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Short communication

E-cigarette use is associated with a self-reported diagnosis of prediabetes in never cigarette smokers: Results from the behavioral risk factor surveillance system survey

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ABSTRACT

Background: The use of e-cigarettes is increasing in the US but there is still a paucity of research on the metabolic effects of e-cigarette use. The goal of this work was to determine the association between e-cigarette use and self-reported prediabetes in adult never cigarette smokers.

Method: The 2017 cross sectional Behavioral Risk Factor Surveillance System (BRFSS) survey data was used for the analysis. Current e-cigarette users reported daily or someday use of e-cigarettes and former e-cigarette users reported no current use of e-cigarettes. Participants who reported a history of diabetes, gestational prediabetes/diabetes were excluded. Odds ratios were calculated to determine the association between e-cigarette use and self-reported prediabetes in never cigarette smokers after adjusting for potential confounders.

Results: There were a total of 154,404 participants that met the inclusion criteria. Of those participants, there were 143,952 never, 1339 current and 7625 former e-cigarette users. Current e-cigarette users had an increased odds of reporting a diagnosis of prediabetes 1.97 (95% CI 1.25–3.10) compared to never e-cigarette users. After stratifying by gender, men and women had an increased odds ratio of reporting a diagnosis of prediabetes 2.36 (95% CI 1.26–4.40) and 1.88 (95% CI 1.00–3.53) respectively when compared to never e-cigarette users. There was no association between former e-cigarette use and a self-reported diagnosis of prediabetes.

Conclusion: Our findings show that e-cigarette use may be associated with self-reported prediabetes. Further evaluation is needed in prospective studies.

1. Introduction

The use of e-cigarettes is increasing rapidly especially among young adults in the United States (US), and an estimated one-third of current e-cigarette users are never or former cigarette smokers (McMillen et al., 2015). E-cigarettes are perceived by the public to be safer than cigarettes(Pearson et al., 2012), but studies have shown that e-cigarette aerosol can contain nicotine and other toxicants that are found in cigarette smoke(Fagan et al., 2017; Goniewicz et al., 2018). The deleterious effects of e-cigarette use on metabolic parameters have not yet been studied thoroughly in humans; however, animal models show that e-cigarette liquids, even without nicotine, can induce weight and metabolic changes such as hyperglycemia that are similar to cigarette smoking (Verhaegen and Van Gaal, 2017).

Prediabetes is a state of intermediate hyperglycemia, and defined by the American Diabetes Association as a fasting plasma glucose of 100–125 mg/dL or 2-h plasma glucose value during a 75-g oral glucose tolerance test of 140–199 mg/dL, or hemoglobin A1c (HbA1c) levels of 5.7–6.4% (Association, 2019). An estimated 84.1 million people age 18 years or older in the US had prediabetes in 2015 based on their fasting glucose or HbA1c level (Centers for Disease Control and Prevention, 2017) and about 5–10% of people with prediabetes become diabetic annually(Tabák et al., 2012).

Prediabetes has been shown to be associated with multiple comorbidities, including stroke, cardiovascular disease, coronary heart disease, chronic kidney disease, erectile dysfunction, polyneuropathy, sensory/small fiber neuropathy and diabetic retinopathy (Huang et al., 2016; Tabák et al., 2012)

Cigarette smoking and dual use of cigarette and e-cigarettes have been shown to be associated with prediabetes and increased HbA1c

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Table 1
Demographics and medical history of never smokers stratified by e-cigarette use.

