

# Association between Non-Cigarette/Smokeless Tobacco and Hypertension in the National Health Interview Survey: A Pseudo-Panel Analysis

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## ABSTRACT

This study sought to examine assumption between having ever used non-cigarette tobacco or smokeless tobacco, and a diagnosis of hypertension among a sample of 13, 086 United States adults participating in the National Health Interview Series from 2012-2014. A pseudo-panel analysis of data extracted from the Integrated Health Interview Series Survey was conducted. The generalized linear mixed model was used to quantify the effect of a history of non-cigarette tobacco, smokeless tobacco, and socio-demographic predictor variables on the response variable, a diagnosis of hypertension. The transformed data, based on the pseudo-panel technique, resulted in fifty-seven (57) birth cohorts and followed in 2012, 2013, and 2014. The mean age was 51.6 years ( $\pm 12.4$ ). The findings of this study revealed that the odds of hypertension diagnosis for non-cigarette tobacco users was 0.8846 times lower (95% CI: 0.7907, 0.9896) than non-users after adjusting for possible confounders such as age, language, education, income and years of smoking. Our study suggested that the association between the use of non-cigarette tobacco and the diagnosis of hypertension among the sample population is consistent enough to assume a less plausible association between the two variables.

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## 1. INTRODUCTION

Tobacco use is a major risk for hypertension and cardiovascular disease (CVD) and is the most important cause of premature death in the United States [1]. Non-cigarette tobacco and smokeless tobacco have been shown to increase the risk of CVD in comparison to non-smokers [1]. Hypertension on its own is a major risk factor for CVD morbidity and mortality [2]. Tobacco-related illnesses and hypertension in the US costs more than \$300 billion [3] and \$46 billion [4] a year respectively. Many studies have examined an association between hypertension and tobacco smoking (cigarette and non-cigarette) but the exact relationship has remained unclear [1],[5],[6]. Experts have projected that tobacco use will kill an estimated 1 billion people in the 21st century [7]. Tobacco use in other forms, besides cigarette, will also contribute to increased morbidity and mortality rates globally [7].

The continued use of non-cigarette tobacco is promoted by some tobacco companies under the claim of a negligible or smaller health risk, hence non-cigarette tobacco (NCT) which fall under the three broad categories of other smoked products, smokeless tobacco and nicotine products are less regulated than cigarettes [6],[8]. In order to minimize passive exposure to smoke and to reduce harm attributed to inveterate smokers, smokeless tobacco (ST) was introduced as a substitute for cigarette smoking, and a major adjunct for smoking cessation [9]. Experts have, however, disagreed, warning that some non-cigarette tobacco products are still harmful since these contain certain ingredients, including glycyrrhizinic acid that leads to potassium wasting and sodium retention which act as buffers for the facilitation of nicotine absorption. These have been found to cause an aggravation of hypertension and increase the risk for chronic diseases including CVD [1],[7]-[10],[11]. While some researchers have found no difference in the prevalence of hypertension among users of non-cigarette tobacco products [12]-[14], others have found an association between the use of non-cigarette tobacco and hypertension [10],[15]-[17].

In the United States, the statistics for those who use NCT is unavailable. However, an estimated 8.1 million people (3.2% of the total population) use ST, most users being males, age 18 -25 years [1]. The use of ST is commonest among Native Americans (7%) and Whites (4.3%) as well as among lower socio-economic groups, including blue-collar/unskilled/unemployed workers and non-college graduates whose health statuses may already be influenced by other social determinants of health [1]. In the 12-17 year age group, data from 2002-2007 shows a more than 10-fold higher prevalence of use among boys (6.3%) than girls (0.4%) [1]. Despite some claims that smokeless tobacco is less harmful than cigarette smoking, the fact still remains that users are exposed to harmful chemicals that could heighten their risk for several health problems just as with cigarette smoking [9].

