Electronic cigarette use and smoking initiation in adolescents and young adults: evidence synthesis

Uso eletrônico de cigarros e iniciação de fumo em adolescentes e jovens: síntese de evidências

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ABSTRACT

Objective: this study aimed to synthesize evidence about electronic cigarette use by adolescents and young adults and future conventional cigarette smoking.

Methods: the search for evidence was carried out in the following databases: PubMed, EMBASE, LILACS, Cochrane Library, Health System Evidence and BIREME for the structured question.

Results: The use of electronic cigarettes by adolescents and young adults is a risk factor for smoking initiation in adulthood with odds ratio OR 5.69 (CI 4.82-6.71).

Conclusion: The evidence can be used to maintain the ban on selling, importing, and advertising electronic smoking devices in Brazil.

Keywords: Adolescent; E-cigarette; Tobacco; Risk factors; Smoking

RESUMO

Objetivo: analisar evidência sobre o uso de cigarros eletrônicos por adolescentes e jóvens adultos e iniciação futura do uso de cigarros convencionais.

Métodos: a busca por evidências foi realizada nas bases PubMed, EMBASE, LILACS, Cochrane Library, Health System Evidence and BIREME para a pergunta estruturada.

Resultados: O uso de cigarro eletrônico por adolescentes e jovens adultos é um fator de risco para a iniciação do tabagismo na vida adulta *odds ratio* OR 5,69 (IC 4,82-6,71)

Conclusão: Conclusão: As evidências podem ser utilizadas para manter a proibição de venda, importação e publicidade de dispositivos eletrônicos para fumar no Brasil.

Descritores: Adolescente; Cigarro eletrônico; Tabaco; Fatores de risco; Tabagismo.

INTRODUCTION

According to the World Health Organization (WHO), more than 7 million people die from smoking-related illnesses every year, with an estimated 820 and 176 million male and female smokers, respectively, above the age of 15 years worldwide[1].

Brazil loses BRL 56.9 billion (~ US$ 15.29 billion) annually due to smoking, 39.4 billion (~ US$ 10.59 billion) of which is related to medical costs and 17.5 billion (~ US$ 4.7 billion) to lost productivity. Taxes on cigarette sales only cover 23% of the losses generated by cigarette smoking, meaning that for every BRL 1.00 (~ US$ 0.27) of taxes, BRL 4.00 (~ US$ 1.07) is spent on the damage caused by tobacco consumption, which translates into 156,216 preventable deaths per year in Brazil [2].

Knowledge of e-cigarettes and experimentation among adults and adolescents doubled between 2008 and 2012 in several countries [3]. Around 2.1 million adults use e-cigarettes, 700,000 of whom are former smokers and 1.3 million so-called dual users of both conventional and e-cigarettes[4].

Electronic cigarettes are categorized as an electronic smoking device (ESD), which heats and vaporizes an aerosol solution that typically contains nicotine, although nicotine-free devices are also available[5]. A number of agencies have conducted studies on the risks involved in using ESDs, such as the effects of the vapor on health and nicotine poisoning through ingestion or skin contact with the e-liquid [6].

In 2009, the National Health Surveillance Agency (ANVISA) published Resolution RDC 46, banning the sale, import and advertising not only of e-cigarettes, but all ESDs [7]. This was a precautionary measure, since there were no toxicology studies or specific scientific tests at the time to prove that ESDs could be used as tools to quit smoking.

Electronic smoking devices are subject to product safety legislation in the following countries: Bulgaria, the Czech Republic, Italy, Latvia, Slovenia, Spain and Cyprus. Their sale, use and advertising is allowed in the United States, although regulations vary between states[5].

Despite constant pressure from the tobacco industry for their approval in different countries, the 7th session of the Conference of the Parties (COP7) on tobacco control recommended banning e-cigarette use or regulating it, in accordance with the laws of individual countries[8]. Given the magnitude of the topic, this study aims synthesize evidence about electronic cigarette use by adolescents and young adults and future conventional cigarette smoking.

METHODS

This is an evidence syntesis of cohort studies that evaluated the influence of electronic cigarette use by adolescents and young adults on smoking initiation.

The research question was developed according to PECO, whereby the population (P) is adolescents and young adults who have never smoked tobacco; exposure (E) refers to electronic cigarettes; comparison (C) is non-exposure to e-cigarettes; and the outcome (O) smoking initiation[9].

The searches were performed between October and November 2017 on six electronic databases, namely PubMed, EMBASE, LILACS, Cochrane Library, Health System Evidence and BIREME. A manual search was carried out in January 2018 to find new publications.