	Never e-cigarette user n = 143,952 % (95% CI %)	Current e-cigarette user n = 1339 % (95% CI %)	Former e-cigarette user n = 7625 % (95% CI %)
Gender			
Male	43.1 (42.5 - 43.6)	68.8 (64.7 - 72.9)	56.6 (54.5 - 58.7)
Female	56.9 (56.4 - 57.5)	31.2 (27.1 - 35.3)	43.4 (41.3 - 45.5)
Age groups			
18 to 24 years	14 (13.6 - 14.5)	67.3 (63.1 - 71.6)	52 (49.9 - 54.1)
25 to 34 years	17.3 (16.9 - 17.8)	21.2 (17.5 - 24.8)	28.3 (26.5 - 30.2)
35 to 44 years	16.9 (16.5 - 17.4)	6.9 (4.3 - 9.4)	9.8 (8.6 - 10.9)
45 to 54 years	18.4 (18 - 18.8)	2.5 (1.2 - 3.7)	5.6 (4.8 - 6.5)
55 years and older	33.3 (32.8 - 33.8)	2.2 (1.3 - 3.1)	4.3 (3.7 - 4.9)
Race and ethnicity			
White only, Non-Hispanic	62.5 (61.9 - 63.1)	60.2 (55.6 - 64.8)	57.7 (55.6 - 59.8)
Black only, Non-Hispanic	13.7 (13.3 - 14.2)	13.7 (10.2 - 17.1)	14.6 (13.1 - 16.2)
Other race or multiracial, Non-Hispanic	7.8 (7.5 - 8.2)	10.4 (7.7 - 13.2)	8.3 (7.2 - 9.4)
Hispanic	15.9 (15.4 - 16.4)	15.7 (12.1 - 19.2)	19.4 (17.5 - 21.2)
Education level			
Did not graduate High School	10.3 (9.9 - 10.8)	11.2 (7.8 - 14.7)	7 (5.7 - 8.2)
Graduated High School	25.3 (24.8 - 25.8)	43.6 (38.9 - 48.2)	30.7 (28.7 - 32.7)
Attended College or Technical School	29.2 (28.7 - 29.7)	33.6 (29.5 - 37.7)	38.8 (36.8 - 40.8)
Graduated from College or Technical School	35.1 (34.6 - 35.6)	11.6 (9.2 - 14.1)	23.5 (21.9 - 25.1)
Other factors			
Currently married	55.3 (54.7 - 55.8)	13.6 (10.7 - 16.6)	21.8 (20.2 - 23.4)
Body Mass Index (BMI)[a]	27.6 (27.6 – 27.7)	26.4 (25.8– 27.0)	26.6 (26.4 – 26.9)
Consumed fruits or vegetables at least once a day	90.3 (90 - 90.7)	82.8 (78.6 - 87)	84 (82.3 - 85.8)
Participated in 150 minutes (or vigorous equivalent minutes) of physical activity per week	51.6 (51 - 52.2)	55.1 (50.3 - 59.9)	52 (49.9 - 54.2)
Heavy alcohol drinker[a,b]	3.4 (3.2 - 3.6)	9.6 (7 - 12.2)	9.7 (8.5 - 10.9)
Currently using smokeless tobacco products	2.3 (2.2 - 2.5)	7.6 (5.5 - 9.7)	5.6 (4.8 - 6.4)
Strength Activity Frequency per Week[a]	1.4 (1.3 – 1.4)	2.2 (2.0 – 2.4)	1.9 (1.8 – 2.0)
Medical history	2.5 (2.3 - 2.6)	1.5 (0.6 - 2.4)	2.3 (1.7 - 2.9)
History of COPD			
Currently has Asthma	7.5 (7.2 - 7.8)	10.1 (7.3 - 12.8)	9.9 (8.7 - 11.1)
History of heart disease[c]	3.5 (3.3 - 3.7)	1.4 (0.3 - 2.6)	0.8 (0.6 - 1.1)
History of high cholesterol	26.4 (25.9 - 26.9)	10.7 (7.5 - 14)	14 (12.6 - 15.5)
History of high blood pressure	26 (25.5 - 26.4)	13.6 (10.4 - 16.9)	14.2 (12.8 - 15.5)
Tested blood sugar in past 3 years	57.7 (57.1 - 58.3)	33.9 (29.5 - 38.2)	40.4 (38.3 - 42.4)
History of depression[d]	13.2 (12.8 - 13.5)	24.1 (20.5 - 27.7)	20.1 (18.5 - 21.6)
Outcome			
History of prediabetes	9.4 (9.1 - 9.7)	5.6 (3.3 - 7.8)	5.2 (4.3 - 6.1)

