

Weight of the Evidence: Demonstrating NJOY ACE[®] Products are APPH

Kate Vergara, Ph.D., MPH
Science Lead for NJOY PMTAs
Scientific Strategy and Advocacy



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— FAMILY OF COMPANIES —



A Portfolio Approach to Harm Reduction

Advance Altria's harm reduction vision through smoke-free product platforms



**Smokeless
Tobacco Products**
e.g., Copenhagen®

**Modern Oral
Tobacco Products**
e.g., on!® Nicotine Pouches

**Heated
Tobacco Products**
e.g., PLOOM®*

**E-Vapor
Products**
e.g., NJOY®



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*PLOOM® is currently unavailable for sale in the United States. Horizon Innovations LLC is a joint venture between Philip Morris USA Inc. and JTI (US) Holding Inc. for the commercialization of Ploom® in the U.S. market.

NJOY ACE Portfolio

Marketing Granted Order



April 26, 2022



June 21, 2024

Pending PMTA Review



NJOY ACE 2.0 Products include device access restrictions



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The First and Only Authorized Non-Tobacco Flavored ENDS

FDA Authorizes Marketing of Four Menthol-Flavored E-Cigarette Products After Extensive Scientific Review

“ This action is further reinforcement that authorization of an e-cigarette product **is possible** when sufficient scientific evidence has been submitted to the agency to justify it. ”

Brian King, Ph.D., M.P.H.
Director of the FDA's Center for Tobacco Products
June 21, 2024

“ Based upon our **rigorous scientific review**, in this instance, the strength of evidence of benefits to adult smokers from completely switching to a less harmful product was sufficient to outweigh the risks to youth. ”

Matthew Farrelly, Ph.D.
Director of the Office of Science
in the FDA's Center for Tobacco Products

Source: [FDA Authorizes Marketing of Four Menthol-Flavored E-Cigarette Products After Extensive Scientific Review](#) | FDA



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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)
- Biomarker Studies
- Abuse Liability Studies
- Human Factors Assessment