Many epidemiological studies have examined the association between cigarettes and hypertension but in recent years, only minimal research has been done on the health effects of non-cigarette tobacco [18],[19]. Given the morbidity, mortality and cost associated with smoking, it is expedient to establish the role of ST products in the development of CVD risk factors such as hypertension [6]. The purpose of this study was to examine the association between ever smoked non-cigarette tobacco in one's lifetime and a diagnosis of hypertension in a nationally-representative sample of US adults.

## **2. RESEARCH METHOD**

### **2.1. Study design and population**

Data was extracted from the Integrated Health Interview Series (IHIS) dataset which comprise of repeated cross-sectional samples for 2012, 2013, and 2014. The IHIS is derived from the National Health Interview Survey (NHIS) public use datasets. The NHIS is the principal source of information on the health of the US population and is a cross-sectional household interview survey. The sampling plan follows a multistage area probability design that permits the representative sampling of households and noninstitutionalized individuals with oversampling of Blacks and Hispanics.

### **2.2. Variables definition and measures**

The data for this study was extracted from the Integrated Health Interview Series (IHIS) dataset which comprise of repeated cross-sections for 2012, 2013, and 2014. The IHIS is based on original data from National Health Interview Survey (NHIS) public dataset. The variables used from the IHIS dataset included: ever told had hypertension on 2+ visits (HYP2TIME), age (AGE), language of interview (INTERVLANG), education attainment (EDUCREC2), person's total earnings (EARNINGS), ever smoked non-cigarette tobacco products (NONCIGEV), and ever used smokeless tobacco (SMKLSEV). Apart from HYP2TIME that was used as the response variable, the rest were predictor variables. Hypertension was defined as two or more occasions of elevated blood pressure at office visits per national guidelines [20] Educational attainment was defined as: 1 = never attended/kindergarten, 2 = grade 1, 3 = grade 2, 4 = grade 3, 5 = grade 4, 6 = grade 5, 7 = grade 6, 8 = grade 7, 9 = grade 8, 10 = grade 9, 11 = grade 10, 12 = grade 11, 13 = 12th grade, no diploma, 14 = high school graduate, 15 = GED or equivalent, 16 = some college, no degree, 17 = AA degree: Technical/vocational/occupational, 18 = AA degree: Academic program, 19 = Bachelor's degree (BA, AB, BS, BBA), 20 = Master's degree (MA, MS, Meng, Med, MBA), 21 = Professional degree (MD, DDS, DVM, JD), and 22 = Doctoral degree. Language of interview was categorized as English, Spanish, English and Spanish or Other. Earnings were classified as: 1= \$01 to \$4999, 2 = \$5000 to \$9999, 3 = \$10000 to \$14999, 4 = \$15000 to \$19999, 5 = \$20000 to \$24999, 6 = \$25000 to \$34999, 7 = \$35000 to \$44999, 8 = \$45000 to \$54999, 9 = \$55000 to \$64999, 10 = \$65000 to \$74999, and 11 = \$75000 and over.

### 2.3. Statistical analyses

Frequencies and percentages were descriptive measures used to summarize the categorical variables, while mean and standard deviation were used to describe the continuous variable (AGE). In the modeling process, age was transformed to a value on a logarithm scale. The generalized linear mixed model (GLMM) with a logit link was used to quantify the effect of each of the predictors on the response variable. A detailed description of the model is shown under 2.4. Quite importantly, the use of the IHIS dataset has one main drawback because some subjects were not followed through time, hence historical information on subjects were not available. This drawback imposes limitation to the use of panel data models. To overcome this limitation, Deaton (1985) [21] suggests following cohorts due to the accessibility of household surveys. We therefore constructed a pseudo-panel by pulling individual subjects sharing common year of birth from one survey year to another in accordance with [21]. Each year of birth forms a birth cohort. The birth cohort for each individual subject can be obtained by subtracting the age of the subject from the year he/she participated in the survey.

