



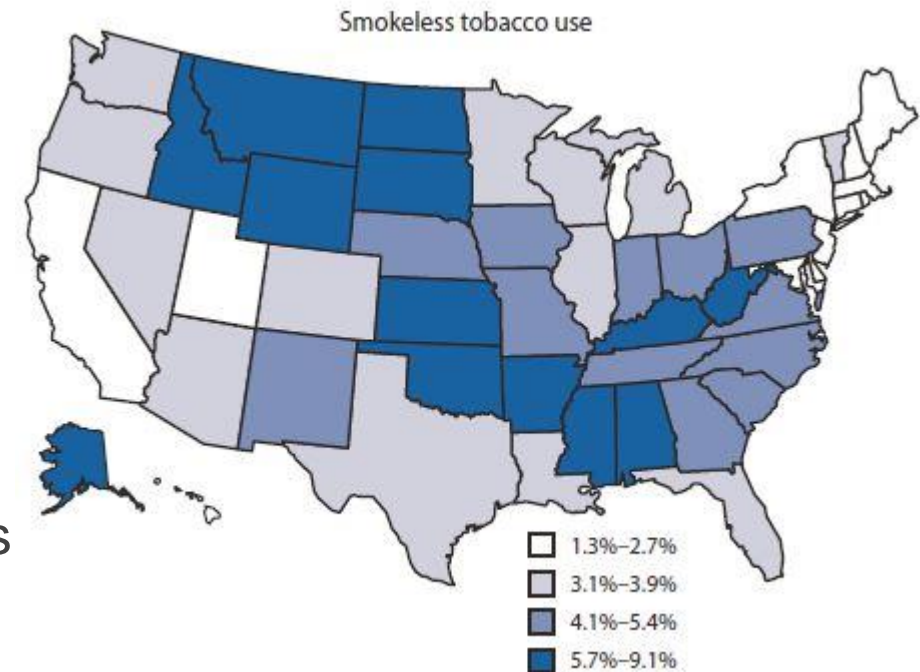
REDUCING HARM FROM SMOKELESS TOBACCO WITH TOBACCO-FREE NICOTINE POUCHES

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Smokeless Tobacco (ST) Use in the U.S.

- ST is used by 3.4% of adults and 5.5% of high school students in the U.S. [1]
- ST is used at 2.5x higher rates in rural areas [2]
- ST use is associated with increased risks of cancer of the mouth, esophagus, and pancreas as well as heart disease and periodontal disease/tooth decay
 - Cancer risk is primarily due to tobacco-specific nitrosamines and other components of tobacco [4].
- There is potential to reduce the harm from ST use by switching to tobacco-free oral nicotine products



State-Specific Prevalence of Smokeless Tobacco Use [3]

Tobacco-Free Nicotine Pouches (TFNPs)?

- Contain 1-12mg of nicotine in salt form as well as flavorings, sweeteners, and alkaline agents to raise pH during use
- At least a dozen brands sold globally:
 - U.S.: Dryft, On!, Velo, Zyn
 - Europe-only: Ace, LOOP, LYFT, POSE, Shiro, Skruf, YOYO, White Fox
- In the U.S.:
 - Convenience store sales exceeded \$40 million in 2019 [5]
 - Online orders of 400,000 cans/month in April/May 2020 reported by one online retailer that expects to sell 1 million cans/month by end of 2020 [6]

