# Alternative Nicotine Delivery System Use Among Women & Girls

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- No Conflicts of Interest

# Objective

- Alternative nicotine delivery devices, namely e-cigarettes, are commonly used and heavily studied products.

- However, there is limited experimental evidence of the how these products are used by women.

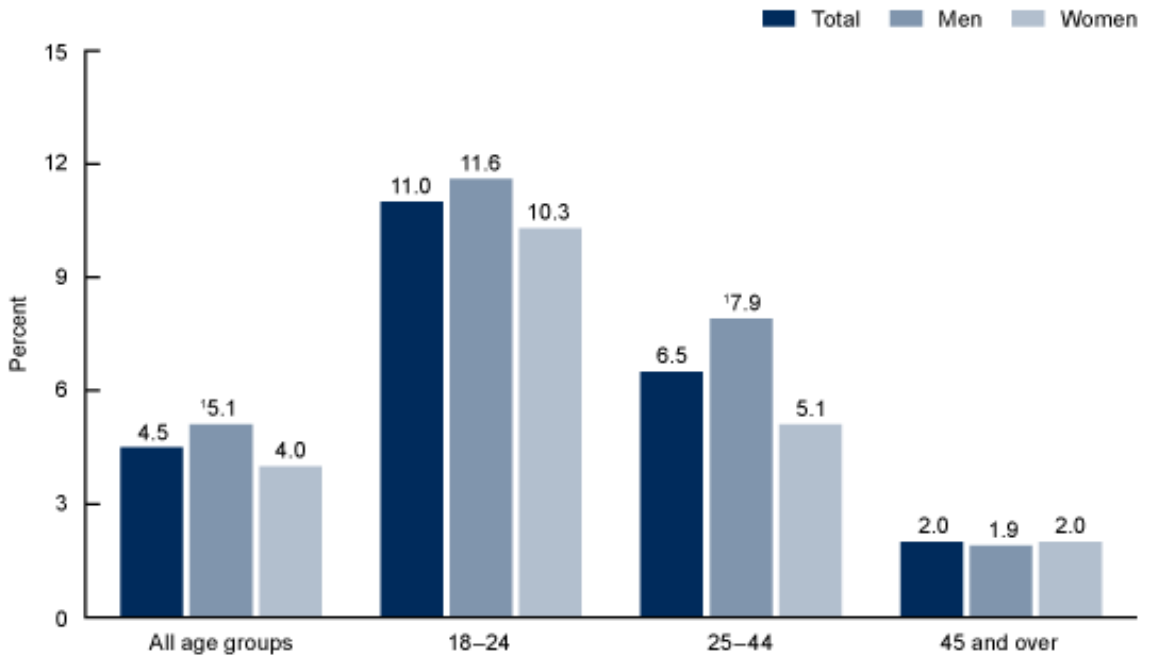
- The goal of today's talk is to…
  - Review human laboratory research on use of e-cigarettes among women
  - Identify the gaps in the research and our knowledge
  - Discuss ways to address these research gaps

# Sex & Gender

- When examining research with women, important to distinguish between sex and gender
- Sex refers to biological variable and can include male, female, intersex
- Gender is the social construct which our understanding of continues to evolve and is non-binary, includes several classifications includes men, women, non-binary, agender, etc.
- Sex & Gender can sometimes be conflated in tobacco research, important to distinguish where possible

# E-cigarettes & Women: Rates of Use

- Among adult data,
  - Women's e-cigarette use is 4.0%.
  - Lower than male use
  - Rates of use decrease as age increases
- Among youth data,
  - High school females have higher use than males (15.4% v. 12.8%)
  - Middle school females have higher use than males (5.3% v. 3.8%)




[1]Significantly different from women ($p < 0.05$).