POPULATION HARM REDUCTION

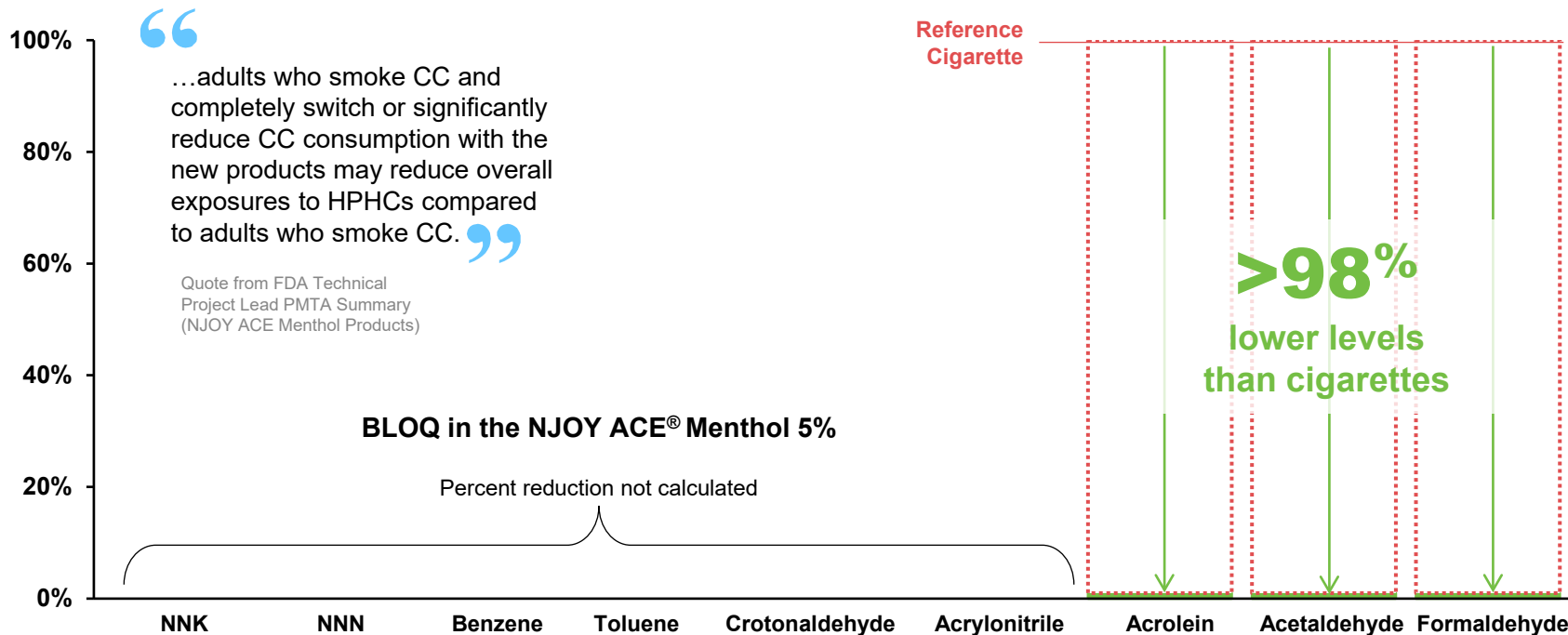


IMPACT on the POPULATION

- Risk Perceptions (absolute and relative)
- Impact of Product on Users
- Impact on Non-Users
- Overall Impact on the Population
- Environmental Assessment



HPHCs in NJOY ACE® Menthol 5% are Not Detected or Substantially Reduced Compared to Cigarettes



HPHC=harmful and potentially harmful constituents; NNK=4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN=N-nitrososonicotine.

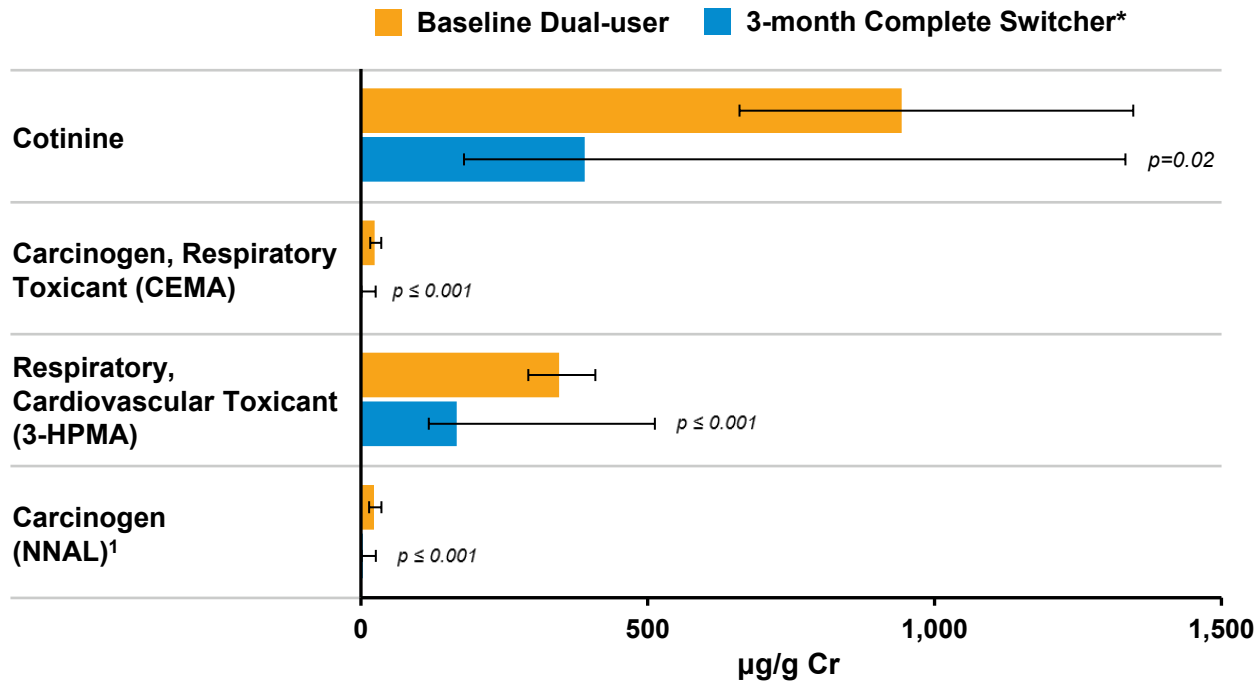
Source: Report Evaluation of HPHCs in NJOY ACE POD Aerosols after 6 to 9 months Storage; Percent reductions based on non-intense use scenarios and ambient storage conditions HPHC levels in Menthol 5% NJOY ACE products at 6 months compared to cigarette mainstream smoke levels measured under ISO conditions.