### 2.4. Generalized Linear Mixed Model

This part of the study outlines the main features of the GLMM. The GLMM contains both fixed effects and random effects. It is an extension of the generalized linear model (GLM) by adding random effects to the linear predictor component. A GLM is a regression model defined within the distributional structure of the exponential family and is given as follows:

$$f_Y(y) = \exp\left(\frac{y\theta - \psi(\theta)}{\phi} + c(y, \phi)\right) \quad (1)$$

where  $\mu = E[y] = \psi'(\theta)$ ,  $\text{Var}[y] = \phi\psi''(\theta) = \phi V(\mu)$ .  $V(\mu)$  captures the relationship between  $E[y]$  and  $\text{Var}[y]$ . The GLM can therefore be represented as:

$$g(\mu) = \eta = X\beta \quad (2)$$

where  $\beta$ ,  $p$ -dimensional vector;  $X$ ,  $(m \times p)$  vector of predictors;  $g$ , a link function;  $\eta$ , a linear predictor.  $\beta$  estimates are obtained by using an iterative numerical approach to solve maximum likelihood equations. GLMMs extend GLMs by including random effects  $Zu$  to the linear predictor shown in (2). The random effects allow cohort-specific prediction, heterogeneity between cohorts, and structural correlation within cohorts. Conditional on a  $q$ -dimensional vector  $u_i$  of random effects for cohort  $i$ , GLMM assumes for the  $j^{\text{th}}$  response on cohort  $i$ ,  $y_{ij}$  are:

$$y_{ij}|u_i \sim f_{Y_{ij}|u_i}(y_{ij}|u_i), \quad u_i \sim f_U(u_i),$$

$$f_{Y_{ij}|u_i}(y_{ij}|u_i) = \exp\left(\frac{y_{ij}\theta_{ij} - \psi(\theta_{ij})}{\phi} + c(y_{ij}, \phi)\right) \quad (3)$$

The following relations hold:

1.  $\mu_{ij} = E[y_{ij}|u_i] = \psi'(\theta_{ij})$
2.  $\text{Var}[y_{ij}|u_i] = \phi\psi''(\theta_{ij}) = \phi V(\mu_{ij})$

A function of  $\mu_{ij}$  which is linear in both  $\beta$  and  $u_i$  is given by:

$$g(\mu_{ij}) = X'_{ij}\beta + Z'_{ij}u_i \quad (4)$$

Where  $X_{ij}$  and  $Z_{ij}$  are  $p$  and  $q$  dimensional vectors of known predictors for fixed and random effects respectively. The random effects signify the impact of cohort  $i$  on its repeated observation that is not captured by the observed predictor. With these random effects, the idea is that, the sampled cohorts are thought to represent a population of all possible cohorts and most often assumed to follow a normal distribution with zero mean and variance  $\sigma_u^2$ .

## 2.5. Estimation

The likelihood associated with (3) is given by:

$$L(\beta, D|y) = \int f_{Y|U} f_U(u) du \quad (5)$$

Maximum likelihood estimation and estimation of  $\beta$  and  $D$  are hampered by the integral in (5), therefore approximate techniques are used for the estimation. Techniques such as the Laplace, pseudo likelihood, and numerical integration have been proposed in the literature [22]. In our case, we used numerical integration based on the adaptive Gauss-Hermite quadrature [23]. To estimate the relationship between HYP2TIME and the six (6) predictors, the present study assumes a normal distribution for the random effects and a logit link for  $g$ . The logit link was appropriate because our response variable “HYP2TIME” can take one of two possible values representing “yes” or “no” to ever told had hypertension on 2+ visits. To determine statistical significance, we used odds ratio estimated from the GLMM with the logit link and the associated  $(1 - \alpha)\%$  confidence interval where  $\alpha$  represents the level of significance. RStudio version 0.99.446 (RStudio, Inc.) statistical package was used for the analysis.