National Center for Health Statistics, National Health Interview Survey

# Alternative Nicotine Delivery Devices: E-cigarettes

Cig-a-like

Vape Pens

Mods/APV

Rechargeable pod devices


Disposables

Disposable Devices

Refillable Devices

Disposable Devices

# E-cigarettes


**Size/Shape**

**Device Type**

**Flavor**

**Nicotine**

- **Cost**
- **Availability**
- **Popularity/Social Perception**

# E-cigarettes


**Flavor**

**Nicotine**

# E-cigarettes & Women


**Nicotine**

- Nicotine in e-cigarettes is characterize by two main components: concentration and type.
- Nicotine concentration, or the amount of nicotine in e-cigarettes varies with concentrations ranging anywhere from 3mg/ml to 80mg/ml.
- Nicotine in e-cigarettes is available in two formulations, freebase or nicotine salt.
  - Nicotine salt allows for higher concentrations of nicotine and have been demonstrated to be less irritating and have higher appeal.
  - Nicotine salt is more commonly available in e-cigarettes currently on the market.

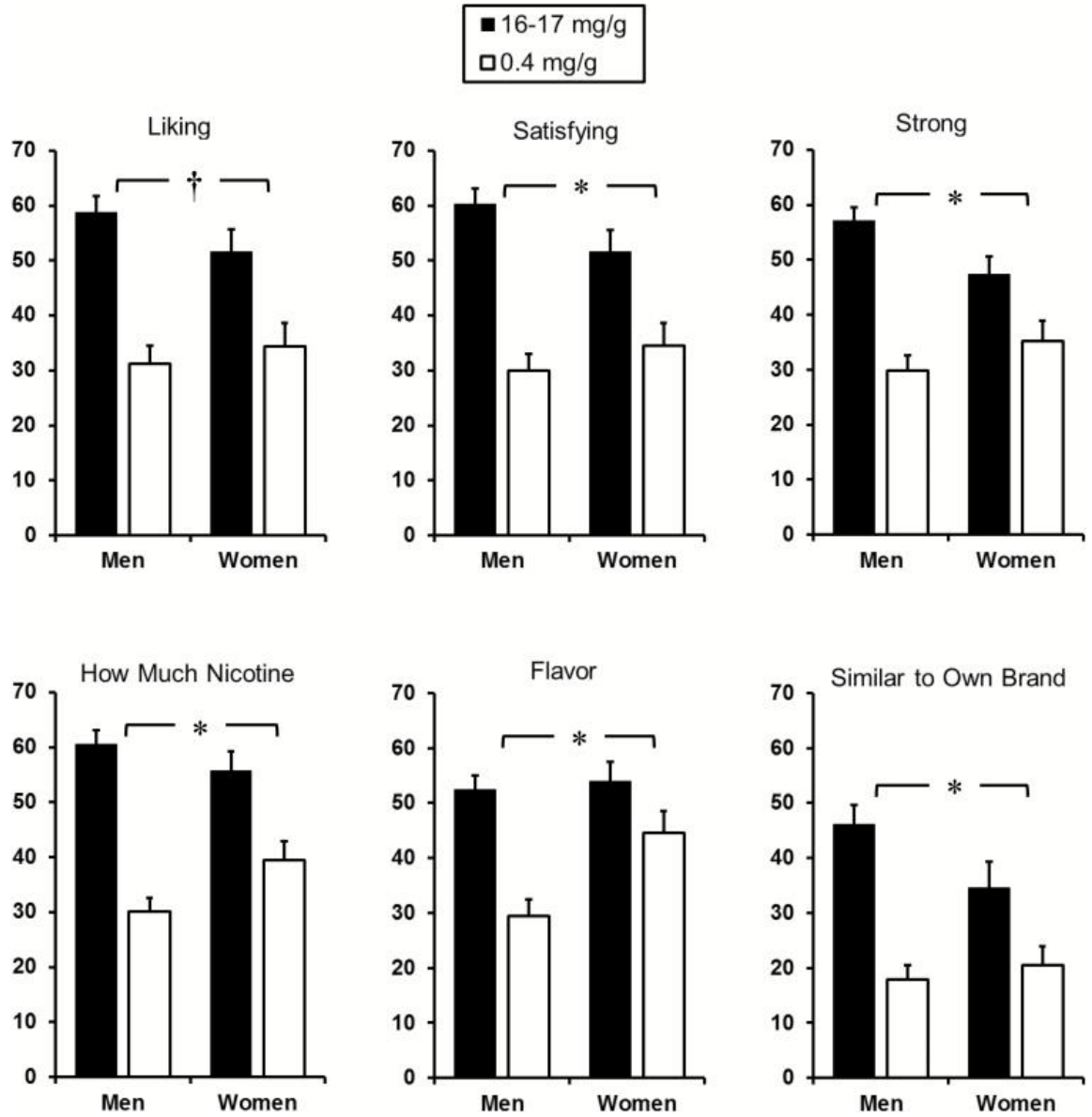
# E-cigarettes & Women

- There is limited data on differences by sex or gender in response to nicotine concentration or type in e-cigarettes.