The search strategy used the terms “adolescent”, “e--cigarette”, “tobacco”, “risk factors”, and “smoking”, which were adjusted according to the specificities of each database. Mendeley was used to remove duplicate studies and organize the references. The inclusion criteria were studies that assessed only adolescents and young adults, the use of e-cigarettes correlated with smoking initiation, and systematic reviews with or without meta-analyses or cohort studies.

Investigations that addressed other populations, such as adults, the elderly, pregnant women and children, smoke products, respiratory or cardiovascular diseases, literature reviews and cross-sectional studies were excluded. There were no restrictions on language or year of publication. Young people who had smoked conventional cigarettes were excluded from the baseline. Only studies that reported on e-cigarette use in the previous 30 days and did not include conventional smokers were considered in the analysis.

Studies were initially selected by two independent reviewers after reading the titles and abstracts, with disagreements resolved by consensus. The full articles were read independently by the reviewers and disagreements regarding exclusions were also

resolved by consensus. The following data were then collected and systematized on Excel spreadsheets: title, intervention, primary outcome, result and limitations.

The quality of the cohort studies was determined using the ROBINS-I[10] and the Newcastle-Ottawa Scale (NOS)[11] check list, a qualitative assessment that considers the selection of study groups. The quality of the systematic review was determined using the AMSTAR2[12] checklist.

RESULTS

A total of 1082 studies were identified on the six databases and manual search, and

162 duplicates were excluded, leaving 920.

After reading the titles, 75 papers were chosen for the abstracts to be read and 65 were then eliminated. The 10 remaining studies were read in their entirety and another seven were then removed. Study selection was based on the inclusion criteria. At the end of the selection process, 2 cohort studies were added to one systematic review (which had also 2 cohort studies).

Characterization of the studies included

The 2 cohort studies added to the systematic review showed and low risk of bias. In order to standardize we included studies that reported e--cigarette use in the previous 30 days at baseline. Table 1 summarizes the characteristics of the studies included.

In the cohort study by Hammond *et al*. (2019)[13]England, and the United States. Design: Repeat cross sectional surveys. Setting: Online surveys in Canada, England, and the US. Participants: National samples of 16 to 19 year olds in 2017 and 2018, recruited from commercial panels in Canada (n=7891, in addition to being more prone to smoking traditional cigarettes, young people who reported e-cigarette use in the last 30 days at baseline were also more likely to be daily smokers at follow-up. According to the author, the fact that e-cigarette use precedes cigarette smoking may be because the former are more readily available to Canadian youth[13]England, and the United States. Design: Repeat cross sectional surveys. Setting: Online surveys in Canada, England, and the US. Participants: National samples of 16 to 19 year olds in 2017 and 2018, recruited from commercial panels in Canada (n=7891.

Watkins *et al*. (2018)[14]and even infrequent smoking in adolescence is associated with established adult smoking. Noncigarette tobacco use is increasing and could stimulate subsequent conventional cigarette smoking in youths. <h3>Objective</h3> To estimate the longitudinal association between noncigarette tobacco use and subsequent cigarette smoking initiation among US youth. <h3>Design, Setting, and Participants</h3> In this prospective cohort study of the Population Assessment of Tobacco and Health (PATH studied the association between e-cigarette use and subsequent cigarette smoking from 2014 to 2015. The cohort consisted of 13,651 adolescents aged between 13 and 17 years at baseline, and follow-up was 1 year after initial data collection. At baseline, at least 851 teenagers (9.1%) who had never smoked had tried some type of smoke product other than cigarettes and 242 (2.2%) had used it in the 30 days before baseline. The most frequently used product in this case was the electronic cigarette. Adolescents who were nonsmokers at baseline were twice as likely to begin using e-cigarettes as those who had already done so (OR 2.53; 95% [CI], 1.80 – 3.56) [14]and even infrequent smoking in adolescence is associated with established adult smoking. Noncigarette tobacco use is increasing and could stimulate subsequent conventional cigarette smoking in youths. <h3>Objective</h3> To estimate the longitudinal association between noncigarette tobacco use and subsequent cigarette smoking initiation among US youth. <h3>Design, Setting, and Participants</h3> In this prospective cohort study of the Population Assessment of Tobacco and Health (PATH.