## 3. RESULTS AND ANALYSIS

### 3.1. Descriptive Statistics

Of 13,086 participants involved in the study, 4,284 (32.74%), 4,140 (31.64%), and 4,662 (35.63%) were from 2012, 2013, and 2014 survey years respectively. The transformed data based on the pseudo-panel technique resulted in fifty-seven (57) birth cohorts and each cohort was followed in 2012, 2013, and 2014. The youngest and the oldest participants were 21 and 79 years old respectively. Also, the average age of participants was 51.6 years with a standard deviation of 12.4 years.

Figure 1 shows the proportion of participants for each of the 57 birth cohorts who had hypertension during the 2012, 2013, and 2014 surveys. Each line represents a birth cohort and the proportions for all the birth cohorts range from 0.40 (2012 survey) to 1.00 (2014 survey). The minimum and the maximum proportions during the 2012 survey were associated with the 1991 (0.40) and the 1935 (1.00) birth cohorts respectively. While the minimum and maximum proportions during the 2013 survey were respectively connected to the 1988 (0.41) and 1945 (0.98) birth cohorts. In the 2014 survey, the minimum and the maximum proportions were 0.52 and 1.00 respectively linked to the 1989 and the 1939 birth cohorts. Broadly speaking, the proportions among all the 57 birth cohorts were consistently above 0.4 apart from that of 1991 during the 2012 survey.

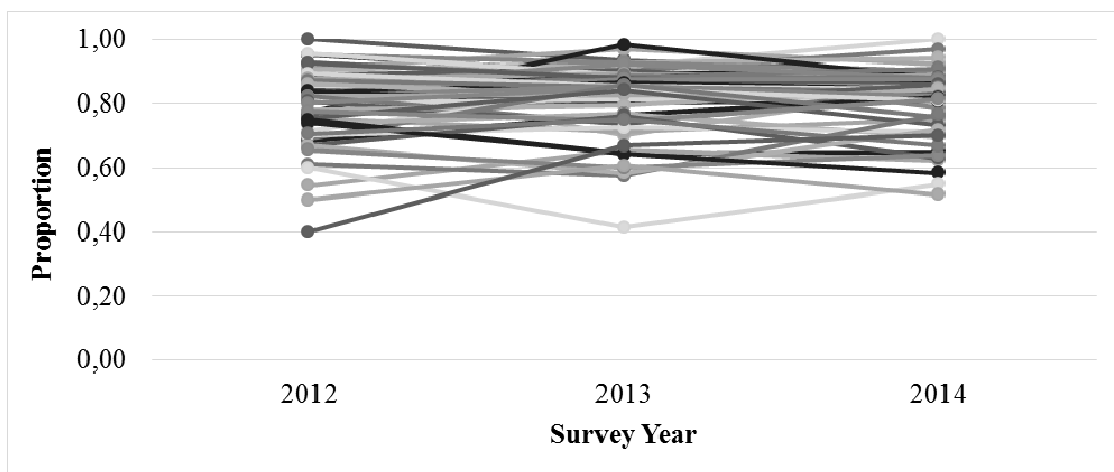


Figure 1. Proportion with hypertension in each birth cohort

Figure 2 displays the proportion of participants who had hypertension by educational attainment. Large variations in proportions were observed at grade 2 during the 2013 and 2014 survey years. It can further be observed that, the variabilities tend to dwindle and proportions move closer to each other as we move from lower level of EDUCREC2 to higher levels with some minor departure starting from the third

highest level in 2012. Almost all the proportions during the three survey years consistently were above 0.60 in exception of one which was observed at grade 2 (0.33) during 2013 survey.

