



Harm Reduction Opportunity of on! PLUS™ Nicotine Pouches

Jennifer H. Smith and Katy M. Webb

FDLI – Tobacco & Nicotine Products Regulatory Science Symposium

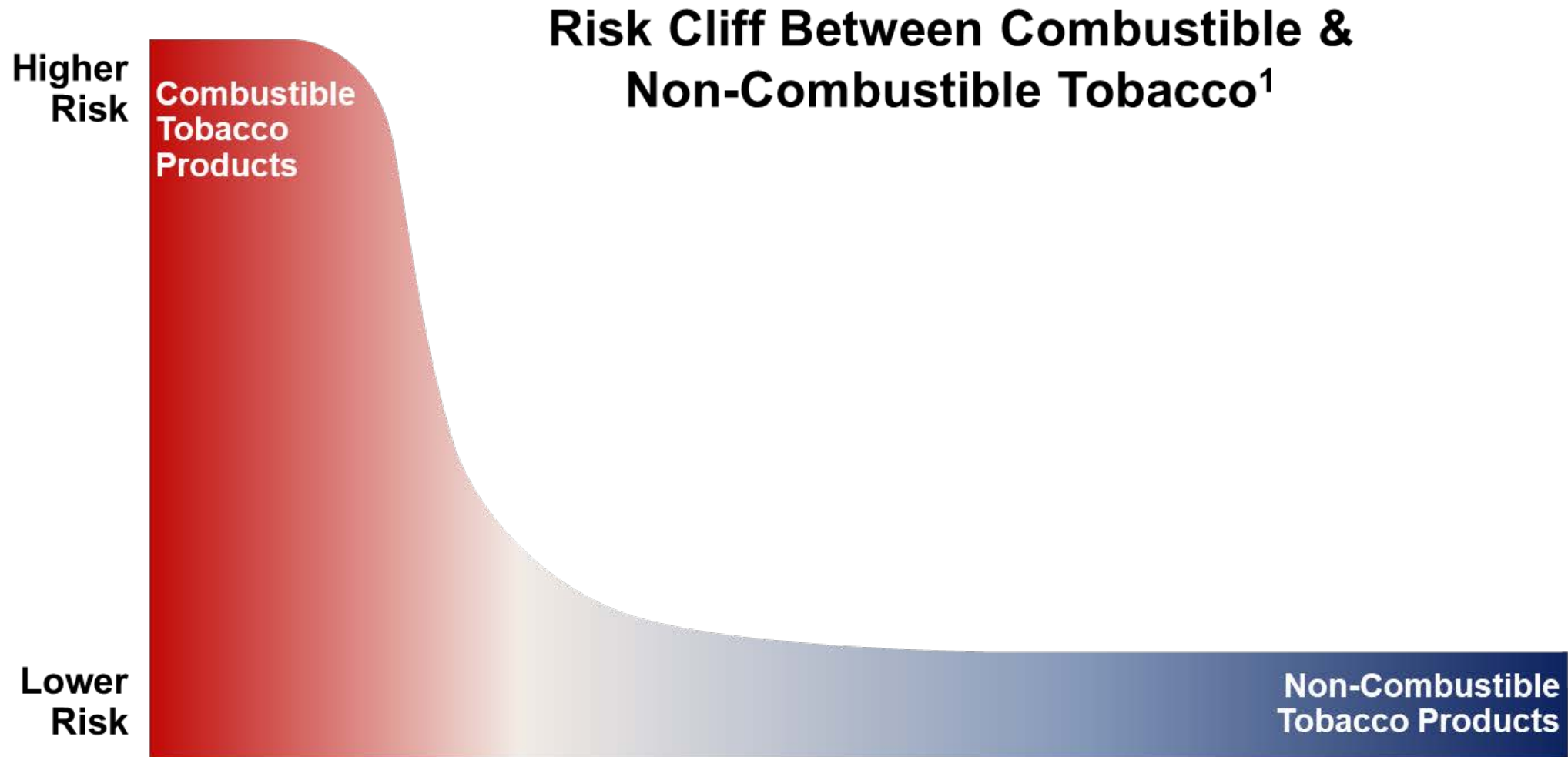
October 30, 2025



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Tobacco Harm Reduction Focuses on Moving Adults Who Smoke Down the “Risk Cliff”

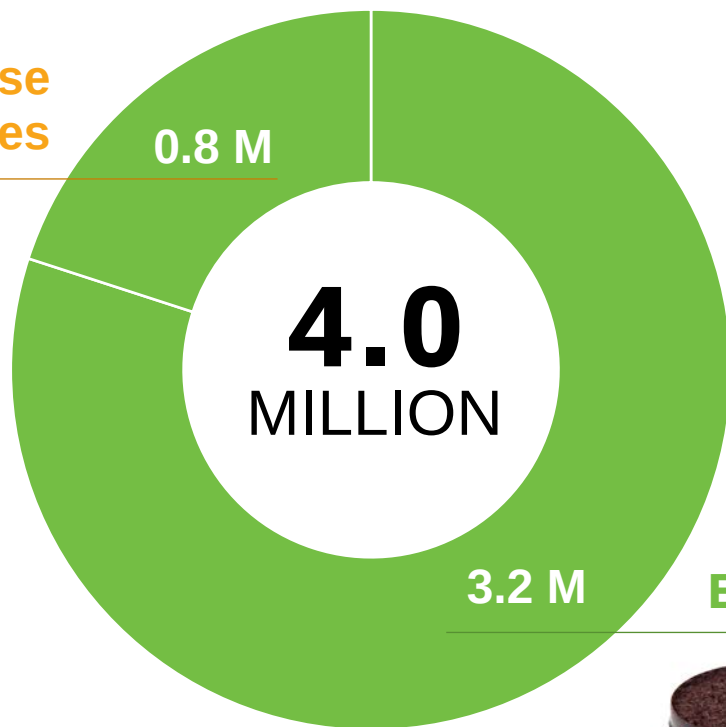


¹Adapted from Nutt, et. al. Estimating the Harms of Nicotine-Containing Products Using the MCDA Approach. Eur. Addict Res 2014; 20:218-225.



on! PLUS™ Presents a Harm Reduction Opportunity for Adults Who Exclusively Use MST and Adults Who Use MST & Cigarettes Concurrently

Dual use
with cigarettes



Exclusive MST



Age 21+ ATCT: Jul 2024 to Jun 2025, 3.2 million adults in the U.S. used MST products exclusively, and 0.8 million adults used MST products and cigarettes concurrently.
MST=moist smokeless tobacco.



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Scientific Framework to Demonstrate APPH

CONSTITUENT REDUCTION



THE PRODUCT

- Chemistry Manufacturing and Controls
- Product Stability
- Chemical characterization

INDIVIDUAL RISK REDUCTION



EXPOSURE and HEALTH RISK

- Toxicology & Risk Assessment
- Health risk assessment (absolute and relative)
- Human Studies
- Human Factors Assessment

POPULATION HARM REDUCTION



IMPACT on the POPULATION

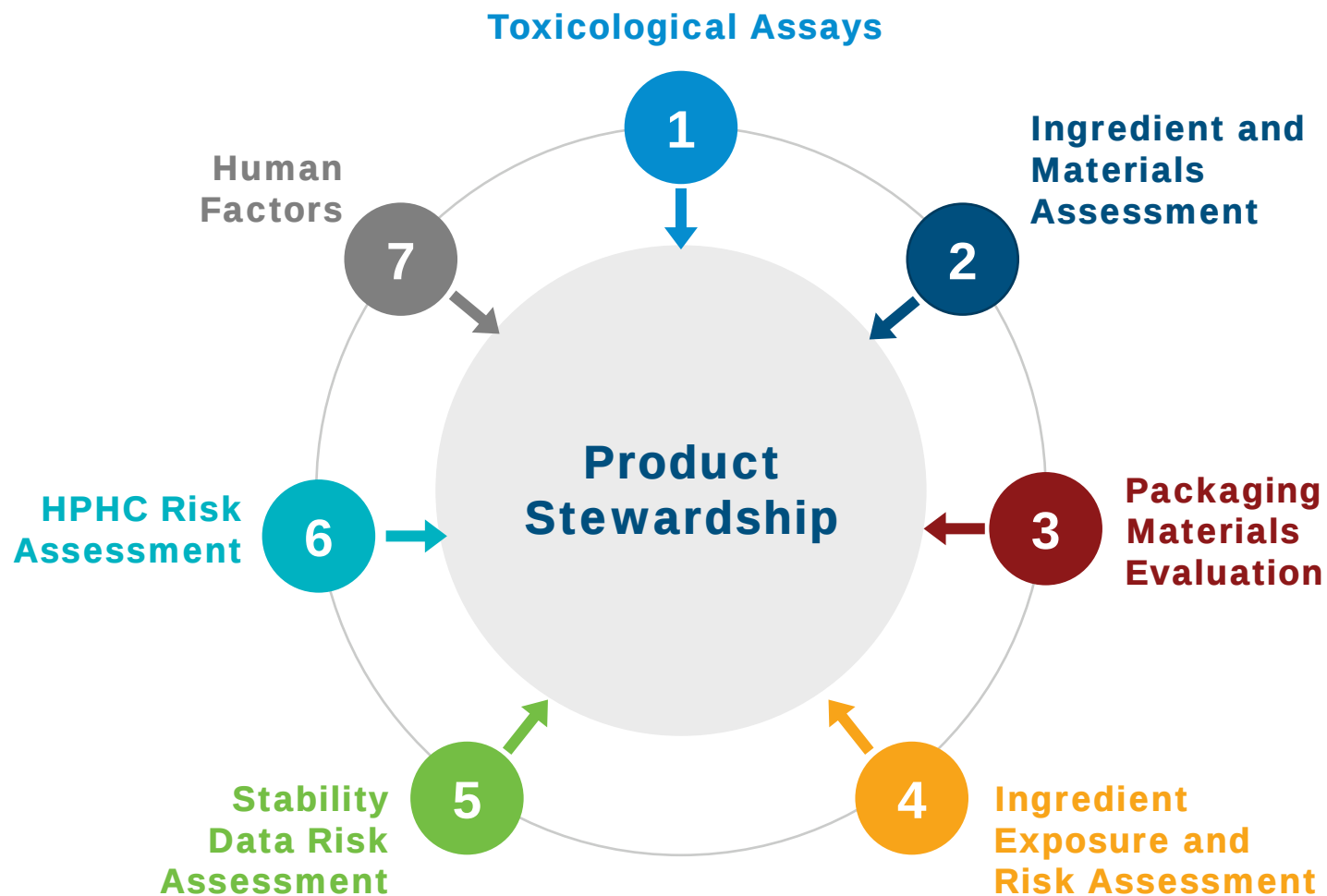
- Risk perceptions (absolute and relative)
- Impact of product on users
- Impact on non-users
- Overall impact on the population
- Environmental Assessment