Biomarkers of Exposure are Significantly Reduced Among Switchers Based on Real World Evidence

“...biomarker data from the NJOY User Study suggests that adults who exclusively use the new products will have lower HPHC exposures compared to adults who dually use CC and the new products.”

Quote from FDA Technical Project Lead PMTA Summary (NJOY ACE Menthol Products)



* Indicates that biomarker levels were significantly lower than dual-users ($p < 0.05$); Data represented as Least Square Means \pm 95% CI from Statistical Model.
3-HPMA=3-Hydroxypropylmercapturic Acid; CEMA=Cyanoethyl mercapturic acid; NNAL=4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol). ¹NNAL is expressed as ng/g Cr.
Source: NJOY ACE Biomarker Substudy Final Report



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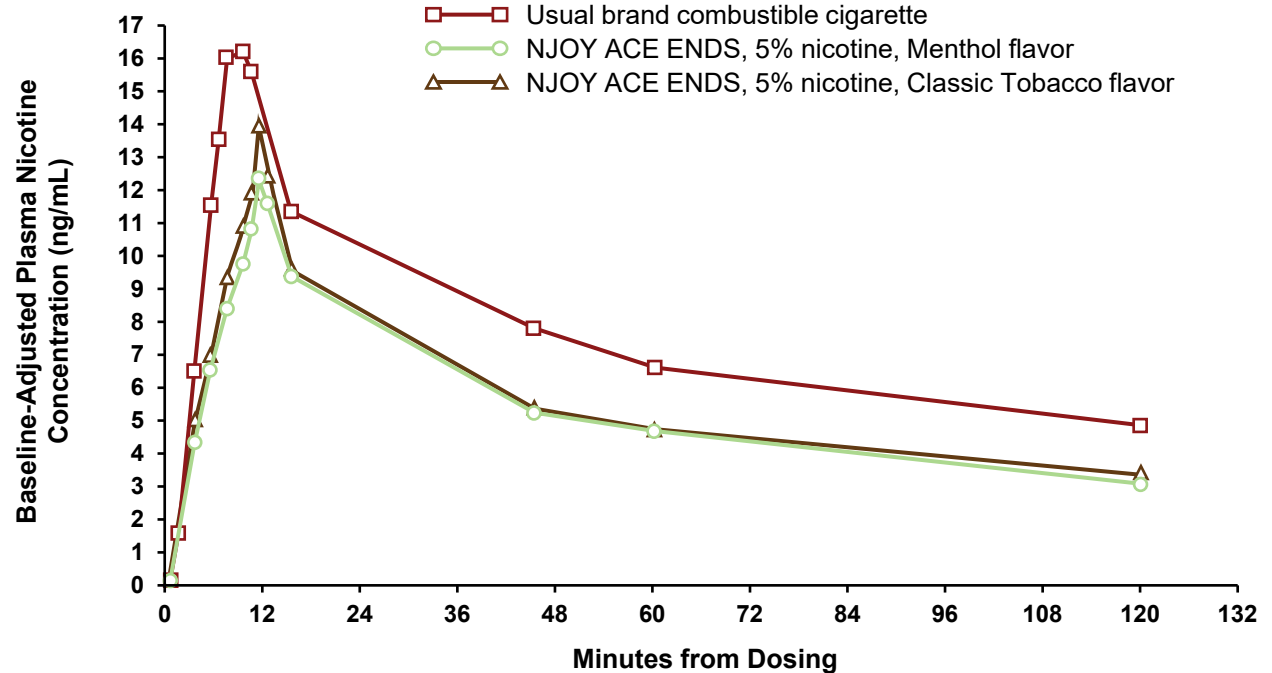
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Nicotine PK Indicates NJOY ACE[®] Abuse Liability Not Likely to be Higher Than Cigarettes