The study by Unger ***et al.*** (2016)[15]respectively, and/or: (b was extracted from the systematic review by Soneji, 2017 [16]in part, on whether e-cigarette use affects the risk of cigarette smoking. Objective: To perform a systematic review and meta-analysis of longitudinal studies that assessed initial use of e--cigarettes and subsequent cigarette smoking. Data Sources: PubMed, EMBASE, Cochrane Library, Web of Science, the 2016 Society for Research on Nicotine and Tobacco 22nd Annual Meeting abstracts, the 2016 Society of Behavioral Medicine 37th Annual Meeting & Scientific Sessions abstracts, and the 2016 National Institutes of Health Tobacco Regulatory Science Program Conference were searched between February 7 and February

17, 2017. The search included indexed terms and text words to capture concepts associated with e-cigarettes and traditional cigarettes in articles published from database inception to the date of the search. Study Selection: Longitudinal studies reporting odds ratios for cigarette smoking initiation associated with ever use of e-cigarettes or past 30-day cigarette smoking associated with past 30-day e-cigarette use. Searches yielded 6959 unique studies, of which 9 met inclusion criteria (comprising 17389 adolescents and young adults and reported that Hispanic young adults had smoked cigarettes one year after using e-cigarettes. No results were provided for cross-sectional assessments. The findings showed that young adults who had used e-cigarettes in the last 30 days at baseline were three times more likely to progress to cigarette smoking (OR 4.71 [95%] CI (2.27 – 9.77) [15]respectively, and/or: (b. In this meta-analysis, the crude OR 4.73 [95%] CI (2.30 – 9.72) was recalculated, but we were unable to obtain the same result presented in Soneji's systematic review [16]in part, on whether e-cigarette use affects the risk of cigarette smoking. Objective: To perform a systematic review and meta-analysis of longitudinal studies that assessed initial use of e-cigarettes and subsequent cigarette smoking. Data Sources: PubMed, EMBASE, Cochrane Library, Web of Science, the 2016 Society for Research on Nicotine and Tobacco 22nd Annual Meeting abstracts, the 2016 Society of Behavioral Medicine 37th Annual Meeting & Scientific Sessions abstracts, and the 2016 National Institutes of Health Tobacco Regulatory Science Program Conference were searched between February 7 and February 17, 2017. The search included indexed terms and text words to capture concepts associated with e-cigarettes and traditional cigarettes in articles published from database inception to the date of the search. Study Selection: Longitudinal studies reporting odds ratios for cigarette smoking initiation associated with ever use of e-cigarettes or past 30-day cigarette smoking associated with past 30-day e-cigarette use. Searches yielded 6959 unique studies, of which 9 met inclusion criteria (comprising 17389 adolescents and young adults.

The study by Hornick *et al* (2016)[17], taken from Soneji's systematic review [16]in part, on whether e-cigarette use affects the risk of cigarette smoking. Objective: To perform a systematic review and meta-analysis of longitudinal studies that assessed initial use of e-cigarettes and subsequent cigarette smoking. Data Sources: PubMed, EMBASE, Cochrane Library, Web of Science, the 2016 Society for Research on Nicotine and Tobacco 22nd Annual Meeting abstracts, the 2016 Society of Behavioral Medicine 37th Annual Meeting & Scientific Sessions abstracts, and the 2016 National Institutes of Health Tobacco Regulatory Science Program Conference were searched between February 7 and February 17, 2017. The search included indexed terms and text words to capture concepts associated with e-cigarettes and traditional cigarettes in articles published from database inception to the date of the search. Study Selection: Longitudinal studies reporting odds ratios for cigarette smoking initiation associated with ever use of e-cigarettes or past 30-day cigarette smoking associated with past 30-day e-cigarette use. Searches yielded 6959 unique studies, of which 9 met inclusion criteria (comprising 17389 adolescents and young adults, used data from an extended abstract presented at a scientific event because the full article could not be found in the literature. The authors concluded that cigarette smoking increased among e-cigarette users when compared to those who did not use the device (12.2% vs 1.4%) crude OR 11.18 [95%] CI (5.41 – 23.13) [17]. In order to confirm the data presented in the systematic review, the crude OR was recalculated (9.84 [95%] CI (6.89 – 14.06), producing data that differed substantially from Soneji's review [16]in part, on whether e-cigarette use affects the risk of cigarette smoking. Objective: To perform a systematic review and meta-analysis of longitudinal studies that assessed initial use of e-cigarettes and subsequent cigarette smoking. Data Sources: PubMed, EMBASE, Cochrane Library, Web of Science, the 2016 Society for Research on Nicotine and Tobacco 22nd Annual Meeting abstracts, the 2016 Society of Behavioral Medicine 37th Annual Meeting & Scientific Sessions abstracts, and the 2016 National Institutes of Health Tobacco Regulatory Science Program Conference were searched between February 7 and February 17, 2017. The search included indexed terms and text words to capture concepts associated with e-cigarettes and traditional cigarettes in articles published from database inception to the date of the search. Study Selection: Longitudinal studies reporting odds ratios for cigarette smoking initiation associated with ever use of e-cigarettes or past 30-day cigarette smoking associated with past 30-day e-cigarette use. Searches yielded 6959 unique studies, of which 9 met inclusion criteria (comprising 17389 adolescents and young adults.

