Electronic Nicotine Delivery Systems (ENDS) use during a six-year period is not associated with self-reported chronic obstructive pulmonary disease (COPD) after proper adjustment of cigarette smoking history: A longitudinal analysis of PATH data

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The Public Health Burden of COPD

• Chronic Obstructive Pulmonary Disease (COPD) is a chronic and progressive disease encompassing emphysema and chronic bronchitis\(^1\)

• COPD is characterized by restrictive airflow to the lungs and an abnormal inflammatory response,\(^2\) usually caused by exposure to noxious particles or gases\(^3\)

• COPD is the fourth leading cause of mortality in the US\(^4\)

• COPD is projected to be responsible for 9.4 million COPD-attributable deaths and more than $800 billion in direct medical costs by 2038\(^5\)
Cigarette Smoking and COPD

• Cigarette smoking is the primary risk factor for COPD,\textsuperscript{3,6} and the risk of COPD is \textbf{200\% higher} among people who currently smoke than people who never smoked cigarettes\textsuperscript{7}

• Years of chronic smoking are needed to develop COPD,\textsuperscript{8} and more than 20\% of people who ever smoked are expected to be diagnosed with COPD\textsuperscript{2,6}

• In addition to smoking status, \textit{smoking duration} and \textit{smoking intensity} are both important covariates in models predicting COPD risk\textsuperscript{9}
ENDS use and COPD

• There is concern that ENDS product use may increase the risk of COPD\(^\text{10}\)

• Some cross-sectional studies have examined the ENDS-COPD association,\(^\text{11-14}\) but these studies carry the risk of reverse causation:
  1. Can’t determine if ENDS use occurred before or after the COPD diagnosis
  2. People who smoked cigarettes might have switched to ENDS after experiencing negative health effects\(^\text{15-17}\)
  3. Most adult ENDS users either currently smoke or formerly smoked cigarettes\(^\text{18-19}\)
Study Objective

• Examine the prospective association between ENDS use and self-reported incident COPD among adults aged 40+ in the US

Address some of the limitations in previous research by:
1. Examining the incidence of COPD prospectively, limiting concerns with reverse causation
2. Including ENDS use as a time-varying measure that was lagged one wave (t-1) to ensure that ENDS use preceded the COPD outcome
3. Controlling for the potential confounding effect of time-varying smoking status and baseline cigarette-pack-years, which previous published studies have not done
Methods

- **Data**: W1-W5 of the Population Assessment of Tobacco and Health Study (PATH), a nationally representative longitudinal study of the US civilian population

- **Analytic Sample**: Adult respondents aged 40+ at baseline (Wave 1) who reported no history of COPD at baseline and participated in at least one follow-up interview
  
  - Each of the 9,861 individuals (N) contributed a separate row of data for each discrete-time interval (T), until they reported COPD or were right censored
  
  - Person-period data set, based on N x T, had 33,679 observations
Methods

Dependent variable: self-reported COPD

• We examined the incidence of self-reported COPD at each follow-up wave based on the following question: “In the past 12 months, has a doctor, nurse, or other health professional told you that you had…(1) COPD, (2) chronic bronchitis, (3) emphysema?”

• Consistent with the clinical definition of COPD, respondents who reported having any of these conditions were considered to have COPD
Methods

- **Time-varying ENDS exposure (t-1):**
  - Every day or someday use of ENDS products among established users (ever fairly regular use of ENDS)

- **Sociodemographic covariates:**
  - Sex
  - Race/ethnicity
  - Household income
  - Education

- **Baseline COPD risk factors:**
  - Obesity (BMI >30) and asthma

- **Time-varying smoking status (t-1):**
  - Based on established use (100 cigarettes in life) & every day / some day use measure
  - Never, former, current use

- **Baseline cigarette pack-years (CPY):**
  - Duration X intensity

- **Time-varying exposure to second hand-smoke, SHS, (t-1):**
  - Past 7-day ‘close exposure’ to second-hand smoke (range 0-100 hours)
Statistical Analysis

- Multivariable discrete time survival models

- Discrete-time hazard models were estimated using a complimentary log-log link function

- All analyses used W1 weights, including full-sample and 100 replicate weights
  - Variances were computed using the balanced repeated replication method with Fay’s adjustment set to 0.3
  - Sensitivity analyses were conducted using the ‘all waves weights’
Key Baseline Characteristics – Analytic sample