Abuse Liability

“...the new product's abuse liability is similar to CC among adults who are experienced with ENDS use, suggesting that the new product may be a suitable substitute for CC among adults who smoke CC and who want to quit.”

Quote from FDA Technical Project Lead PMTA Summary (NJOY ACE Menthol Products)



CC=combustible cigarette; ENDS=electronic nicotine delivery system.



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Longitudinal Cohort Study Demonstrates Significant Switching Potential for NJOY ACE



NJOY User Study

“

The NJOY User Study demonstrated that **switching from combusted cigarettes to the new ENDS products does occur among current adult smokers.**

The applicant has therefore demonstrated the potential for these products to benefit adult smokers as compared to continued exclusive cigarette use.

”

Quotes from FDA Technical
Project Lead PMTA Summary
(Emphasis added)

ENDS=electronic nicotine delivery system.



Longitudinal Cohort Study Overview



POPULATION HARM REDUCTION

PROSPECTIVE LONGITUDINAL ONLINE OBSERVATIONAL SURVEY

Evaluating the Effectiveness of NJOY ACE® ENDS on Reduction and Switching From CC Use



PURPOSE

Assesses relationship between the frequency of combustible cigarette smoking, switching from combustible cigarettes to ENDS, and the purchasing and use of NJOY ENDS products*

STUDY DESIGN

National purposive sample of 8,002 US adult subjects aged 21+ years who first used NJOY ACE® within the 12-month period prior to completing the baseline survey

COHORTS

Primary Outcomes Cohort

Baseline and 3-month timepoints

Secondary Outcomes Cohort

Baseline, 3-month and 6-month time-points

*When the study began in 2019, the following NJOY ACE products were available: NJOY ACE Classic Tobacco 2.4% and 5%, Rich Tobacco 5%, Menthol 2.4% and 5%, Blueberry 2.4% and 5%, Watermelon 2.4% and 5%. The NJOY ACE Blueberry and Watermelon products were removed from the market pursuant to the FDA Enforcement announced in January 2020.
CC=combustible cigarette; ENDS=electronic nicotine delivery system.