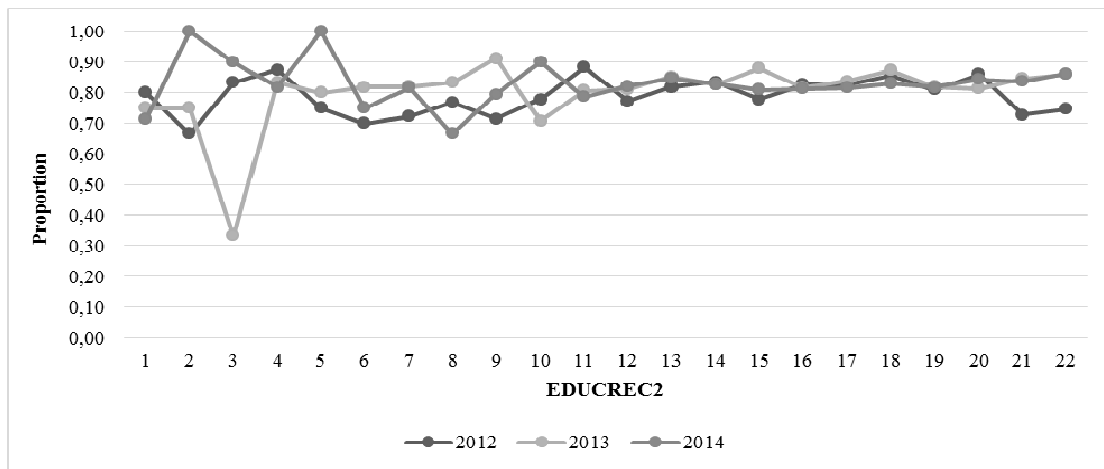


Figure 2. Proportion with hypertension by educational attainment

Figure 3 shows the proportion of participants who had hypertension by language of interview within the 3-year span of the survey in the Spanish ethnic populations. There was also an observed increase in hypertension diagnosis among individuals who speak other languages apart from English and Spanish in 2014 (Figure 3). It could further be observed that clear understanding of diagnosis and possible diagnostic implications based on language had positive effect on the proportion of observed hypertension diagnosis amongst the English speaking populations with no observed changes within the 3 years of survey.

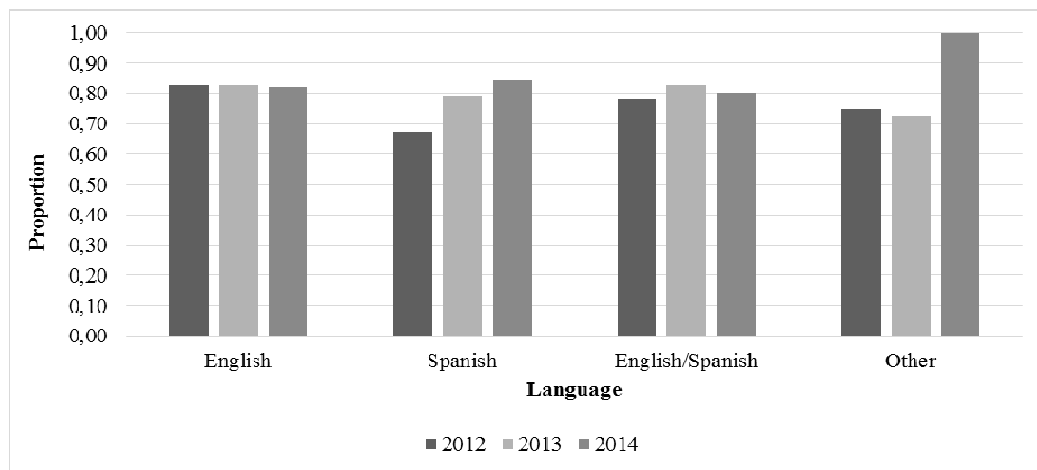


Figure 3. Proportion responded yes to HYP2TIME by INTERVLANG

Figure 4 displays the proportion of participants with hypertension diagnosis by earnings. The lowest proportions were observed among earning groups 4, 3, and 6 in 2012, 2013, and 2014 respectively. Further, the highest proportions were recorded among earning groups 2, 5, and 1 in 2012, 2013, and 2014 respectively.