Using a Product Stewardship Approach to Evaluate on! PLUS™ Nicotine Pouches



CONSTITUENT REDUCTION



- **Chemically & Microbiologically Stable**
- **Toxicological Risk Is Substantially Lower Than Cigarettes and MST and Similar to Commercial OTDN Products**

HPHC=Harmful or Potentially Harmful Constituent; OTDN=oral tobacco derived nicotine



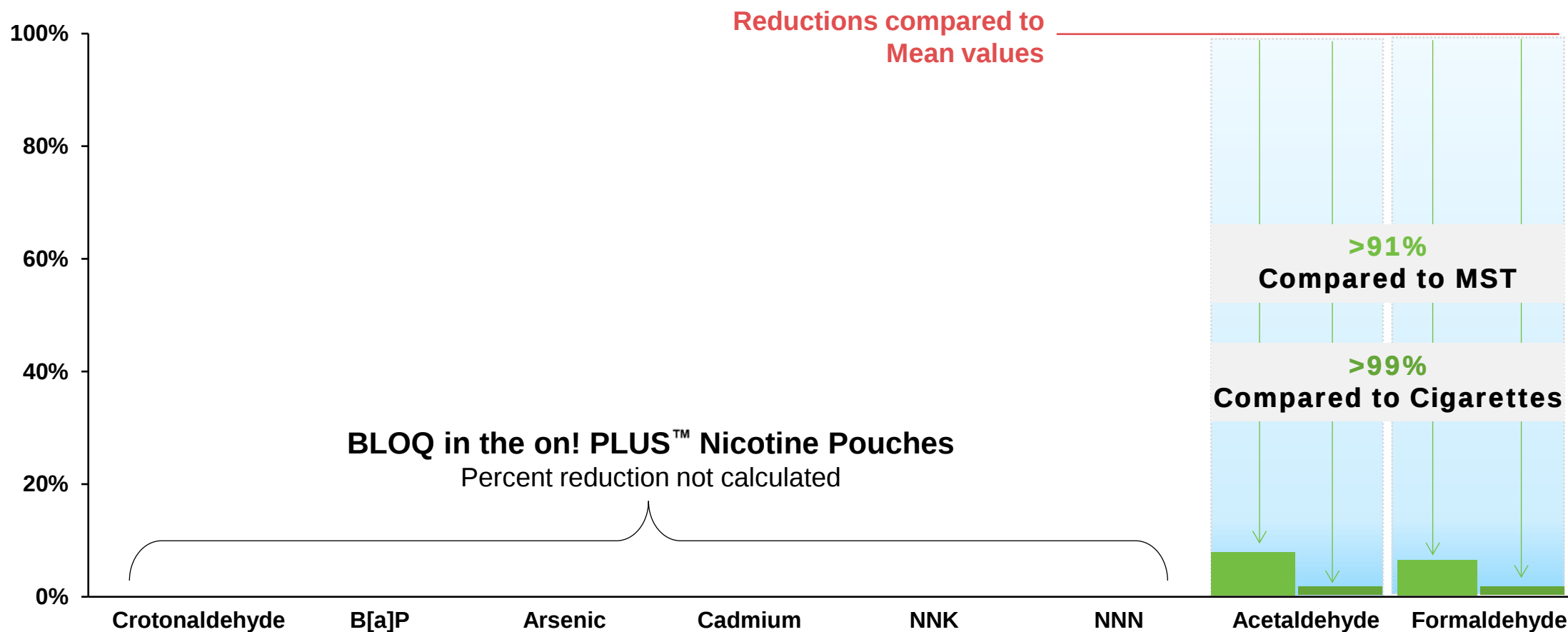
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HPHCs in on! PLUS™ Products Are Not Detected or Substantially Reduced Compared to MST and Cigarettes



CONSTITUENT REDUCTION



Disease association as identified by FDA in Established List, US FDA, Federal Register Vol. 77, April 2012.

B[a]P=Benzo[a]pyrene; BLOQ=below limit of quantitation; HPHC=harmful and potentially harmful constituents; MST=moist smokeless tobacco; NNK=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN=N-nitrosornicotine.

Source: Percent reductions based on maximum HPHC levels across Mint, Wintergreen and Tobacco on! PLUS™ products compared to MST values from Data source: Summary of 2014 and 2015 Smokeless Market Surveys, RDM JAB 2016 281. Data for comparison are on wet weight basis (WWB). The original data were presented in unit/g. We convert the data to unit per portion based on the assumption of a 2 g portion size for a typical use of MST product. The ranges are from RJRT's MRTPAs MR0000068–MR0000073, Section 6.1.5, Table 6.1.5-11.



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Tobacco Abuse Liability Framework

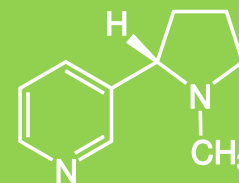


INDIVIDUAL RISK REDUCTION

Relative to other tobacco/nicotine products with known Abuse Liability

NICOTINE EXPOSURE

Pharmacokinetics (PK) and Pharmacodynamics (PD)



SUBJECTIVE EFFECTS

Product Liking, Satisfaction, Craving, and Withdrawal



USE PATTERNS

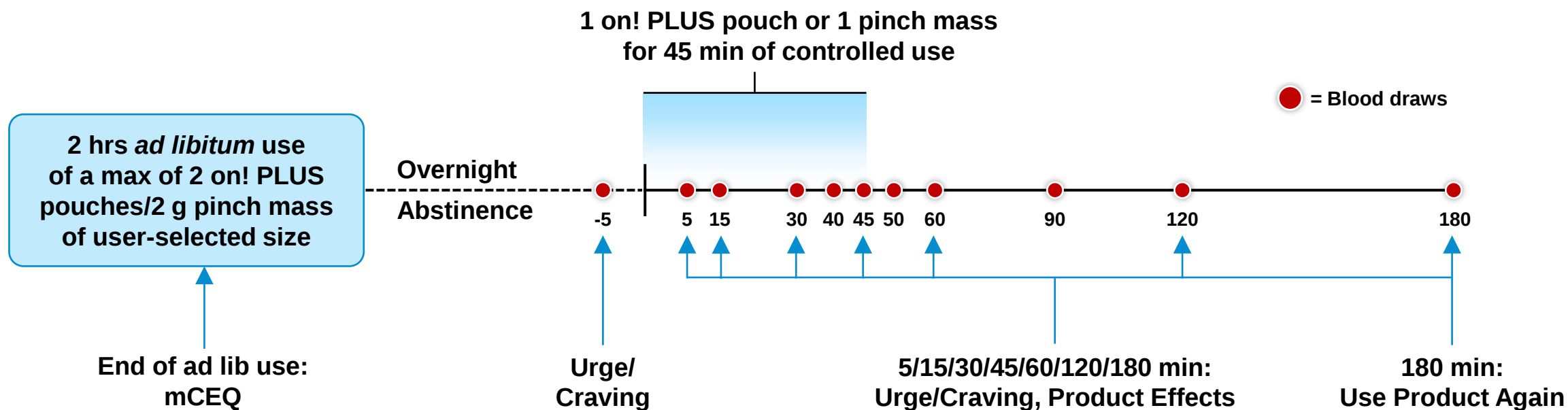
Topography, Actual Use, Use Not as Intended



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PK Study Design



mCEQ = Modified Cigarette Evaluation Questionnaire
Urge and Craving = modified from the Minnesota Nicotine Withdrawal Scale

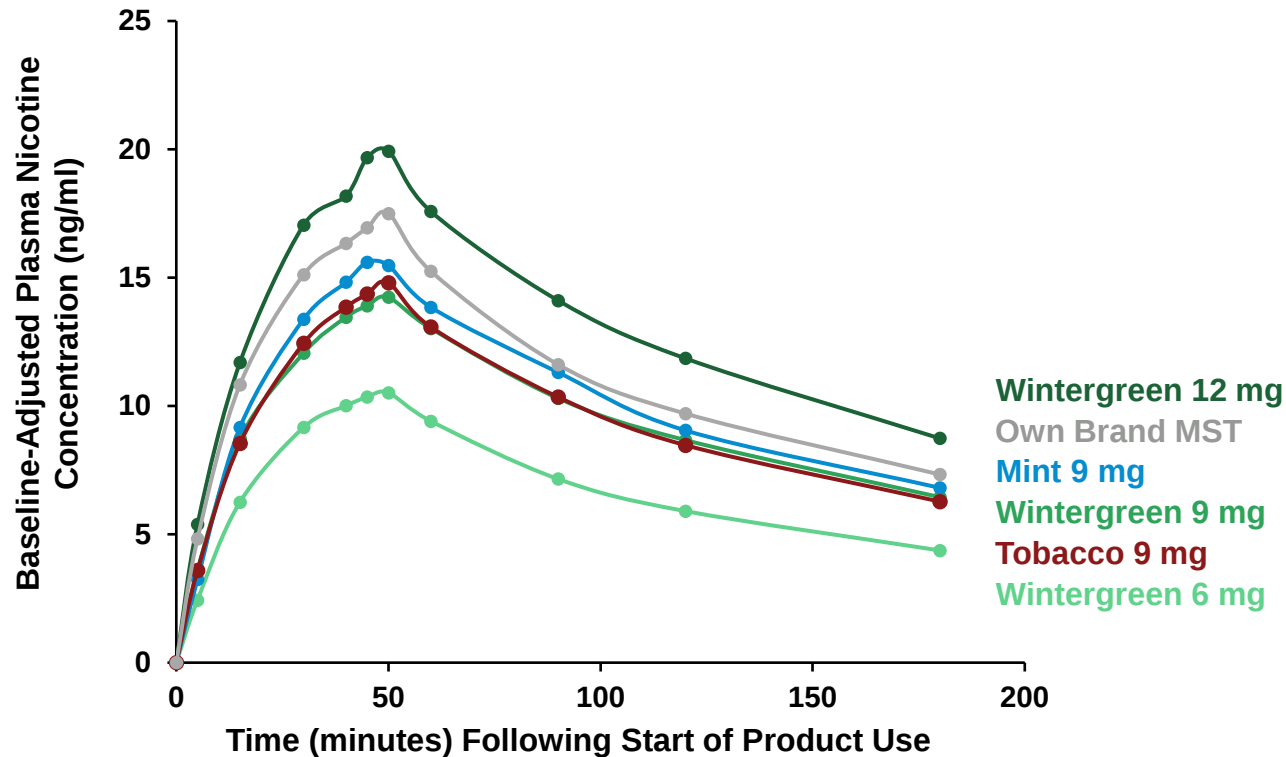


The on! PLUS™ Portfolio Delivers a Wide Range of Nicotine



INDIVIDUAL RISK REDUCTION

Plasma Nicotine: Overall Population



Pharmacokinetic Study

- n=54
- 45-minute product use
- Adults who use >2 g product pinch mass
- Flavor does not impact nicotine exposure

on! PLUS™ and own brand MST products; n=54; PK Study Number ALCS-REG-22-03

*Nighbor et al., (2023) A Comparison of Use Topography and Nicotine Pharmacokinetics Among Loose and Portioned Smokeless Tobacco Users, Nicotine & Tobacco Research, <https://doi.org/10.1093/ntr/ntac195>