[a] Mean (95% CI).
[b] Men having more than 14 drinks per week, and women having more than 7 drinks per week.
[c] Participants reported ever been told by a by a doctor, nurse, or other health professional that they have heart attack and/or angina and/or coronary heart disease.
[d] Participants reported ever been told by a doctor, nurse, or other health professional that they have a depressive disorder, including depression, major depression, dysthymia, or minor depression.

levels in adults without a history of diabetes (Aeschbacher et al., 2014; Choi et al., 2018). Nicotine that can be found in e-cigarette liquids (Fagan et al., 2017) has been shown to negatively affect pancreatic beta cells, increase HbA1c levels and induce hyperinsulinemia(Clair et al., 2011; Eliasson et al., 1996; Xie et al., 2009). Furthermore, e-liquids with or without nicotine have been shown to induce hyperglycemia and affect glucose homeostasis in rats (El Golli et al., 2016a).

The goal of this study was to examine the association between e-cigarette use and self-reported prediabetes in a representative population of adult never cigarette smokers in the United States who have no known history of diabetes. Based on the fact that e-cigarette liquids and nicotine found in e-cigarette liquids can affect glucose homeostasis, we hypothesized that e-cigarette use will be associated with an increased odds of self-reported prediabetes after adjusting for other potential confounding factors.

2. Method and materials

2.1. Data source

The 2017 cross-sectional Behavioral Risk Factor Surveillance System (BRFSS) survey data was used for the analysis (Centers for Disease Control and Prevention (CDC), 2017,-b). BRFSS is a collaborative project between the Centers for Disease Control and Prevention (CDC) and all states in the US and participating US territories. The BRFSS survey is designed to collect data on health-related risk behaviors, chronic health conditions, and use of preventive services from the noninstitutionalized adult population (≥ 18 years) residing in the US. It includes a core set of questions that is used by all the states and optional modules that can be included by the different states. Data in BRFSS is self-reported and collected using landlines and cellphones. To collect the data, landlines numbers are randomly selected using a disproportionate stratified sample design and data is collected from a randomly selected adult in the household. Also, cellphone numbers are randomly selected using cellphone sampling frames and data is collected from an adult who answers the cellphone and who resides in a private or college housing. More information about BRFSS design can be found elsewhere (Centers for Disease Control and Prevention (CDC), 2017,-a)

The prediabetes questionnaire was an optional module in the 2017 survey, therefore only the 47 states and US territories that reported data on the prediabetes module were used for the analysis (N = 355,585).

2.2. Exclusion criteria

Participants who were current or former smokers of conventional

Table 2
Results of the multivariable regression analyses for never smokers who had a blood sugar test within the past 3 years[a].

	Odds ratio (95 % CI)
Entire cohort (n = 71,541)	
Never e-cigarette user (n = 68,719)	Ref
Current e-cigarette user (n = 352)	1.96 (1.13 - 3.40)
Former e-cigarette user (n = 2470)	1.20 (0.91 - 1.58)
Male cohort (n = 28,070)	
Never e-cigarette user (n = 26,607)	Ref
Current e-cigarette user (n = 213)	2.34 (1.13 - 4.86)
Former e-cigarette user (n = 1250)	1.39 (0.92 - 2.10)
Female cohort (n = 43,471)	
Never e-cigarette user (n = 42,112)	Ref
Current e-cigarette user (n = 139)	1.76 (0.79 - 3.92)
Former e-cigarette user (n = 1220)	1.11 (0.77 – 1.59)

[a] Adjusted for all confounders listed in Table 1.

cigarettes (N = 149,892) or who had a history of diabetes (N = 48,677), gestational prediabetes (N = 2979) or gestational diabetes (N = 2581) were excluded from the analysis.