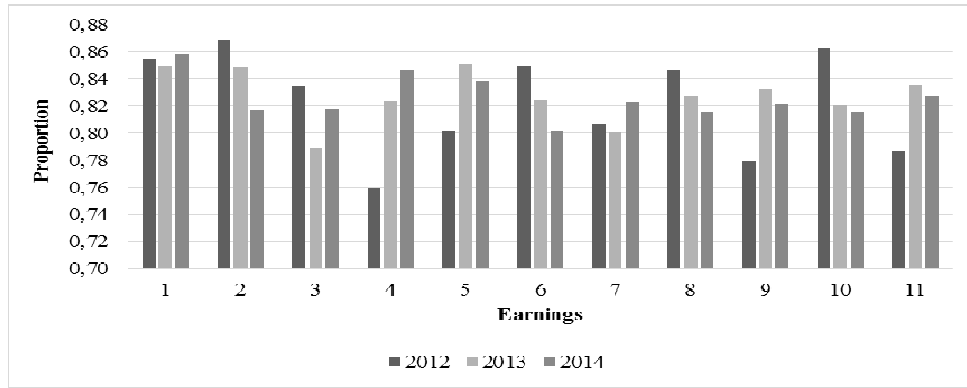


Figure 4. Proportion responded yes to HYP2TIME by EARNINGS

Figures 5 and Figure 6 display the proportion of participants that had a hypertension diagnosis by ever smoked non-cigarette tobacco products and ever used smokeless tobacco respectively. The proportion with hypertension diagnosis increased marginally from 0.83 in 2012 to 0.84 in 2014 among those who had never used NCT. However the proportion declined from about 0.81 to 0.79 between 2012 and 2014 for those who had ever used NCT. Also, the proportion with hypertension diagnosis rose by 1% (0.82 to 0.83) between 2012 and 2014 among those had never used ST. While, the proportion had ever used ST but had a hypertension diagnosis dropped by 3% (0.81-0.78) from 2012 to 2014.