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Diversity of Behaviors Within Tobacco Consumers

Results of standard in-clinic abuse liability studies do not necessarily reflect real world usage patterns

	Mean	SD
Average Pinch Mass (g)	4.3	2.19
Average Duration of Use (min)	74	33.9

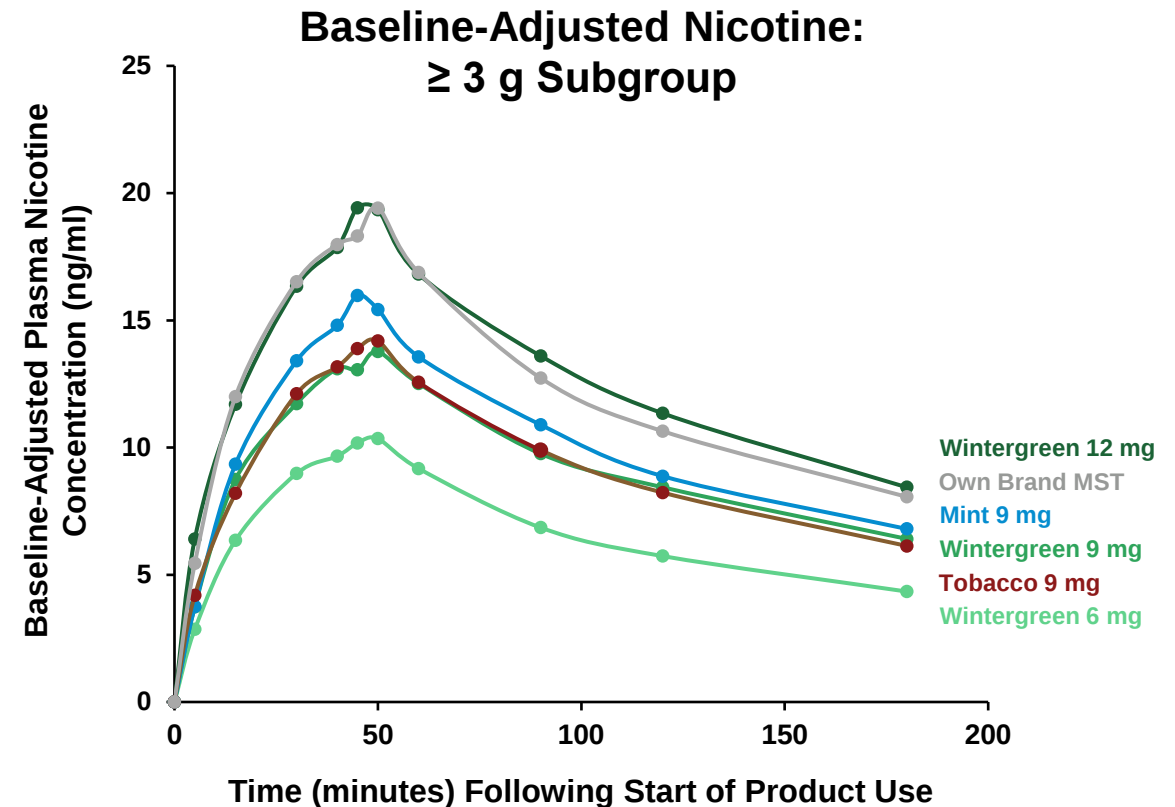
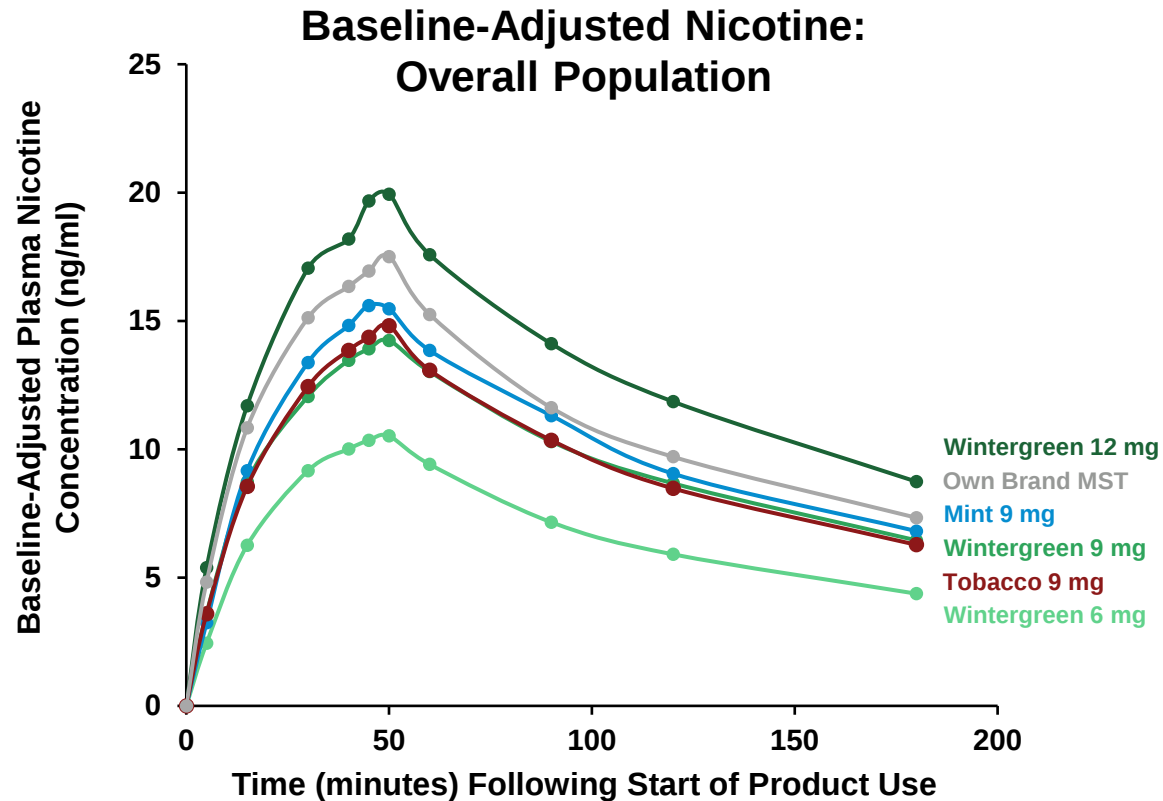
N=168. Webb et al. "Impact of Factors Related to Loose and Pouched Moist Smokeless Tobacco Product Use Behavior on Biomarkers of Exposure to Nicotine and N-Nitrosornicotine". Contributions to Tobacco & Nicotine Research, 2025.
<https://doi.org/10.2478/cttr-2025-0008>



The on! PLUS™ Portfolio Delivers a Wide Range of Nicotine: Subgroup Analysis



INDIVIDUAL RISK REDUCTION



Pharmacokinetic Study using on! PLUS™ and own brand MST products; PK Study Number ALCS-REG-22-03; Overall population, n=54; ≥ 3 g subgroup n=32; MST=moist smokeless tobacco.



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Diversity of Behaviors Within Tobacco Consumers

Results of standard in-clinic abuse liability studies do not necessarily reflect real world usage patterns

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<https://doi.org/10.2478/cttr-2025-0008>

PK Study

45-minute duration

for both OBMST and on! PLUS™



Actual Use Study

~13-17* minutes

average use time for on! PLUS™

*Adult Dippers (n=456) average=16.66 (95% CI=15.46–17.86) minutes; Adult Dual Users of MST products and cigarettes (451) average=13.13 (95% CI=12.12–14.13) minutes; ALCS Final Report Number: ALCS-REG 2022-03-00645, "Tobacco Product Portfolio/Actual Use Study of on! PLUS Nicotine Pouches; OBMST=own brand MST;



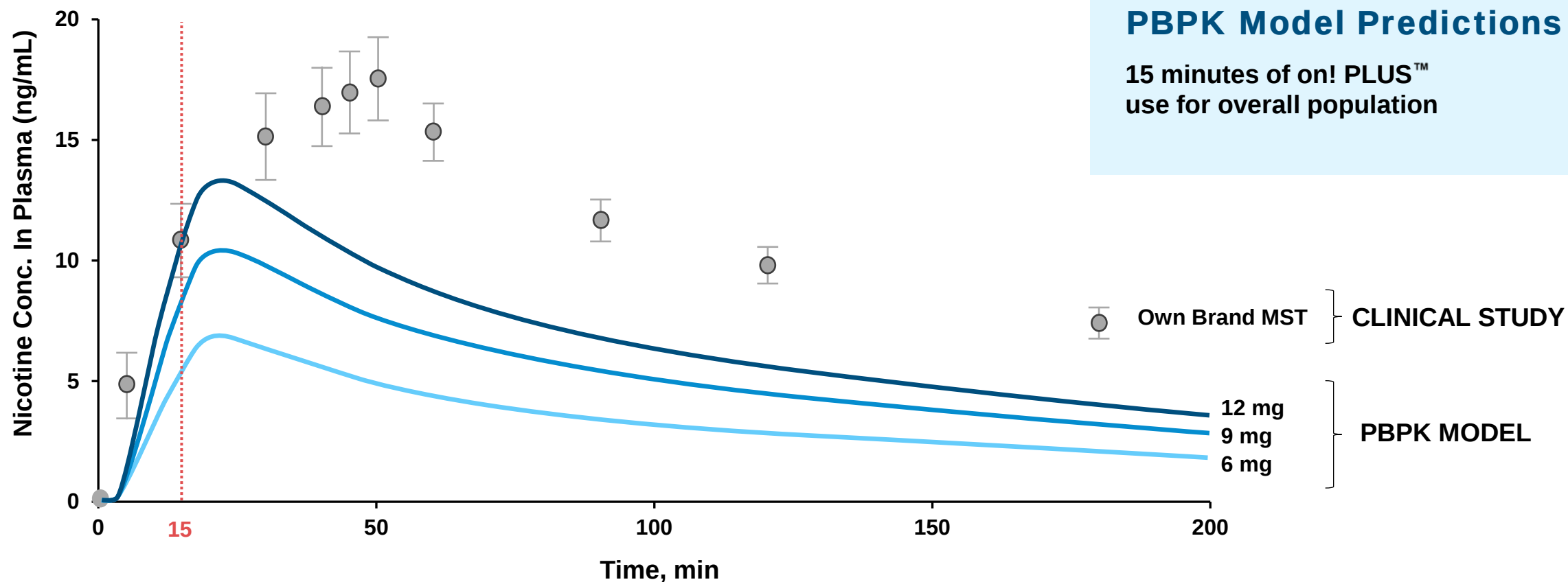
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PBPK Modeling: Nicotine PK Indicates on! PLUS™ Nicotine Exposure Not Likely to be Higher than MST