  - Studies from non-e-cigarette products can inform potential sex/gender differences in response to nicotine concentration.
  - Studies examining response to nicotine type demonstrate mechanisms in which women may be uniquely affected.

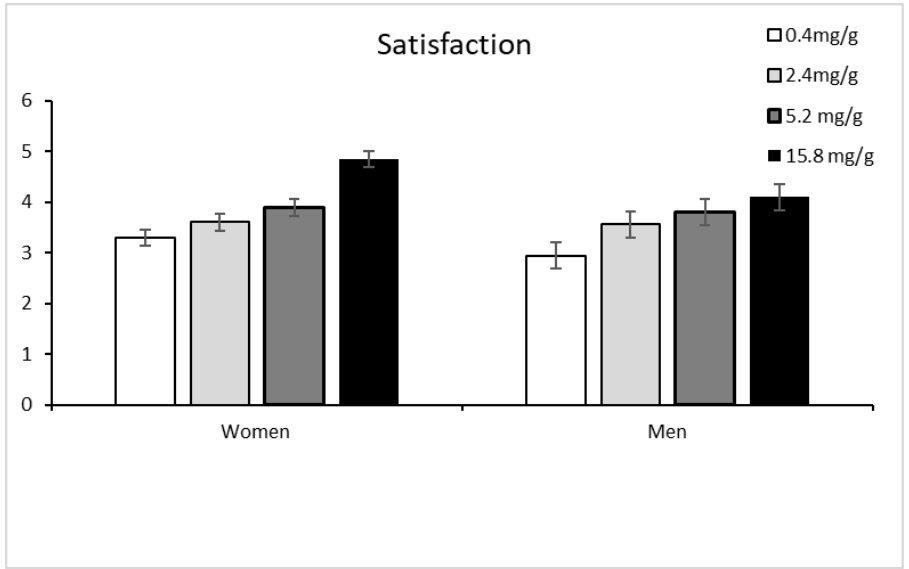
# Nicotine in E-cigarettes & Women: Concentration

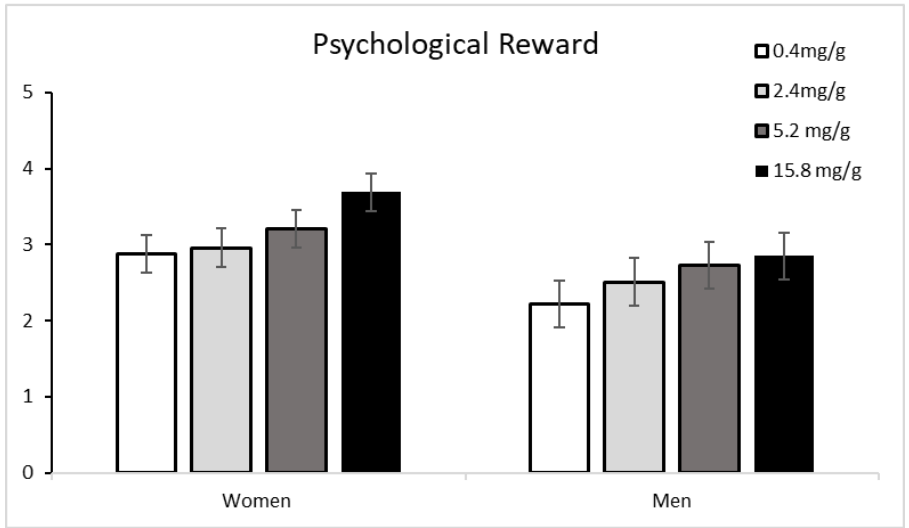
- Some cigarette research suggests that women may be less sensitive to changes in nicotine concentration compared to men.
  - Cigarette cessation trials using nicotine replacement therapy have demonstrated a pattern of poorer cessation outcomes among women
  - Laboratory research suggests women may be poorer at nicotine discrimination than men.
    - Nicotine nasal spray studies –
      - Women were worse at distinguishing nicotine nasal spray from nicotine free nasal spray
      - Women were less confident in the accuracy of their discrimination
    - Studies with combustible cigarettes show mixed results - some show differences in discrimination of sensory effects (Perkins et al., 2018), while others do not (Streck et al., 2020).