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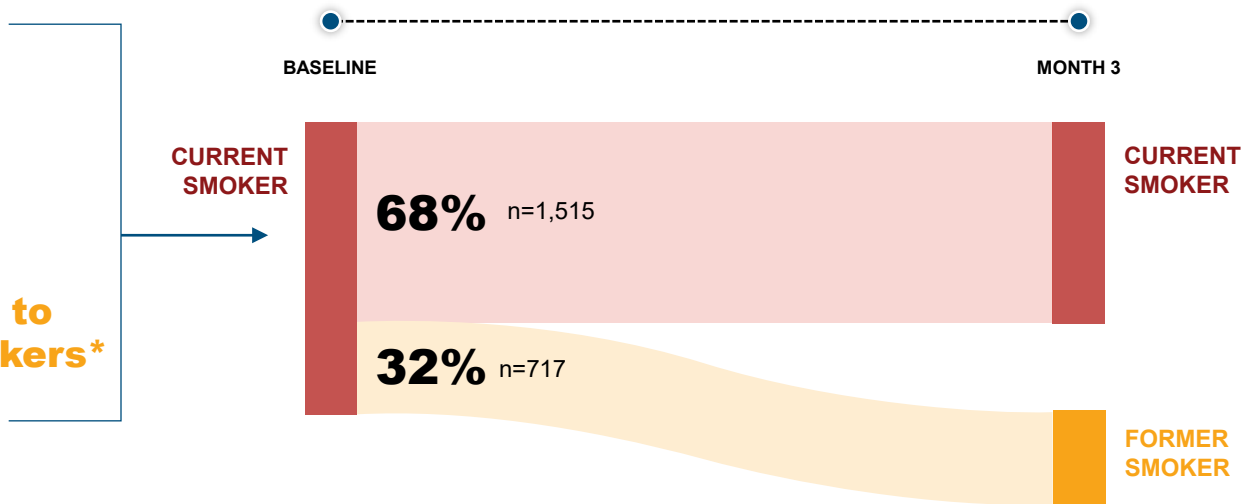
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Real World Evidence Demonstrates Switching Success with NJOY ACE®



POPULATION HARM REDUCTION

32%
of Adult
Smokers
(21+ at Baseline)
transitioned to
Former Smokers*



* Indicates switching rate calculated based on the number of participants initially using NJOY ACE at baseline and completing survey at three months (per protocol population).
Source: Prospective Longitudinal Cohort Study Figure 7-1.



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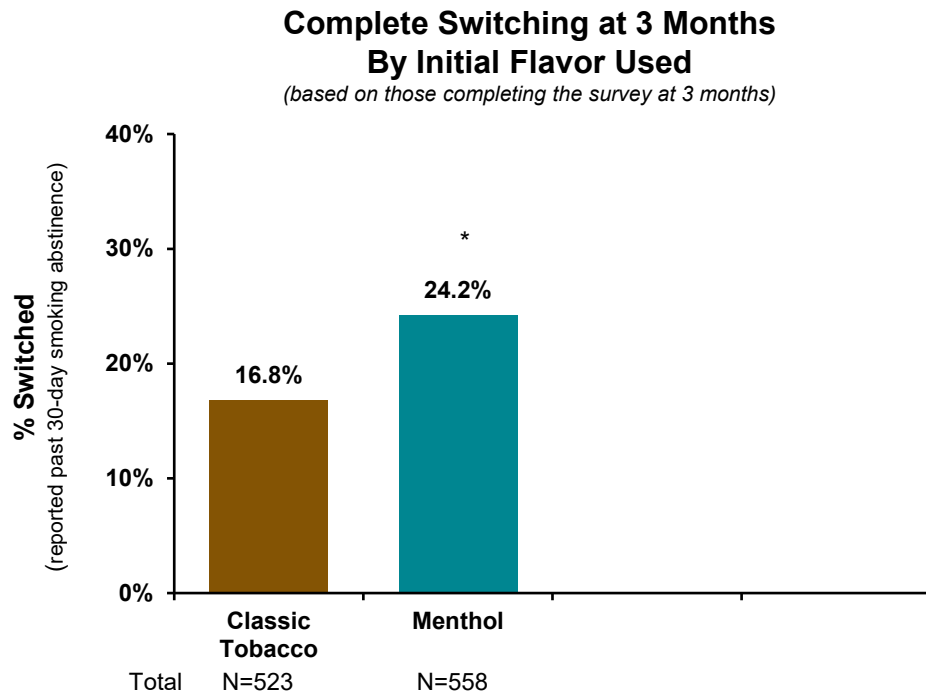
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Flavored NJOY® ACE Products More Effective in Promoting Complete Switching Relative to Tobacco-Flavored



POPULATION HARM REDUCTION



*Statistically significantly greater than Classic Tobacco-flavored NJOY ACE products
Analysis shows per protocol 30-day point prevalence abstinence for initially used NJOY ACE flavor.
Source: NJOY ACE User Survey Supplemental Blueberry and Watermelon Report; Initial Used NJOY Flavor.