INDIVIDUAL RISK REDUCTION



PBPK=Physiologically Based Pharmacokinetics
PK Study Number ALCS-REG-22-03; ; n=54
Actual Use Study Number ALCS-REG 2022-03-00645 found ~13-17 minutes average use time for on! PLUS™

Salehi, A., Sarkar, M.A., Smith, J.H. and Rostami, A.A. (2025), Physiologically Based Pharmacokinetic Modeling to Predict Nicotine Pharmacokinetics of Nicotine Pouches Under Naturalistic Use Conditions. J Clin Pharm, 65: 1297-1309. <https://doi.org/10.1002/jcph.70038>



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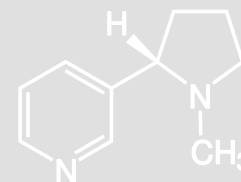
Abuse Liability Framework



INDIVIDUAL RISK REDUCTION

Relative to other tobacco/nicotine products with known Abuse Liability

NICOTINE EXPOSURE
Pharmacokinetics (PK) and
Pharmacodynamics (PD)



SUBJECTIVE EFFECTS
Product Liking, Satisfaction,
Craving, and Withdrawal



USE PATTERNS
Topography, Actual Use,
Use Not as Intended



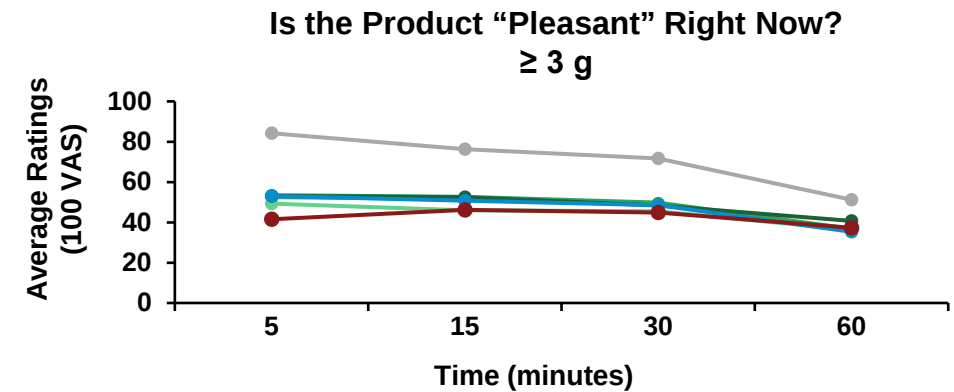
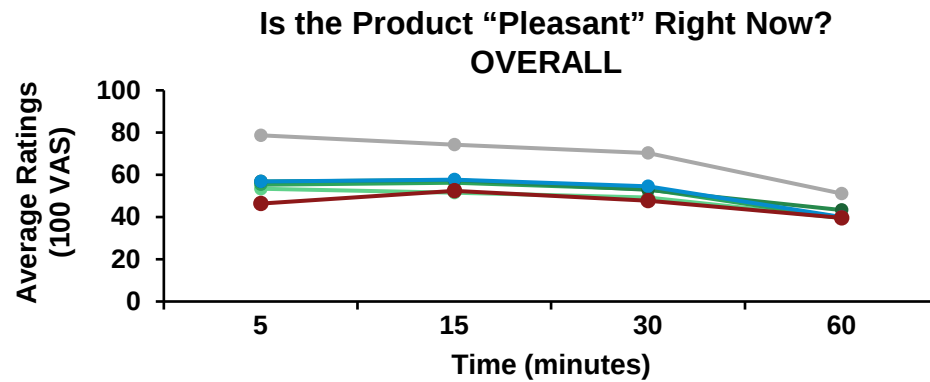
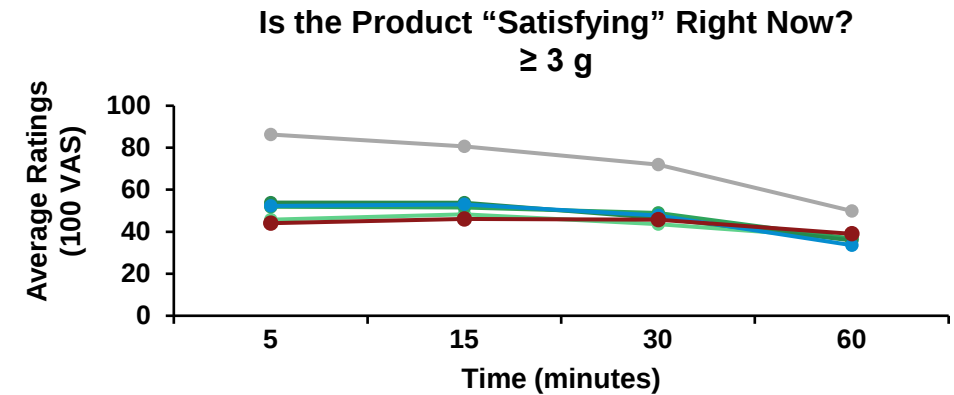
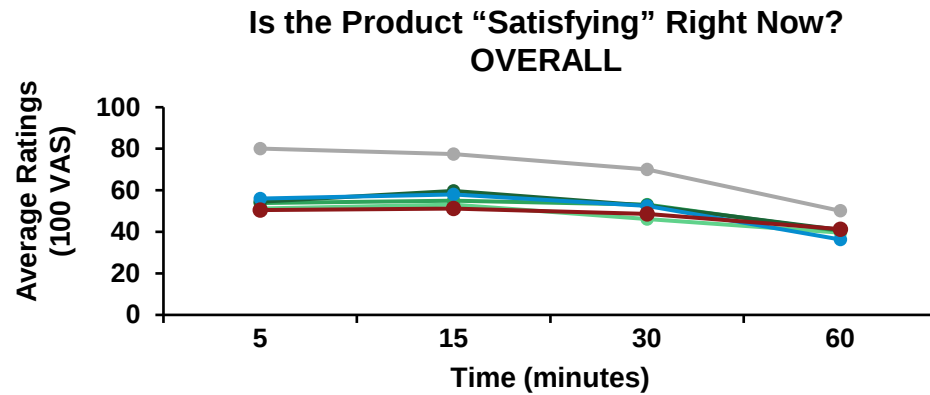
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Adult Dippers Preferred Their Own Brand of MST Over on! PLUS™



INDIVIDUAL RISK REDUCTION

Wintergreen 6 mg Wintergreen 9 mg Wintergreen 12 mg Mint 9 mg Tobacco 9 mg Own Brand MST



Pharmacokinetic Study using on! PLUS™ and own brand MST products; PK Study Number ALCS-REG-22-03; n=54; MST=moist smokeless tobacco.



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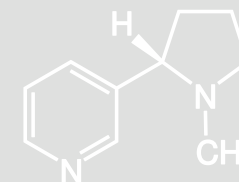
Typical Tobacco Abuse Liability Framework



INDIVIDUAL RISK REDUCTION

Relative to other tobacco/nicotine products with known Abuse Liability

NICOTINE EXPOSURE
Pharmacokinetics (PK) and
Pharmacodynamics (PD)



SUBJECTIVE EFFECTS
Product Liking, Satisfaction,
Craving, and Withdrawal



USE PATTERNS
Topography, Actual Use,
Use Not as Intended

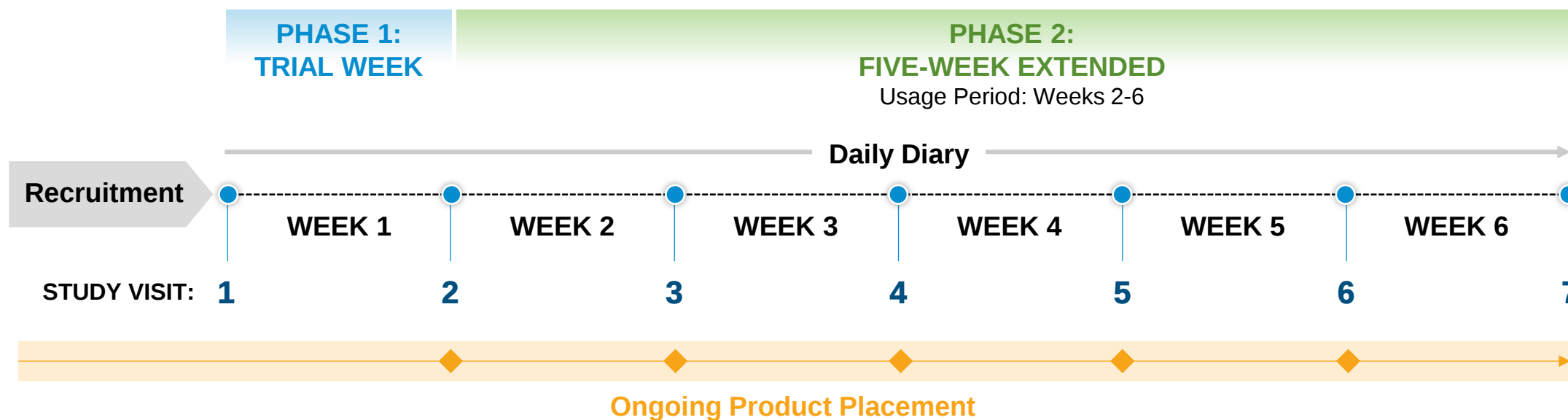


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Actual Use Study Design



INDIVIDUAL RISK REDUCTION



Karelitz, J. L., Newmyer B., and Becker, E., Effect of on! Plus Nicotine Pouch Products on Tobacco Product Use Behaviors Among Adults in the United States Who Use Smokeless Tobacco Exclusively or Dual Use with Cigarettes: A Six-Week Actual Use Study. *In Preparation*.