- 53% female
- 11.4% Hispanic; 11.2% Non-Hispanic Black
- 1.4% ENDS user
- 13.8% current cigarette use; 23.2% former use; 63% never use
- 8.7% with previous asthma diagnosis
- 33.5% with BMI &ge; 30
# Life table describing incidence of self-reported COPD, PATH Adults 40+ W2-W5

## Table

<table>
<thead>
<tr>
<th>Interval</th>
<th>Total</th>
<th>COPD Diagnosis</th>
<th>Censored</th>
<th>Survival Estimate</th>
<th>Hazard Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period 1 (W1-W2)</td>
<td>9861</td>
<td>314</td>
<td>646</td>
<td>0.968</td>
<td>0.024</td>
</tr>
<tr>
<td>Period 2 (W2-W3)</td>
<td>8901</td>
<td>252</td>
<td>719</td>
<td>0.941</td>
<td>0.021</td>
</tr>
<tr>
<td>Period 3 (W3-W4)</td>
<td>7930</td>
<td>158</td>
<td>785</td>
<td>0.922</td>
<td>0.014</td>
</tr>
<tr>
<td>Period 4 (W4-W5)</td>
<td>6987</td>
<td>201</td>
<td>6785</td>
<td>0.896</td>
<td>0.019</td>
</tr>
</tbody>
</table>

- **Risk set N=33,789**
- **Incident cases n=925**
- **Average annualized incidence 0.020 (weighted)**
Main Findings – Incremental Models

Hazard Ratios Predicting Incident COPD

ENDS use - unadjusted

ENDS use - adding adjustment for sociodemographics

ENDS use - adding adjustment for smoking status

ENDS use - adding adjustment for cigarette pack-years
## Final Model – ENDS and cigarette use variables

<table>
<thead>
<tr>
<th></th>
<th>Hazard</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time-varying ENDS use</strong></td>
<td>1.1</td>
<td>.78-1.57</td>
</tr>
<tr>
<td><strong>Time-varying cigarette smoking status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never cigarette use</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>Former cigarette use</td>
<td>0.85</td>
<td>.59-1.23</td>
</tr>
<tr>
<td><strong>Current cigarette use</strong></td>
<td>1.64**</td>
<td>1.17-2.29</td>
</tr>
<tr>
<td>Log cigarette pack-years(^a)</td>
<td>1.79***</td>
<td>1.46-2.19</td>
</tr>
<tr>
<td>Time-varying second-hand smoke exposure(^b)</td>
<td>1.09***</td>
<td>1.04-1.14</td>
</tr>
</tbody>
</table>

\(^a\) – baseline; per 10 pack-year increase  
\(^b\) - per 10-hour increase of exposure in the past 7 days
Final Model - Other Covariates

• COPD self-reported incidence associated with:
  • Increasing age
  • Female sex
  • Non-Hispanic Black race
  • Less than high school or some college education level
  • Prior asthma diagnosis
  • BMI $\geq 30$
More than 90% of sample adults who use ENDS currently or formerly smoked.

Decreasing proportion of never & current smoking and increasing proportion of former smoking among sample adults who use ENDS.
Cigarette pack-years and secondhand smoke exposure in analytic sample by Wave

- Higher baseline mean cigarette smoking pack-years in sample adults who use ENDS
- Higher exposure to second-hand smoke in sample adults who use ENDS
Discussion

• Longitudinal study of COPD incidence in a nationally representative survey

• ENDS use was not associated with incident COPD risk after adjusting for smoking status and cigarette pack-years

• Cigarette smoking status, pack-years, second-hand smoke were all associated with COPD risk

• More than 90% of those in the analytic sample reporting ENDS use also reported current or former cigarette use

• The average pack-years (baseline) and second-hand smoke exposure was significantly higher in those reporting ENDS use
Discussion

Some caveats and limitations:

1. Results were based on approximately 5-years of data. Longer follow-up may be required to understand the role of ENDS use on incident COPD risk.

2. Longer term longitudinal studies are needed, especially as ENDS products continue to evolve.

3. ENDS use was only reported by a relatively small number of respondents.

4. Self-reported data.
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References

References