From Perkins et al., 2018




From Streck et al., 2020



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# Nicotine in E-cigarettes & Women: Concentration

- There is limited investigation of the effect of nicotine concentration in e-cigarettes among women.
  - Generally, among nicotine dependent populations, higher nicotine concentration is associated with higher reward and appeal.
    - At certain levels of nicotine, irritation effects limit appeal and reward associated with nicotine.
    - There is a lack of data examining effects of nicotine concentration by sex or gender.
  - Data from other products suggests women could be less sensitive to differences in nicotine and other product features may influence product perception/perception of nicotine concentration.

# Nicotine in E-cigarettes & Women: Type

- There have been a few laboratory studies looking at e-cigarette nicotine type (free-base v. salt), but these studies do not report effects by sex or gender.
  - Salt nicotine produced higher rates of appeal and lower rates of harshness (Leventhal et al., 2021; Han et al., 2023).
  - Reduction of product harshness has long been a target of the tobacco industry to increase product appeal among women (Carpenter et al., 2005).
  - E-cigarette smoothness & harshness were strongly associated with appeal in women compared to men (Pang et al., 2022).


# E-cigarettes & Women

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# E-cigarettes & Women


**Flavor**

- E-cigarettes come in a variety of flavors with flavors including sweet (candy, dessert, fruit), cooling (menthol, mint), tobacco, and more unique flavors (spiced, alcohol, beverage).
- Flavor includes both "characterizing" flavors (e.g. cherry, strawberry, menthol), but also can include other sensory components, like cooling sensation with no characterizing flavor.
  - Flavors can be multi-component, e.g. sweet flavor that include cooling components
  - The addition of cooling components have been shown to be associated with increased product use (Davis et al., 2021; Leventhal et al., 2023).
- E-cigarette flavor & nicotine level have been shown to interact (e.g. harshness of nicotine reduced by flavor).
- Compared to males, females report higher rates of non-tobacco flavors and females report using e-cigarettes for the availability of flavor options.

# Flavor in E-Cigarettes & Women

- Lab studies have demonstrated that flavor may be uniquely relevant to women in e-cigarettes.
  - Perception of flavor may have a stronger impact on appeal in women.
  - Familiarity of flavor may increase appeal.
  - Menthol/cooling flavor in e-cigarette may be especially influential on appeal among women.

# Flavor in E-Cigarettes & Women

1. Perception of flavor may have a stronger impact on appeal in women.

    - Pang et al., 2022
        - In an examination of 10 e-cigarette flavors tested with nicotine salt and freebase nicotine, ratings of appeal (liking) and sensory experience (sweetness, smoothness, cooling, bitterness, and harshness) were taken.
        - Ratings of smoothness, bitterness, and harshness were more strongly associated with appeal in females v. males.

# Flavor in E-Cigarettes & Women

2. Familiarity of flavor may increase appeal in women.

- Oncken et al., 2015
  - Participants were exposed to tobacco and menthol free base nicotine e-cigarettes separately over two week-long periods.
  - Participants were combusitible cigarette users smoking either non-menthol or menthol flavored cigarettes.
  - Following each exposure, participants completed a lab session in which subjective appeal (liking) and biochemical data (nicotine level) was collected during and after ad-lib e-cigarette use.

# Flavor in E-Cigarettes & Women

2. Familiarity of flavor may increase appeal.

- Oncken et al., 2015
  - Liking for women was influenced by cigarette flavor preference, where men did not display this difference.