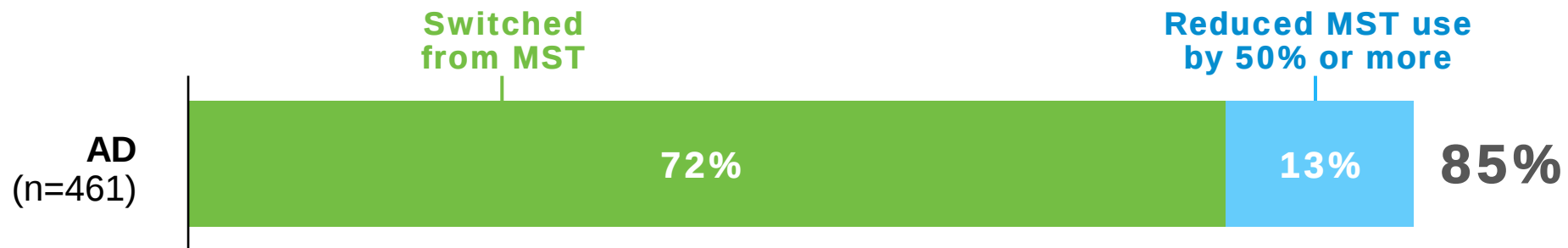
Source: ALCS Final Report Number: ALCS-REG 2022-03-00645, "Tobacco Product Portfolio/Actual Use Study of on! PLUS™ Nicotine Pouches"



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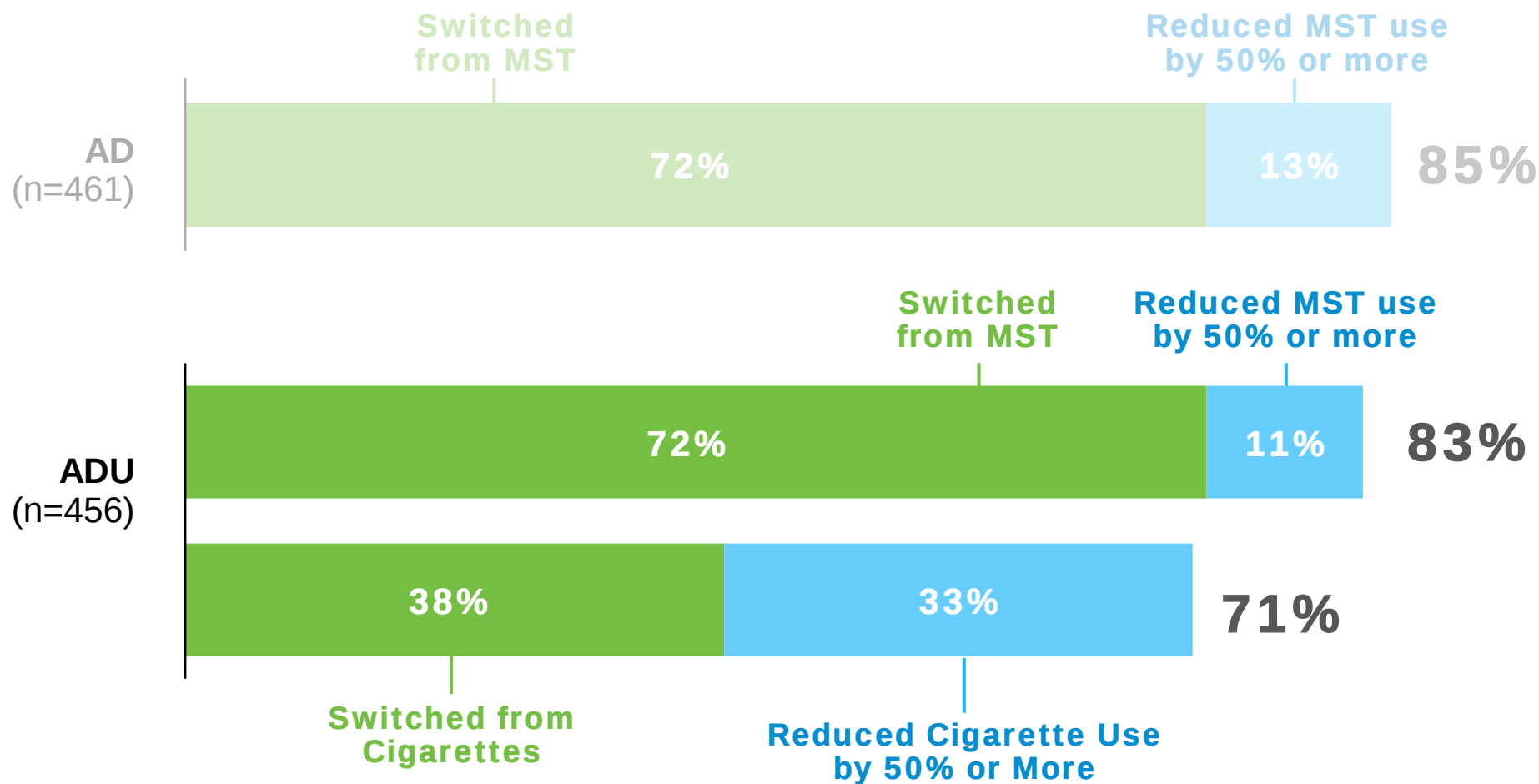
Large Proportions of Adult Tobacco Users Switched or Reduced Their Consumption of Traditional Tobacco Products by 50% or More



AD=adults who use MST products (snuff/dip); ADU=adults who use MST products and combustible cigarettes concurrently (adults who dual use); MST=moist smokeless tobacco.
ALCS Final Report Number: ALCS-REG 2022-03-00645, "Tobacco Product Portfolio/Actual Use Study of on! PLUS™ Nicotine Pouches"
Switching was defined as using the on! PLUS™ and not using MST and cigarettes any day during the last week of Phase 2 (i.e., Week 6) among those who started using on! PLUS™.



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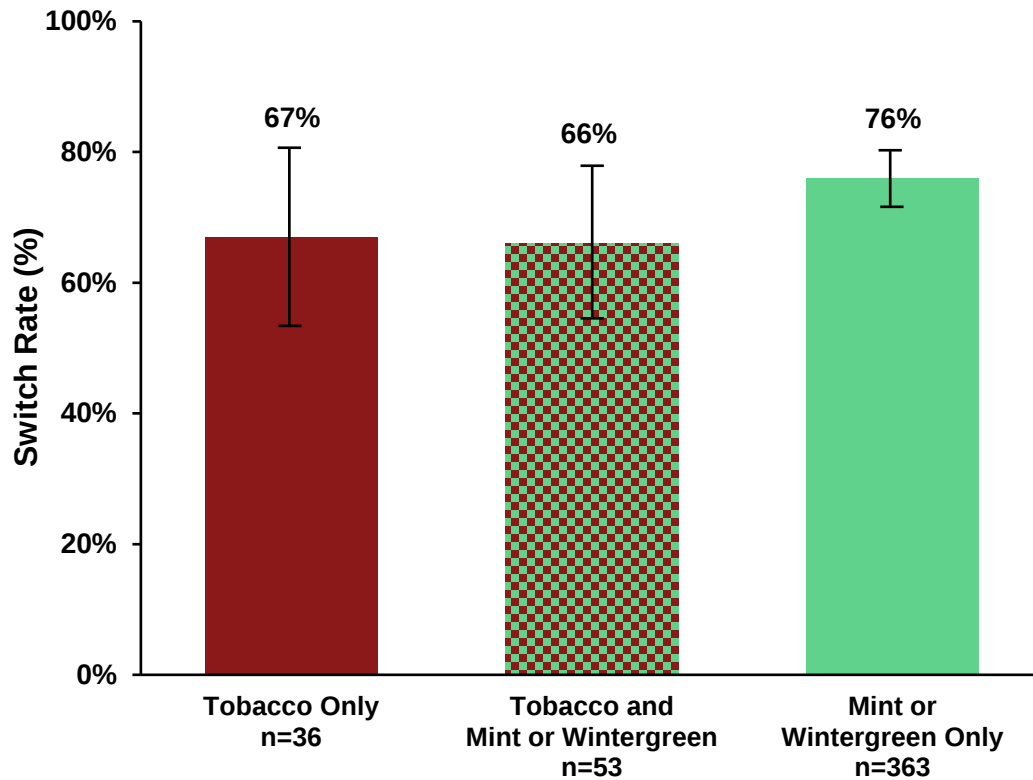


Switching Rates are Similar, But on! PLUS™ Mint and Wintergreen Flavors Have Greater Reach

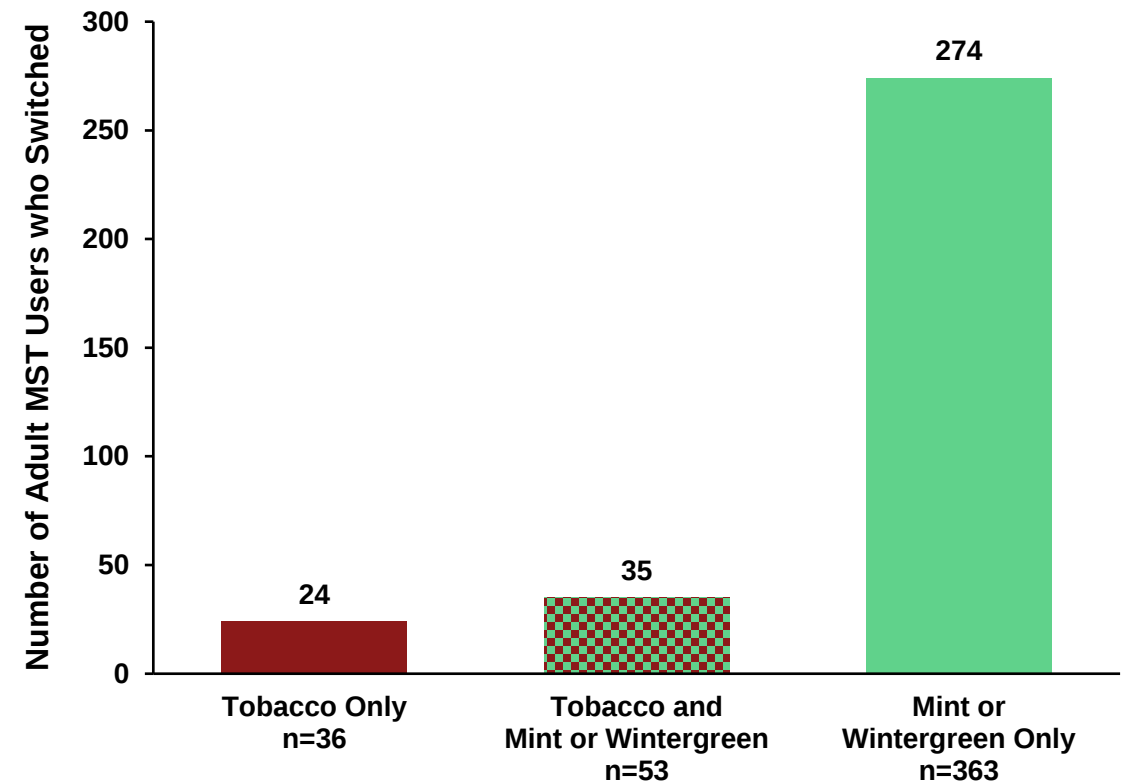


INDIVIDUAL RISK REDUCTION

Switch Rate to on! PLUS™ Among Adult MST Users by on! PLUS™ Flavor Use at Week 6



Number of Adult MST Users Who Switched to on! PLUS™ from MST at Week 6



ATCs=adult tobacco consumers, MST= moist smokeless tobacco, NP=nicotine pouch.
Source: ALCS on! PLUS™ Actual Use Study, 2023 (internal docket 2023-AH-61).