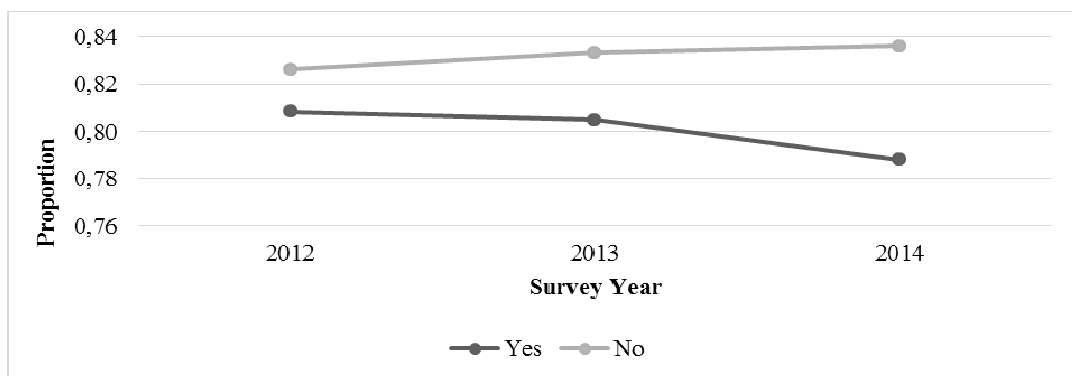


Figure 5. Proportion responded yes to HYP2TIME by NONCIGEV

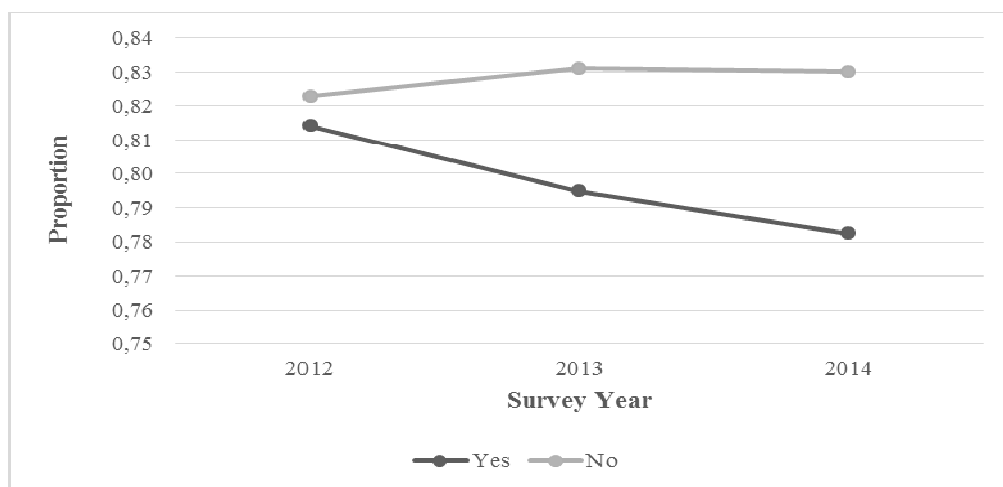


Figure 6. Proportion responded yes to HYP2TIME by SMKLESEV

### 3.2. Odds Ratio Analysis

Table 1 shows the estimated odds ratios and their corresponding 95% confidence intervals from the GLMM model with the logit link. Here, we focus on significant effects. Our analysis revealed that the odds of hypertension diagnosis for those who responded ‘yes’ to the use of NCT was 0.8846 times lower (95% CI .7907, .9896) than those who responded ‘no’, after adjusting for the confounders of age, language, education, income and years of smoking.

Table 1. Estimated GLMM with a Logit Link

Parameter	Estimate	SE	Z ratio	P value	Odds ratio	95% 9CI
Intercept	-5.2516	0.5409	-9.7090	0.0000	0.0052	(0.0018, 0.0151)
Log(AGE)	1.6849	0.0834	20.2090	0.0000	5.3917	(4.5789, 6.3489)
INTERVLANG 2	-0.3056	0.1459	-2.0940	0.0363	0.7367	(0.5534, 0.9807)
INTERVLANG 3	-0.0284	0.2033	-0.1400	0.8888	0.9720	(0.6525, 1.4478)
INTERVLANG 4	0.1609	0.4895	0.3290	0.7424	1.1745	(0.4500, 3.0655)
EARNINGS 2	-0.0273	0.1389	-0.1970	0.8440	0.9730	(0.7411, 1.2775)
EARNINGS 3	-0.2353	0.1275	-1.8460	0.0649	0.7903	(0.6155, 1.0147)
EARNINGS 4	-0.2308	0.1306	-1.7680	0.0771	0.7939	(0.6146, 1.0254)
EARNINGS 5	-0.1011	0.1298	-0.7790	0.4359	0.9038	(0.7008, 1.1656)
EARNINGS 6	-0.1775	0.1165	-1.5230	0.1277	0.8374	(0.6664, 1.0522)
EARNINGS 7	-0.3167	0.1191	-2.6600	0.0078	0.7286	(0.5769, 0.9201)
EARNINGS 8	-0.2218	0.1255	-1.7670	0.0772	0.8011	(0.6264, 1.0245)
EARNINGS 9	-0.3605	0.1324	-2.7230	0.0065	0.6973	(0.5379, 0.9039)
EARNINGS 10	-0.2360	0.1486	-1.5880	0.1122	0.7898	(0.5903, 1.0568)
EARNINGS 11	-0.3572	0.1201	-2.9760	0.0029	0.6996	(0.5529, 0.8852)
EDUCREC2 2	0.2848	0.8946	0.3180	0.7503	1.3295	(0.2302, 7.6769)
EDUCREC2 3	0.2490	0.7071	0.3520	0.7247	1.2827	(0.3208, 5.1286)
EDUCREC2 4	0.5391	0.6469	0.8330	0.4047	1.7144	(0.4825, 6.0922)
EDUCREC2 5	0.4322	0.6945	0.6220	0.5338	1.5406	(0.3949, 6.0099)
EDUCREC2 6	-0.0615	0.5705	-0.1080	0.9142	0.9403	(0.3074, 2.8769)
EDUCREC2 7	0.2629	0.4590	0.5730	0.5668	1.3007	(0.5290, 3.1984)
EDUCREC2 8	-0.0124	0.5706	-0.0220	0.9827	0.9877	(0.3228, 3.0220)
EDUCREC2 9	0.3415	0.4869	0.7010	0.4831	1.4070	(0.5418, 3.6536)
EDUCREC2 10	0.4315	0.4606	0.9370	0.3489	1.5396	(0.6242, 3.7975)
EDUCREC2 11	0.3981	0.4542	0.8760	0.3808	1.4890	(0.6113, 3.6269)
EDUCREC2 12	0.3281	0.4459	0.7360	0.4619	1.3883	(0.5793, 3.6269)
EDUCREC2 13	0.6130	0.4542	1.3500	0.1771	1.8460	(0.7579, 4.4963)
EDUCREC2 14	0.5352	0.4216	1.2700	0.2043	1.7077	(0.7475, 3.9016)
EDUCREC2 15	0.5587	0.4381	1.2750	0.2022	1.7484	(0.7409, 4.1260)
EDUCREC2 16	0.5286	0.4223	1.2520	0.2107	1.6965	(0.7415, 3.8815)
EDUCREC2 17	0.5355	0.4265	1.2550	0.2093	1.7083	(0.7404, 3.9412)
EDUCREC2 18	0.7646	0.4351	1.7570	0.0789	2.1481	(0.9156, 5.0399)
EDUCREC2 19	0.5300	0.4232	1.2520	0.2104	1.6990	(0.7412, 3.8941)
EDUCREC2 20	0.5985	0.4289	1.3950	0.1629	1.8194	(0.7850, 4.2173)
EDUCREC2 21	0.4005	0.4684	0.8550	0.3926	1.4926	(0.5959, 3.7382)
EDUCREC2 22	0.4012	0.4607	0.8710	0.3838	1.4937	(0.6055, 3.6846)
NONCIGEV (YES)	-0.1227	0.0573	-2.1420	0.0322	0.8846	(0.7907, 0.9896)
SMKLSEV (YES)	0.0435	0.0717	0.6070	0.5437	1.0445	(0.9076, 1.2021)
YEAR 2	0.0315	0.0585	0.5390	0.5899	1.0320	(0.9203, 1.1574)
YEAR 3	-0.0131	0.0566	-0.2320	0.8166	0.9870	(0.8833, 1.1028)