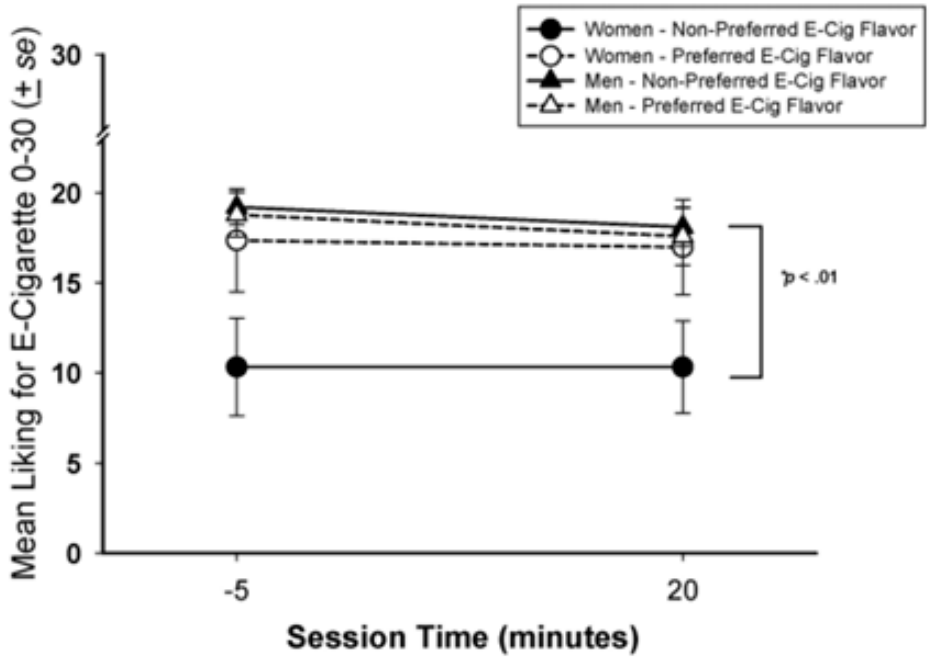


**Figure 3.** Effects of preferred flavor and sex on e-cigarette liking.
*Women receiving nonpreferred e-cigarette reported significantly lower liking scores than the other groups.

# Flavor in E-Cigarettes & Women

## 2. Familiarity of flavor may increase appeal.

- Oncken et al., 2015
  - Nicotine levels were lower for women given their non-preferred e-cigarette flavor.

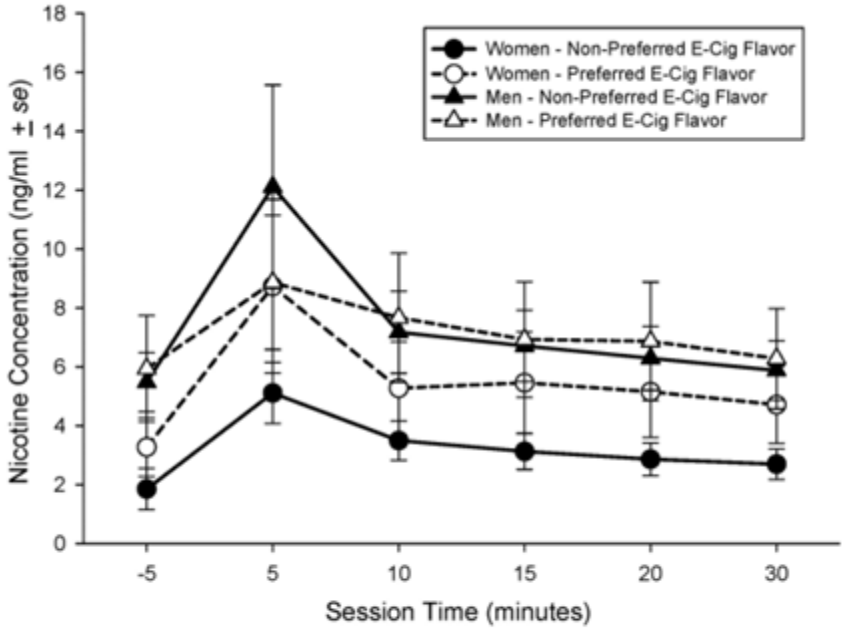


**Figure 2.** Effects of sex and preferred flavor on changes in nicotine concentrations. Nicotine levels for women receiving nonpreferred e-cigarettes (black circles) were significantly lower than the other groups.