2.3. Data and definitions

Data was collected on age, race, gender, marital status, education level, tobacco and alcohol use, food and vegetable consumption, exercise patterns and health status. Never smokers of cigarettes reported having smoked less than 100 cigarettes in their lifetime. E-cigarette use was assessed with the following question: “Have you ever used an e-cigarette or other electronic vaping product, even just one time, in your entire life?” Never e-cigarette users reported “no” to the question and ever e-cigarette users reported “yes” to the question. Ever e-cigarette users were then asked the following question: “Do you now use e-cigarettes or other electronic “vaping” products every day, some days, or not at all”. Current e-cigarette users reported currently using e-cigarettes every day or some days. Former e-cigarette users reported ever using an e-cigarette but not currently using e-cigarettes.

Prediabetes was defined as a “yes” to the question: “Ever been told by a doctor or other health professional that you have pre-diabetes or borderline diabetes?” and participants who tested their blood sugar in the past three years reported “yes” to the following question: “Had a test for high blood sugar or diabetes in the past three years?”

2.4. Statistical analysis

Descriptive statistics for never smokers of cigarettes who were current, former or never e-cigarette users are shown in Table 1. Multivariable logistic regression was used to examine the association between e-cigarette use and self-reported prediabetes after controlling for all the confounders listed in Table 1. For the secondary analysis, subgroup analysis with only participants that reported a test for high blood sugar or diabetes in the past three years was performed. Additionally, e-cigarette use was stratified based on gender, and the association between e-cigarette use and self-reported prediabetes was examined after adjusting for all the confounders in Table 1.

Weights were incorporated into the analysis to account for probability of selection and also to adjust for nonresponse bias and non-coverage errors as detailed elsewhere (Centers for Disease Control and Prevention (CDC), 2017,-c). Weights and analysis for the subpopulations were calculated as detailed elsewhere (Lumley, 2010). All participants with missing values were removed from the analysis. All analyses were conducted using R version 3.4.2.

3. Results

In our cohort, there were 143,952 never e-cigarette users, 1339 current e-cigarette users and 7625 former e-cigarette users. Descriptive statistics and medical history of never, current and former e-cigarette users are shown in Table 1. Among the never smokers used for the analysis, 55.4% (95% CI 54.9–56.0) were female, 55.8% (95% CI 55.3–56.4) had tested their blood sugar in the past 3 years and 9.0 (95% CI 8.7–9.3) had self-reported prediabetes. Among the participants who had a blood sugar test in the past 3 years, 58.9% (95% CI 58.2–59.6) were female and 14.0% (95% CI 13.5–14.5) had self-reported prediabetes.

Compared to never e-cigarette users, the odds ratio for self-reported prediabetes was 1.97 (95% CI 1.25–3.10) for current e-cigarette users and 1.07 (95% CI 0.84–1.37) for former e-cigarette users. After stratifying by gender, among men, the odds ratio of self- reported prediabetes was 2.36 (95% CI 1.26–4.40) for current e-cigarette users and 1.22 (95% CI 0.86–1.74) for former e-cigarette users compared to never e-cigarette users. Among women, the odds ratio of self-reported prediabetes was 1.88 (95% CI 1.00–3.53) for current e-cigarette users and 1.00 (95% CI 0.71–1.40) for former e-cigarette users compared to never e-cigarette users.

Current e-cigarette users who have had a blood sugar test in the past 3 years also had increased odds of self-reported prediabetes compared to never e-cigarette users (Table 2). After stratifying by gender, male current e-cigarette users had increased odds of self-reported prediabetes compared to male never e-cigarette users. There was no statistically significant difference in the odds of self-reported prediabetes for females who were current e-cigarette compared to never e-cigarette users (Table 2).