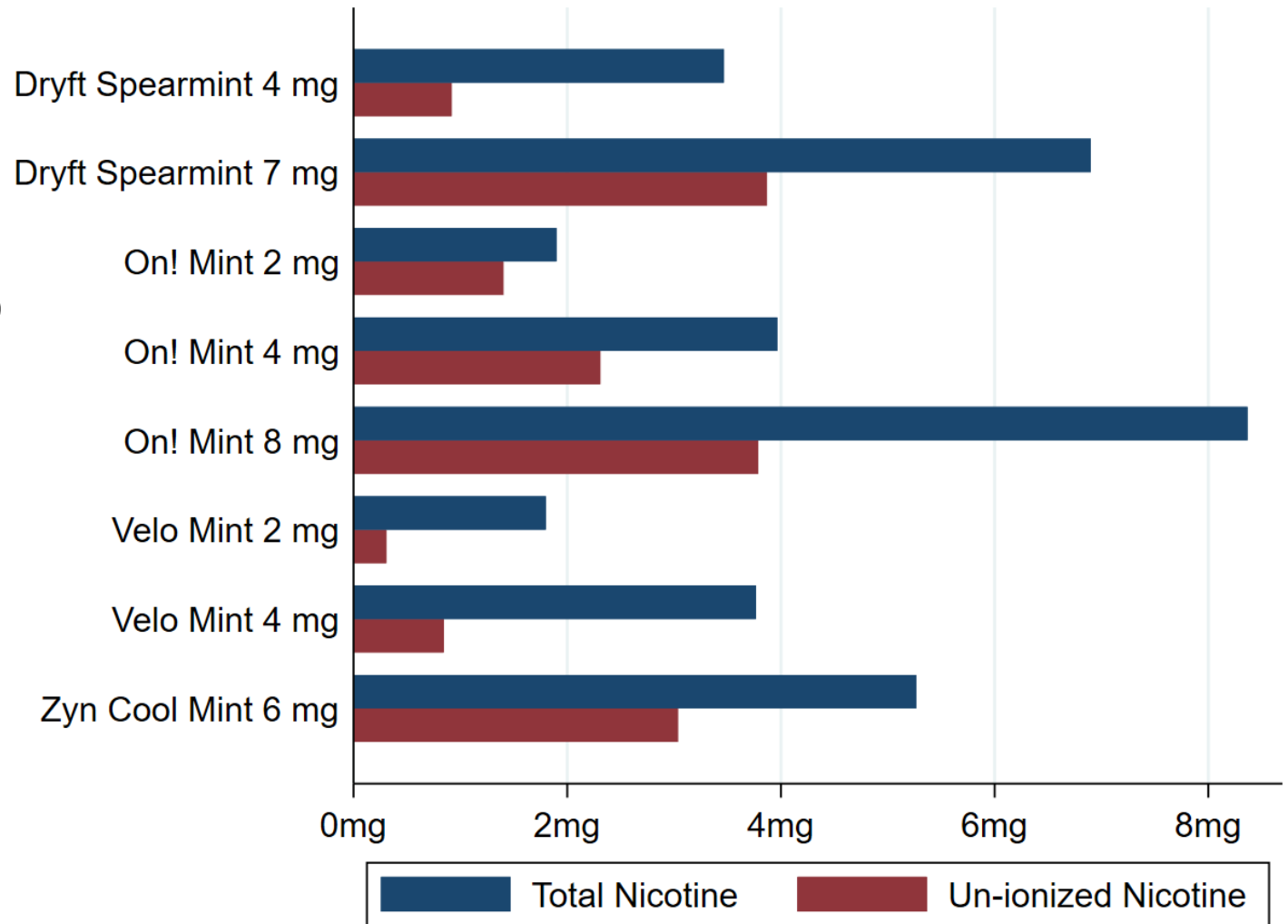


Chemical Analysis Methods

- Eight TFNP products were selected:
 - Dryft Spearmint (4mg, 7mg) [Kretek International/Dryft Laboratories, Made in Sweden]
 - On! Mint (2mg, 4mg, 8mg) [Altria/Helix Innovations, LLC; Made in Sweden]
 - Velo Mint (2mg, 4mg) [R.J. Reynolds Vapor; Made in USA]
 - Zyn Cool Mint (6mg) [Swedish Match, Made in Sweden]
- Nicotine analyzed using LC-MS/MS
- pH measured using two methodologies:
 - Standardized method (SM) for ST: 2g of product in 20mL of distilled water [7]
 - Alternative methodology (AM): 1 pouch (0.23-0.41g) in 20mL of artificial saliva
- Un-ionized nicotine was calculated using Henderson-Hasselbalch equation [7]
 - The pH determines the percent of nicotine in the un-ionized form
 - Un-ionized nicotine is the form most readily absorbed through the buccal lining [8]