# Flavor in E-Cigarettes & Women

3. Menthol/cooling flavor in e-cigarette may be especially influential on appeal among women.

   - Among women, low levels of menthol increases perception of e-cigarette flavor intensity (Rosbrook & Green, 2016).

   - In an examination of four e-cigarettes flavors including menthol, liking of menthol was rated more highly in women compared to men (Mead et al., 2019).

   - In an examination of fruit, menthol, and tobacco flavored e-cigarettes, women rated both fruit and menthol more appealing than tobacco, while males demonstrated a preference for fruit over menthol (Pang et al., 2019).

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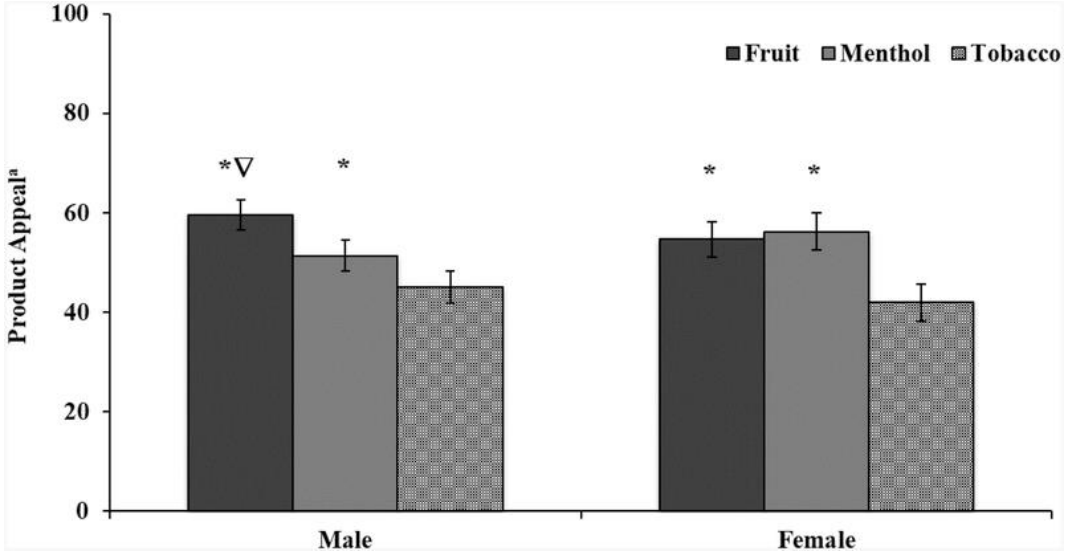


* sig. difference from tobacco, ∇ sig. difference from menthol

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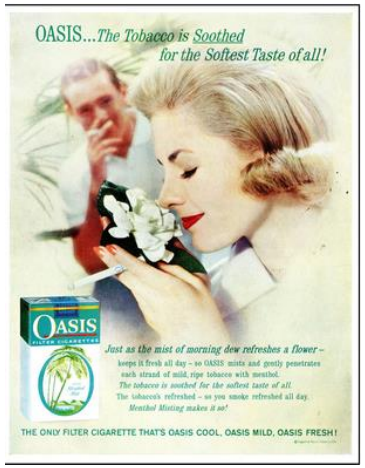





# Gaps in the Literature

- Nicotine & flavor in e-cigarettes is understudied among women.
  - Evidence from cigarette literature suggest nicotine concentration perception may differ by sex or gender, but e-cigarette studies are needed.
  - Nicotine type may be especially relevant to women given effects of irritation & harshness.
  - Lab data on flavor suggests the relevance of menthol flavor and familiarity.
- Examination of reward/reinforcing efficacy is needed across products.

# Challenges for Future Research

- Continued evolution of e-cigarettes
- Population considerations
- Feasibility of isolating e-cigarette features