4. Discussion

Among never cigarette smokers, current e-cigarette users had an increased odds of self-reported prediabetes compared to never e-cigarette users. There was no association between former e-cigarette use and self-reported prediabetes. Stratified analysis showed higher odds of self-reported prediabetes for male current e-cigarette users compared to never e-cigarette users.

Subgroup analysis with participants who have tested their blood sugar in the past 3 years showed similar odds of self-reported prediabetes for current e-cigarette users compared to never e-cigarette users. Stratified analysis with female e-cigarette users, however, showed no association between current e-cigarette use and self-reported prediabetes compared to never e-cigarette use. The lack of association between diabetes risk or elevated HbA1c levels and cigarette or dual use of cigarettes and e-cigarette in women has been reported previously (Beziaud et al., 2004; Choi et al., 2018); therefore, it is not surprising that current e-cigarette use may not be associated with prediabetes in female e-cigarette users compared to never e-cigarette user. The gender difference found may be due to the fact that men are generally less insulin sensitive than women, develop type 2 diabetes at a lower BMI than women and are at a higher risk for prediabetes and diabetes (Geer and Shen, 2009; Logue et al., 2011; Yang et al., 2019)

The association we found between e-cigarette use and prediabetes might be due to the nicotine found in e-cigarette liquids(Fagan et al., 2017). Long-term use of nicotine-containing gum has been shown to be associated with insulin resistance and hyperinsulinemia in middle aged men, and the degree of insulin sensitivity correlated negatively to plasma cotinine levels (Eliasson et al., 1996). Also, cotinine has been shown to be associated with higher HbA1c levels in adults without diabetes (Clair et al., 2011). In vitro studies have shown that nicotine in the presence of palmitate enhanced the production of reactive oxygen species and impaired glucose uptake in skeletal myocytes (Tatebe and Morita, 2011). Fetal and neonatal nicotine exposure in rats resulted in dysglycaemia, pancreatic beta cell dysfunction, increased apoptosis, and loss of beta cell mass (Xie et al., 2009).

The association between e-cigarette use and prediabetes might also be due to the sugar, aldehydes and other flavorants found in the e-liquid

(Fagan et al., 2017). In vitro studies have shown that e-liquid with or without nicotine promoted oxidative stress leading to the disruption of plasma and liver biochemical parameters, thereby altering the liver tissue histology in rats (El Golli et al., 2016b). Furthermore, e-liquids without nicotine induced hyperglycemia in rats, and the mechanism of glucose metabolism disruption was different from that of nicotine containing e-liquid and nicotine alone (El Golli et al., 2016a).

One of the strengths of the study was the large number of respondents available for the analysis, who were nationally representative of the non-institutionalized adults in the US. Another strength was the inclusion of only never smokers of cigarettes, thereby removing the confounding effect of cigarette use on prediabetes. Some of the limitations were the cross-sectional nature of the analysis, the inability to establish a causal relationship between e-cigarette use and self-reported prediabetes by participants and the lack of information on the amount, duration and the last time e-cigarettes were used by participants. Other limitations were the inability to verify the diagnosis of prediabetes from HbA1c levels or glucose levels, the lack of biochemical confirmation of cigarette and e-cigarette use which may lead to the under reporting of use, which may bias the results of the analysis and the potential for recall bias and diagnosis misclassification bias by the participants. Also, there may have been undiagnosed prediabetes in some participants; however, subgroup analysis with participants who had a test for blood sugar in the past 3 years likely reduced the number of participants with undiagnosed prediabetes in the study.

5. Conclusion

In conclusion, current e-cigarette use was associated with self-reported prediabetes. Our findings are a cause for concern because of the growing use of e-cigarettes, and further evaluation is needed in larger prospective studies.

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Contributors

Dr. Atuegwu conceptualized the paper, performed the statistical analyses and drafted the paper. Dr. Perez, Dr. Oncken, Dr. Maheshwari, Dr. Mead and Dr. Mortensen participated in the interpretation of the findings, edited and reviewed the manuscript. All authors contributed to and approved the final draft.

Declaration of Competing Interest

None.

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