Nicotine and Un-ionized Nicotine (SM)

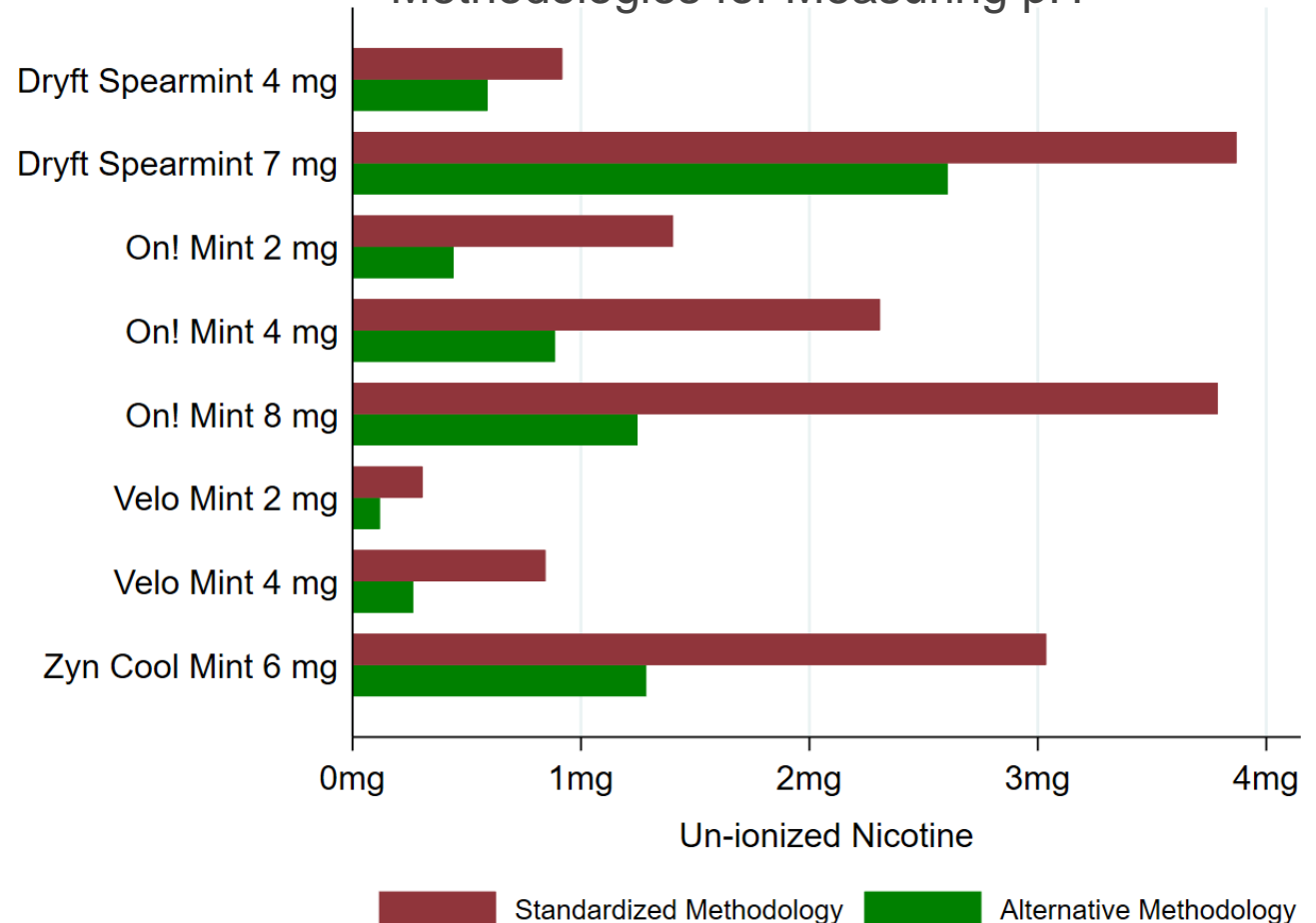
- Total nicotine was close to amount labeled (-13% to +5%)
- The percent of un-ionized nicotine varied from 17% (Velo Mint 2mg) to 74% (On! Mint 2mg)
 - On! Mint **2mg** had more Un-ionized nicotine than Velo Mint **4mg** or Dryft Mint **4mg**
- pH was higher in the brands made in Sweden (Dryft, On!, Zyn) than the American made brand (Velo)