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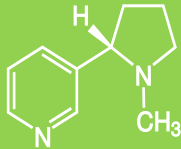
Totality of the Evidence Demonstrates Abuse Liability of on! PLUS™ Is Similar or Lower than MST Products



INDIVIDUAL RISK REDUCTION

NICOTINE EXPOSURE

Pharmacokinetics (PK) and
Pharmacodynamics (PD)



SUBJECTIVE EFFECTS

Product Liking, Satisfaction,
Craving, and Withdrawal



USE PATTERNS

Topography, Actual Use,
Use Not as Intended



The abuse liability of on! PLUS™ is similar or lower than MST products

- Nicotine uptake is likely similar to, or lower than, MST products
- Adult dippers prefer their own brand of MST product to on! PLUS™
- Most dippers/dual users switch to on! PLUS™ or reduce consumption of traditional tobacco products by at least 50%



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Scientific Framework

CONSTITUENT REDUCTION



THE PRODUCT

- Chemistry Manufacturing and Controls
- Product Stability
- Chemical characterization

INDIVIDUAL RISK REDUCTION



EXPOSURE and HEALTH RISK

- Toxicology & Risk Assessment
- Health risk assessment (absolute and relative)
- Human Studies
- Human Factors Assessment

POPULATION HARM REDUCTION

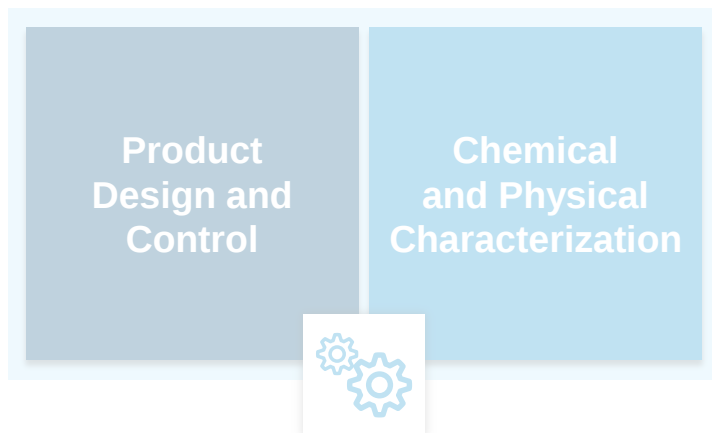


IMPACT on the POPULATION

- Risk perceptions (absolute and relative)
- Impact of product on users
- Impact on non-users
- Overall impact on the population
- Environmental Assessment

Scientific Framework

CONSTITUENT REDUCTION



THE PRODUCT

- Chemistry Manufacturing and Controls
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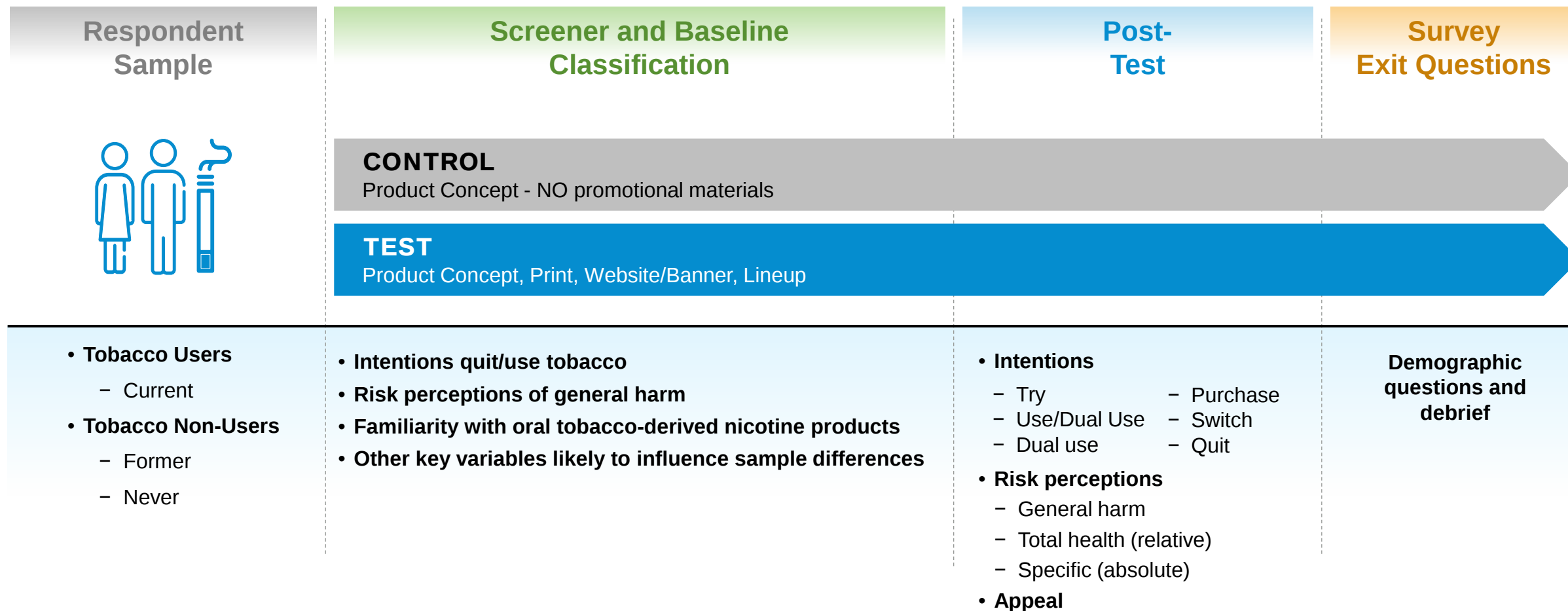


IMPACT on the POPULATION

- Risk perceptions (absolute and relative)
- Impact of product on users
- Impact on non-users
- Overall impact on the population
- Environmental Assessment



Perceptions and Behavioral Intentions Study



Johns, S.E. "No Meaningful Effect of Promotional Materials for a Novel Nicotine Pouch Product on Behavioral Intentions and Risk Perceptions" Poster presented at the 77th Tobacco Science Research Conference, September 8-11, 2024.



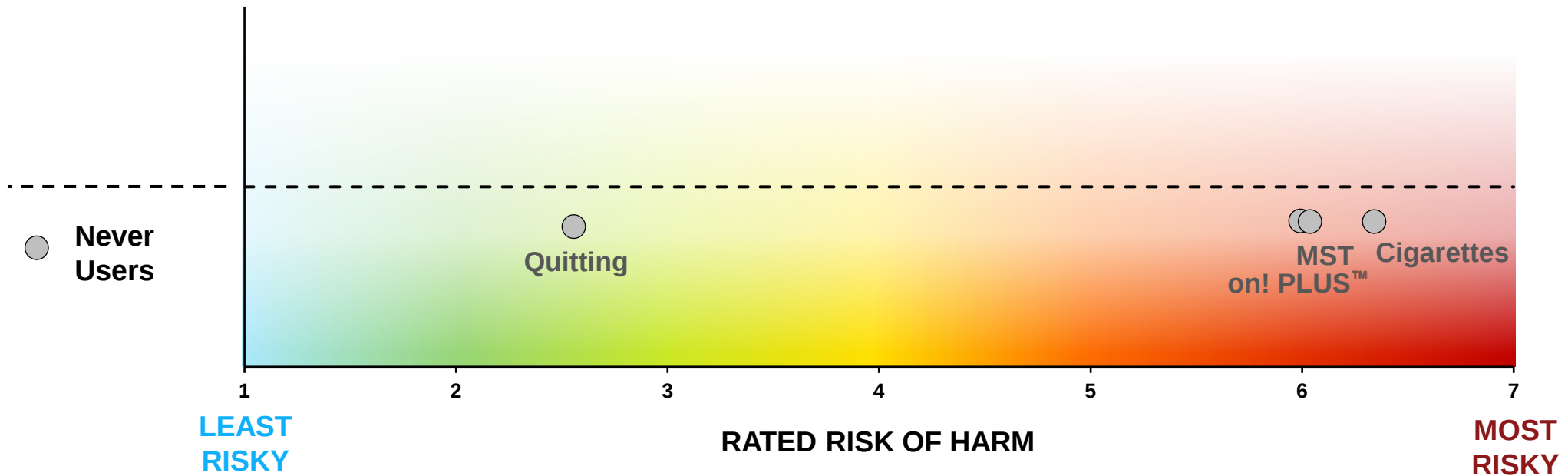
Adult Users and Nonusers Understand that on! PLUS™ Nicotine Pouches Are Not Risk-Free