Methodological quality of the studies

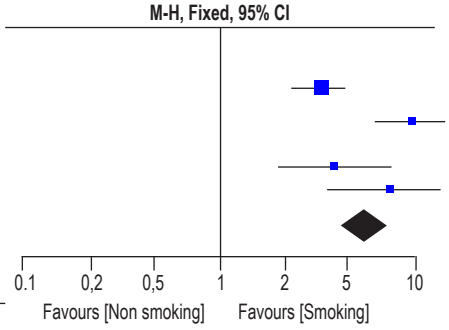
The systematic review was considered high quality AMSTAR 2[12].

The cohorts included were assessed using ROBINS-I[10] and the NOS[11] checklist. The four studies were added and a new the meta-analysis was carried out (Figure 2). The use of electronic cigarettes by adolescents and young adults is a risk factor for smoking initiation in adulthood with crude odds ratio OR 5.69 (CI 4.82-6.71)

Figure 2

Forest plot showing the association between e-cigarette use and smoking initiation in adolescents and young adults

	Exposed to e-cig		Not exposed to e-cig			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Hammond, 2017	136	487	1313	16831	70,9%	4,58 (3,73, 5,63)
Hormik, 2016	94	171	118	1069	19,5%	9,84 (6,89, 14,06)
Unger, 2016	11	42	90	1290	5,6%	4,73 (2,30, 9,72)
Watkins, 2018	10	87	203	10242	4,0%	6,42 (2,30, 9,72)
Total (95% CI)		787		29432	100,0%	5,69 (4,82, 6,71)
Total Events	251		1724			
Heterogeneity: Chi² = 13,70, df= 3 (P= 0.003); I²= 78%						
Test for overall effect Z= 20,66 (P< 0.00001)						



DISCUSSION

This study has added 2 articles to Soneji's systematic review that permitted to construct a meta-analysis graph which indicates that e-cigarette use by adolescents and young adults is a risk factor for smoking initiation. Teenagers and young adults who use electronic cigarettes may learn behavior associated with conventional cigarette smoking, which could result in a natural transition to smoking [16]in part, on whether e-cigarette use affects the risk of cigarette smoking. Objective: To perform a systematic review and meta-analysis of longitudinal studies that assessed initial use of e-cigarettes and subsequent cigarette smoking. Data Sources: PubMed, EMBASE, Cochrane Library, Web of Science, the 2016 Society for Research on Nicotine and Tobacco 22nd Annual Meeting abstracts, the 2016 Society of Behavioral Medicine 37th Annual Meeting & Scientific Sessions abstracts, and the 2016 National Institutes of Health Tobacco Regulatory Science Program Conference were searched between February 7 and February 17, 2017. The search included indexed terms and text words to capture concepts associated with e-cigarettes and traditional cigarettes in articles published from database inception to the date of the search. Study Selection: Longitudinal studies reporting odds ratios for cigarette smoking initiation associated with ever use of e-cigarettes or past 30-day cigarette smoking associated with past 30-day e-cigarette use. Searches yielded 6959 unique studies, of which 9 met inclusion criteria (comprising 17389 adolescents and young adults. Data from the cohort studies analyzed here corroborate those of a recent randomized clinical trial in England, in which 2,836 adolescent e-cigarette users at baseline were strongly associated with smoking initiation (adjusted odds ratio (OR) 4.06 95% CI (2.94 to 5.6) [18]"ISSN":"14683318","PMID":"28818839","abstract":"AbstrAct background In cross-sectional surveys, increasing numbers of adolescents report using both electronic cigarettes (e-cigarettes.

This study found that the adolescents and young adults in the cohorts who reported e-cigarette use in the previous 30 days at baseline were more likely to start smoking. These findings are in accordance with those of other longitudinal studies [19,20]cigarettes, cigars, and hookah. According to a study carried out in 2016, >40% of e-cigarette users became smokers, that is, those who reported using e-cigarettes were 6 times more likely to progress to smoking traditional cigarettes than those who had never used the device [21]never e-cigarette users (n = 152.