Comparing Un-ionized Nicotine using SM and AM

- The AM method resulted in lower pH and un-ionized nicotine and more variability in un-ionized nicotine
- Products differed greatly in their relative pHs under the two methodologies:
 - The pH of Dryft products differed the least
 - The pH of On! products differed the most
- Dryft Spearmint **7mg** had more than 2x the un-ionized nicotine of On! Mint **8mg** (AM) despite having the similar levels using the SM

Comparison of Un-ionized Nicotine Using Two Methodologies for Measuring pH



Discussion

- This is the first study to chemically characterize multiple TFNPs sold in the U.S.
- The un-ionized nicotine (SM) of TFNPs varied from 0.3-3.9mg
 - Range for moist snuff: 0.01-7.8mg/g
 - Average for American snus: 2.2mg/g [9]
- The lower un-ionized nicotine content of TFNPs may be offset by their higher efficiency of nicotine release compared to moist snuff [10-11]
- ST users who switch to TFNPs may decrease or increase their nicotine intake, depending on product selection, nicotine release profile, and use behaviors
- Switching studies are needed to determine the acceptability of TFNPs for ST harm reduction as well as the nicotine intake from TFNPs
- Alternative methodologies may be needed to characterize the chemical properties of TFNPs *in vitro* to better reflect their impacts *in vivo*

References:

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Supplemental Slide: Nicotine, pH, Un-ionized Nicotine

Product	Mass per Pouch (g)	Total Nicotine (mg)	FDA/USTC Standard pH Methodology (Distilled Water)			Alternative pH Methodology (Artificial Saliva)		
			pH	% Un-ionized Nicotine	Un-ionized Nicotine (mg)	pH	% Un-ionized Nicotine	Un-ionized Nicotine (mg)
			Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Dryft Spearmint 4 mg	0.374 (0.011)	3.47 (0.06)	7.58 (0.07)	27% (3%)	0.92 (0.10)	7.33 (0.00)	17% (0%)	0.59 (0.01)
Dryft Spearmint 7 mg	0.369 (0.004)	6.90 (0.40)	8.13 (0.06)	56% (4%)	3.87 (0.38)	7.8 (0.03)	38% (2%)	2.61 (0.21)
Velo Mint 2 mg	0.227 (0.007)	1.80 (0.00)	7.33 (0.01)	17% (0%)	0.31 (0.01)	6.87 (0.01)	7% (0%)	0.12 (0.00)
Velo Mint 4 mg	0.413 (0.007)	3.77 (0.06)	7.48 (0.01)	22% (0%)	0.84 (0.01)	6.90 (0.00)	7% (0%)	0.27 (0.01)
Zyn Cool Mint 6 mg	0.413 (0.007)	5.27 (0.06)	8.15 (0.07)	58% (4%)	3.04 (0.19)	7.53 (0.01)	24% (1%)	1.29 (0.04)
On! Mint 2 mg	0.266 (0.001)	1.90 (0.00)	8.47 (0.08)	74% (4%)	1.40 (0.07)	7.50 (0.02)	23% (1%)	0.44 (0.02)
On! Mint 4 mg	0.259 (0.002)	3.97 (0.06)	8.17 (0.10)	58% (6%)	2.31 (0.22)	7.48 (0.04)	22% (2%)	0.89 (0.06)
On! Mint 8 mg	0.271 (0.003)	8.37 (0.21)	7.94 (0.03)	45% (2%)	3.79 (0.25)	7.26 (0.09)	15% (3%)	1.25 (0.27)