POPULATION HARM REDUCTION

Please rate each item for the risk you feel
it could pose to a person's health

7-pt scale: 1 Not at all risky, 7 Extremely risky



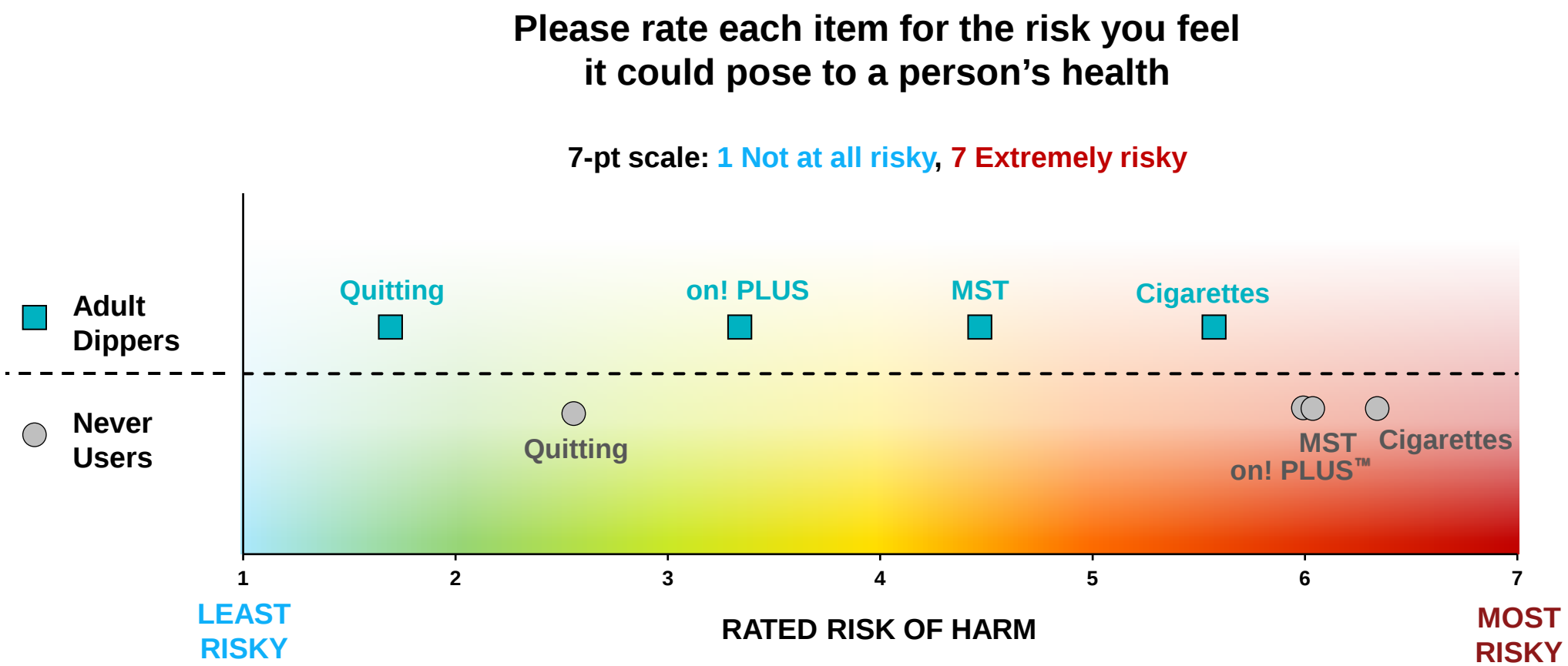
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Adult Users and Nonusers Understand that on! PLUS™ Nicotine Pouches Are Not Risk-Free



POPULATION HARM REDUCTION



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Adult Users and Nonusers Associate Daily Use of on! PLUS™ Nicotine Pouches with Adverse Health Outcomes

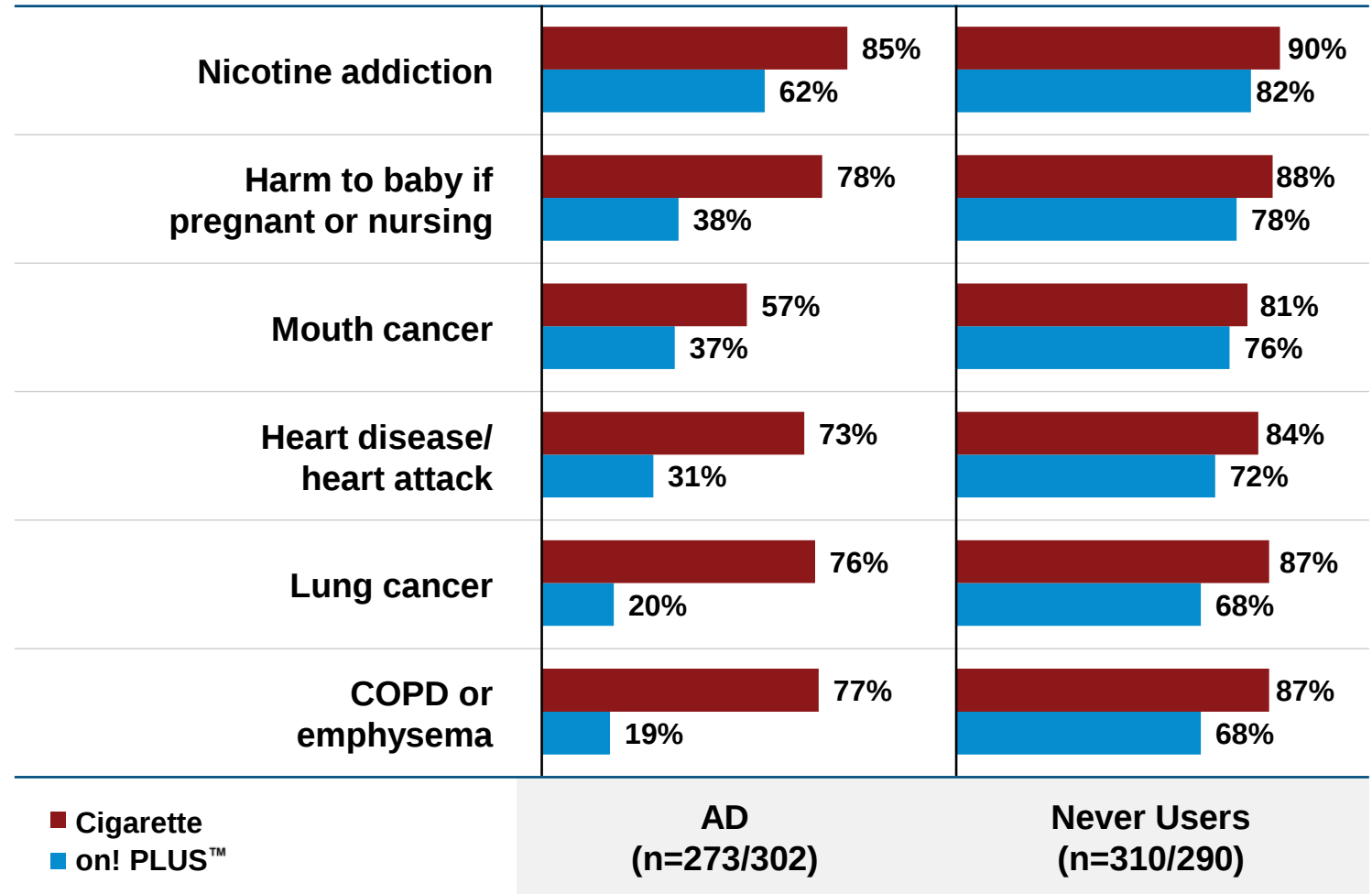
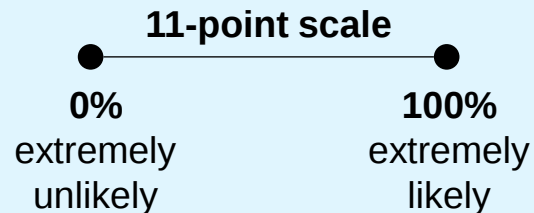


POPULATION HARM REDUCTION

Average score in response to the question:



How likely is it that these things will happen to a person who only (smokes cigarettes, uses on! PLUS™) daily?

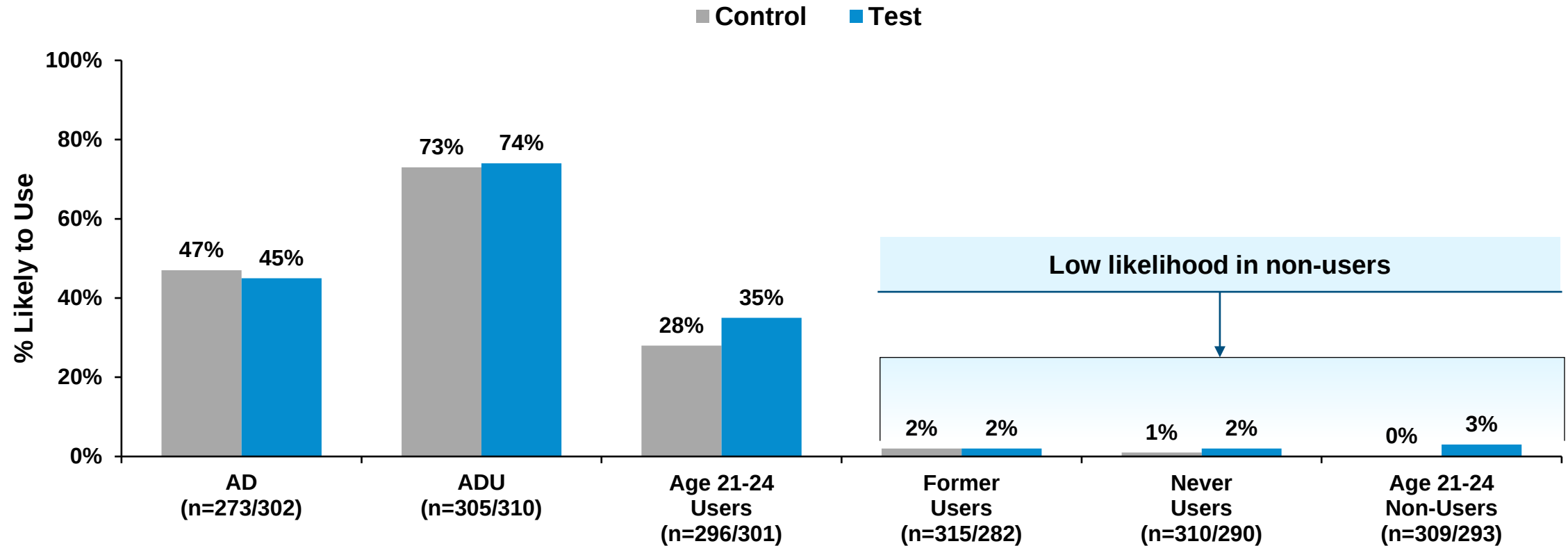


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Low Likelihood of Use of on! PLUS™ among Nonusers of Tobacco Products



POPULATION HARM REDUCTION



Adult Nonusers of Tobacco (inclusive of main sample and oversample of 21-24-year-olds), of which subgroups include: Former Users=adults who have formerly used tobacco products; Never Users=adults who have never used tobacco products; Control=participants viewed product concept only; Test=participants viewed product concept and promotional materials. Likelihood to Use is defined as a score ≥ 3.5 on the intentions to use composite measure, in addition to selecting "yes" for intention to purchase on! PLUS™ nicotine pouches.

AD=adults who use MST products (snuff/dip); ADU=adults who use MST products and combustible cigarettes concurrently (adults who dual use).