## 4. DISCUSSION

This study adopted a pseudo-panel data analysis approach to estimate the effect of NCT and ST use and other socio-demographic variables on the diagnosis of hypertension in cohorts defined by year of birth in a three-year period, 2012-2014. The finding of this study show lower odds of hypertension diagnosis with age among who responded ‘yes’ to the use of NCT compared to those who responded ‘no’. Friedman et al. (1982) [24] reported non-smokers had a higher mean diastolic blood pressure (1mmHg higher) than smokers, regardless of gender. A notable limitation of this study is that the characteristics of the reference group (those who do not use ST and NCT, body mass index [BMI] status) are not known and may have included people who use cigarettes or who were obese. A comparison between non-smokers, smokers and former smokers in the Czech Republic by Pankova et al (2015) [13] showed no difference in the diagnosis of hypertension

despite an adjustment for age and BMI. The authors, however, found the diagnosis of hypertension was more likely in non-smokers compared to former smoker. Another limitation is we did not adjust for all possible confounders that could affect the relationship between NCT, ST, and the diagnosis of hypertension, including body mass index (BMI). Future studies should investigate patients' knowledge of the deleterious effects of non-cigarette tobacco on cardiovascular disease risk.

## 5. CONCLUSION

Given the sodium content of non-cigarette tobacco products, regardless of lower odds of developing hypertension, a large number of aged individuals who use these products should still be considered at risk, in some form, for developing hypertension or poor control of their blood pressure. In screening for tobacco use, healthcare providers should screen for the use of both cigarette and non-cigarette tobacco products in their patients as well as initiate individualized health education messages that target tobacco cessation in all forms.

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