The Brazilian regulatory authority has faced questions over the banning of electronic cigarettes and pressure from the regulated sector to register the devices. The claim of reduced risk seems to be refuted in the face of the real possibility of e-cigarettes leading to smoking in adolescents and young adults. Should this prove to be true, the significant reduction in the number of smokers achieved through health protection measures could be reversed in just a few years.

It is important to underscore that there are no studies to date that demonstrate the safety of ESDs or any benefits from using them. As a result, the sale and import of ESDs is banned in Norway, Argentina and Columbia. Australia does not support ESD use or advocate them as treatment [5], and considers nicotine to be poisonous [4]. Moreover, their use and sale is banned in Singapore, and Canada has warned its citizens against them because their safety, efficacy and quality have not been tested. Electronic cigarettes of any type are prohibited in Lithuania regardless of their nicotine content[22], but are considered medicinal products in Austria, Denmark, Estonia, Germany, Hungary, Portugal, Romania, Slovakia, Finland, and Sweden. However, to our knowledge, e-cigarettes have yet to be formally registered for medicinal purposes[22].

CONCLUSION

Based on this evidence synthesis, the present study found that e-cigarette use by adolescents and young adults is a risk factor for smoking initiation. The evidence can be used to maintain the ban on selling, importing and advertising electronic smoking devices in Brazil.

Despite constant pressure from the tobacco industry for their approval in different countries, the 7th session of the Conference of the Parties (COP7) on tobacco control, held in India in 2016, recommended banning e-cigarette use and their regulation, in accordance with the laws of individual countries[8].

The sale, import and advertising of e-cigarettes and other electronic smoking devices (ESDs) has been banned in Brazil since 2009, when ANVISA published Resolution RDC 46/2009 [7].

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APPENDIX

Table 1

Characteristics of the studies included.

Author	Hammond D. *et al*, 2017	Watkins SL. *Et al*, 2018	Unger JB. et al 2016	Hornik R. et al 2016
Country	Canada	USA	USA	USA
Title	Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study	Association of Noncigarette Tobacco Product Use With Future Cigarette Smoking Among Youth in the Population Assessment of Tobacco and Health (PATH) Study, 2013-2015	E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults.	Prediction of cigarette use from six-month prior electronic and combustible cigarette use for a U.S national sample of 13-25 year olds
Intervention	E-cigarette	E-cigarette	E-cigarette	E-cigarette
Primary Outcome	Smoking initiation after electronic cigarette use (12-month interval)	Smoking initiation after electronic cigarette use (12-month interval).	Smoking initiation after electronic cigarette use (12-month interval)	Smoking initiation after electronic cigarette use (6-month interval)
Results	The cross-sectional results demonstrated that e-cigarette use in the previous 30 days increased (7.2% vs 9.7% $p < 0.001$) between 2013/2014 and 2014/2015. Of the 44,163 students assessed at baseline, e-cigarette use in the previous 30 days was strongly associated with smoking and susceptibility to smoking. In the longitudinal sample (n = 19,130), e-cigarette use in the last 30 days at baseline was associated with smoking initiation – smoking the whole cigarette (adjusted odds ratio [OR] 2.12, 95% [CI] 1.68–2.66) and smoking initiation – daily smoking (adjusted [OR] 1.79, 95% [CI] 1.41–2.28) at follow-up.	The population was 10,284 young people who reported not having smoked conventional cigarettes, 9.1% of whom had tried another smoke product. Those who used e-cigarettes were 2 to 3 times more likely to start smoking than those who had not.	Among the participants who had not smoked cigarettes in the previous month (N=1056, 79% of the sample), 42 (4%) reported using e-cigarettes in the same period in 2014. Those who used e-cigarettes in the last month were 3 times more likely to smoke than those who had not (26% vs. 7%; OR=3.32, [CI] 95% 1.55 - 7.10).	Cigarette smoking increased among young people who had used e-cigarettes at baseline compared to those who had not (12.2% vs 1.4%).
Limitations	The study was only carried out in 2 Canadian cities.	The small number of youths who had used certain products and began smoking cigarettes.	Small sample size. Since an experimental study was not performed, causal inferences could not be made. The data reported in the questionnaires were not biochemically validated.	Low cumulative response rate (35% of initial responses) and potential presence of unobserved confounders.