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Low Likelihood of Appeal and Use of on! PLUS™ Nicotine Pouches among Nonusers of Tobacco Products



POPULATION HARM REDUCTION

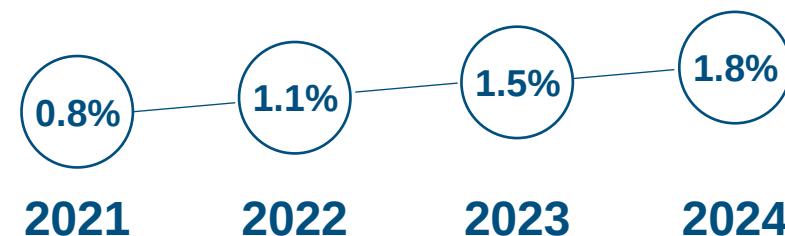
Low likelihood of appeal among nonusers and low intentions to try and use

Adult nonusers understand that on! PLUS™ nicotine pouches are not risk-free

Absolute risk perceptions are
not lowered from exposure
to marketing and advertising

Low likelihood of initiation by youth

Current (past 30-day) Nicotine Pouch Use Among
Middle and High School Student Combined¹



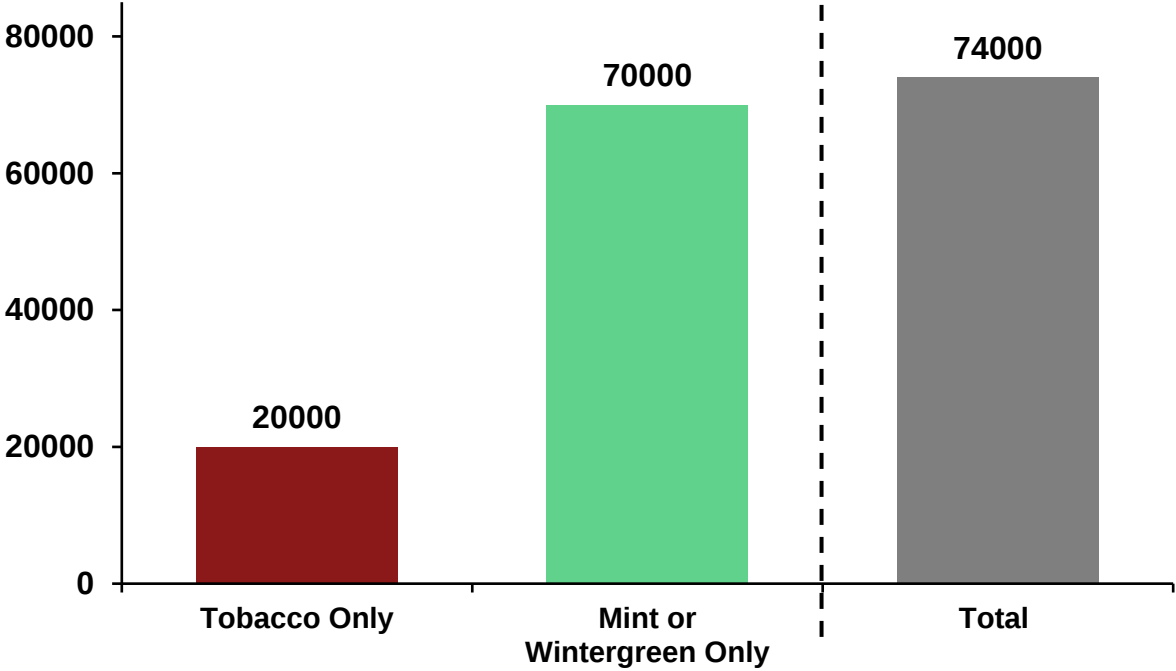
¹Data from National Youth Tobacco Survey 2021-2024– Nicotine pouch use > 1 day in the past 30 days.





Flavor Accounts for Large Share of Public Health Benefit

Population Health Impact Overall and by Flavor Usage
All-Cause Premature Death Prevented by 2100



Switching adjusted based on flavor used in week 6
of actual use study

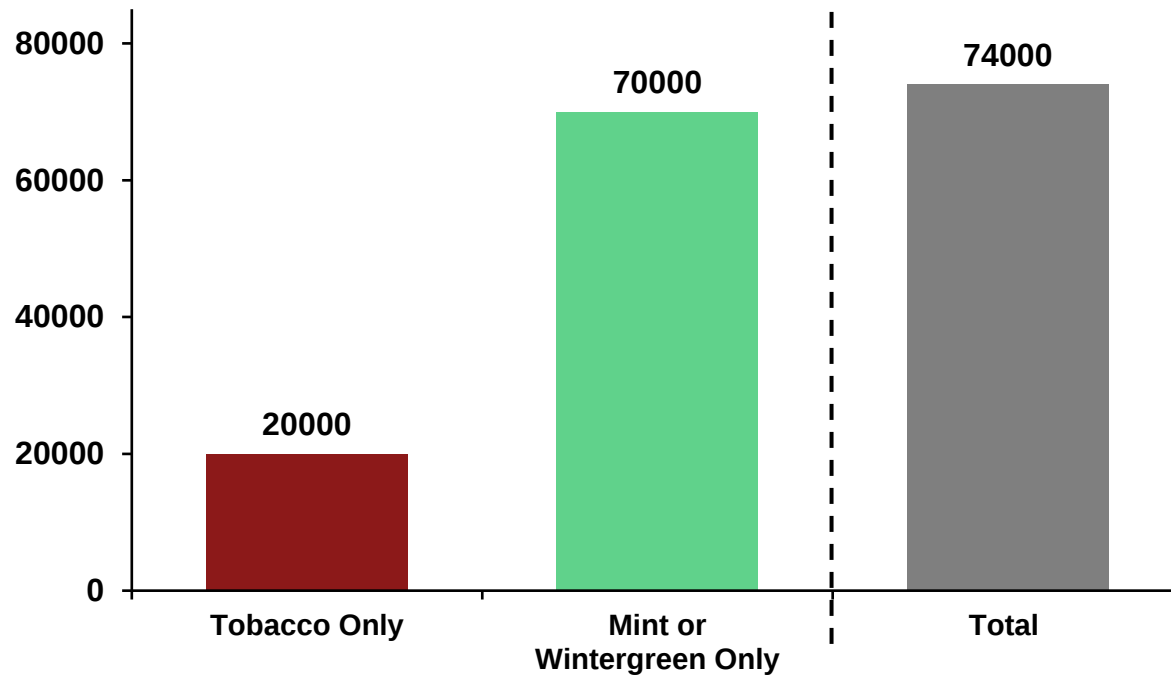
Source: Hannel, T.; Wei, L.; He, Y.; Muhammad-Kah, R.; Largo, E.; Sarkar, M., "Modeling the Population Health Impact of Flavor Variety and Potential Risk of Youth Initiation Resulting from the Marketing of an Oral Nicotine Pouch Product". Poster presented at the 77th Tobacco Science Research Conference, September 8-11, 2024.



Flavor Accounts for Large Share of Public Health Benefit

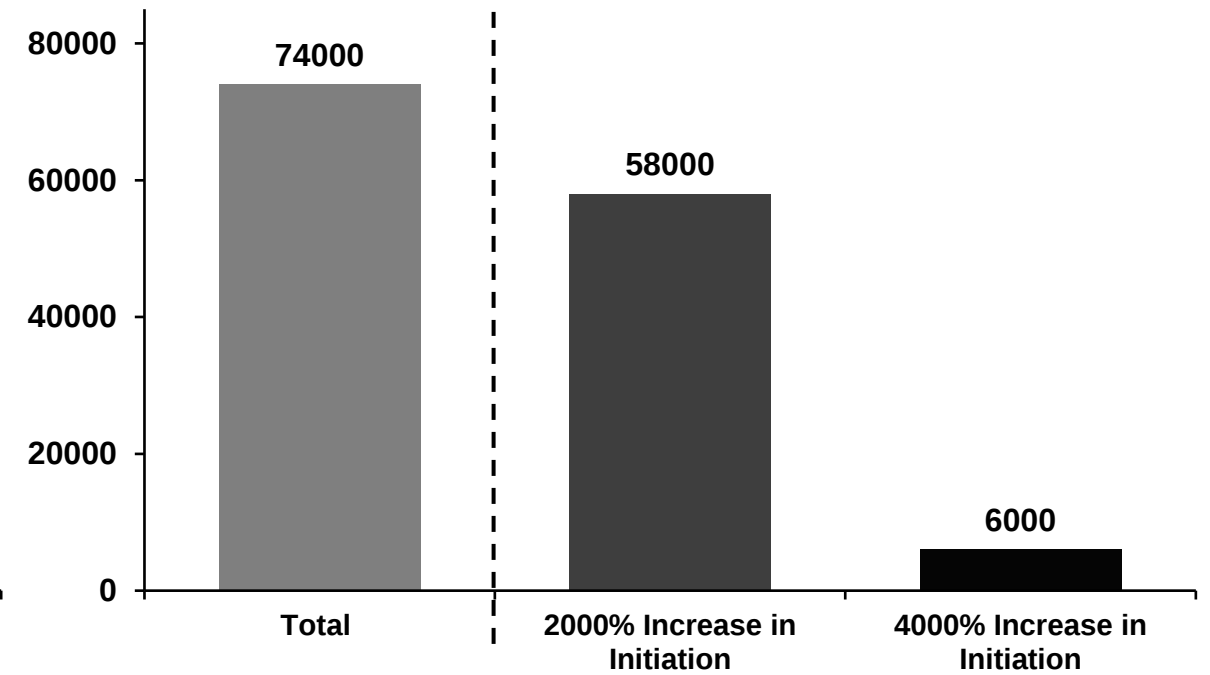
Tipping Point Analysis Shows the Underage Initiation Would Need to Increase Substantially to Shift Balance

Population Health Impact Overall and by Flavor Usage
All-Cause Premature Death Prevented by 2100



Switching adjusted based on flavor used in week 6 of actual use study

Population Health Impact Overall and by Varying Underage Initiation Rates
All-Cause Premature Death Prevented by 2100



Candidate product initiation rate increased among underage (12-20) population

Source: Hannel, T.; Wei, L.; He, Y.; Muhammad-Kah, R.; Largo, E.; Sarkar, M., "Modeling the Population Health Impact of Flavor Variety and Potential Risk of Youth Initiation Resulting from the Marketing of an Oral Nicotine Pouch Product". Poster presented at the 77th Tobacco Science Research Conference, September 8-11, 2024.



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Integration of Multiple Lines of Evidence to Demonstrate APPH*

- ✓ HPHCs eliminated or substantially reduced
- ✓ Abuse liability not likely to be higher than MST products
- ✓ Near real-world evidence demonstrated substantial switching to on! PLUS™
- ✓ Many AD & ADU who did not switch reduced MST and/or cigarettes $\geq 50\%$
- ✓ Appealed to AD & ADU and did not appeal to those who do not use tobacco
- ✓ Likelihood that youth and underage young adults will initiate is low
- ✓ A portfolio of flavors beyond tobacco provides additional reach



Net Population Benefit

APPH

*Appropriate for the Protection of Public Health

HPHC=harmful and potentially harmful constituents; MST=moist smokeless tobacco products; AD=adults who dip (use MST products); ADU=adults who dual use MST products and cigarettes; Cig=cigarette;



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THANK YOU!