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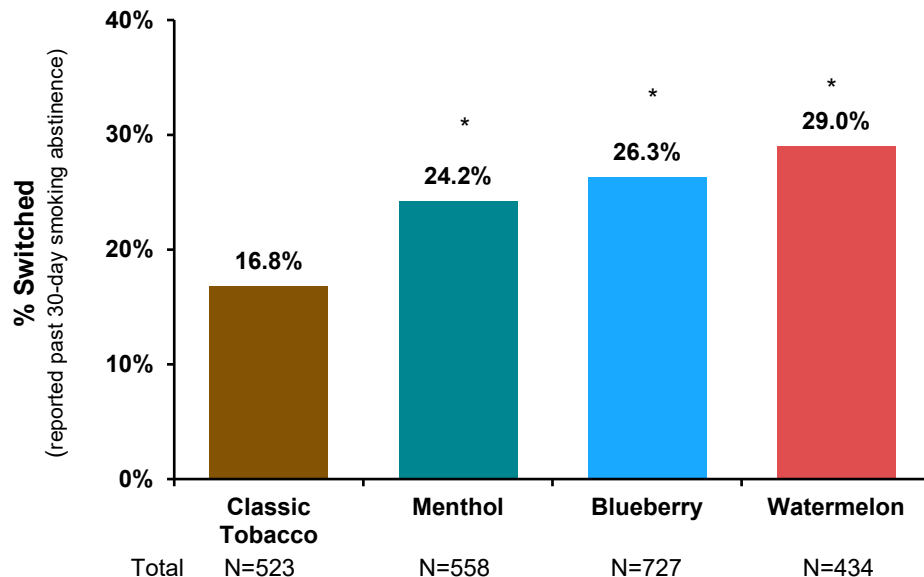
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Flavored NJOY® ACE Products More Effective in Promoting Complete Switching Relative to Tobacco-Flavored

Complete Switching at 3 Months By Initial Flavor Used

(based on those completing the survey at 3 months)



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Source: NJOY ACE User Survey Supplemental Blueberry and Watermelon Report; Initial Used NJOY Flavor.

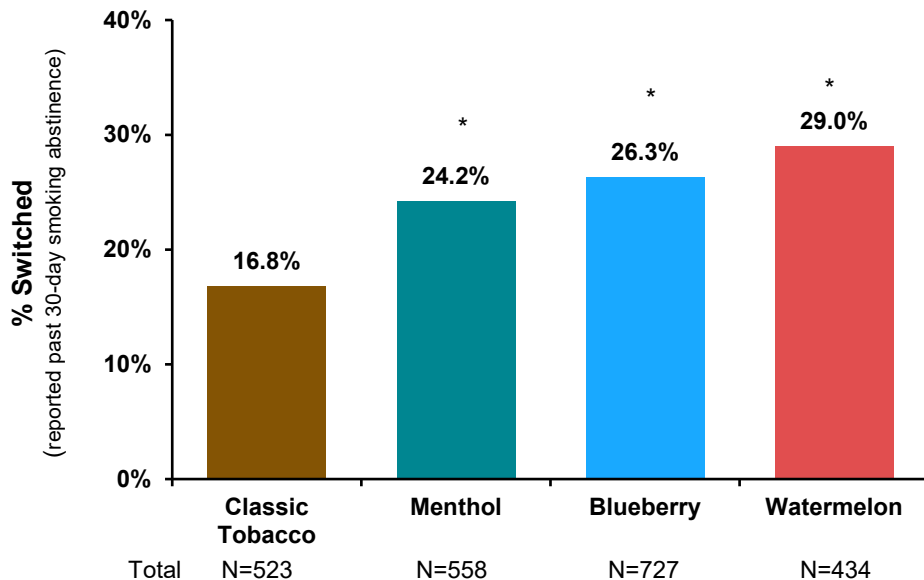




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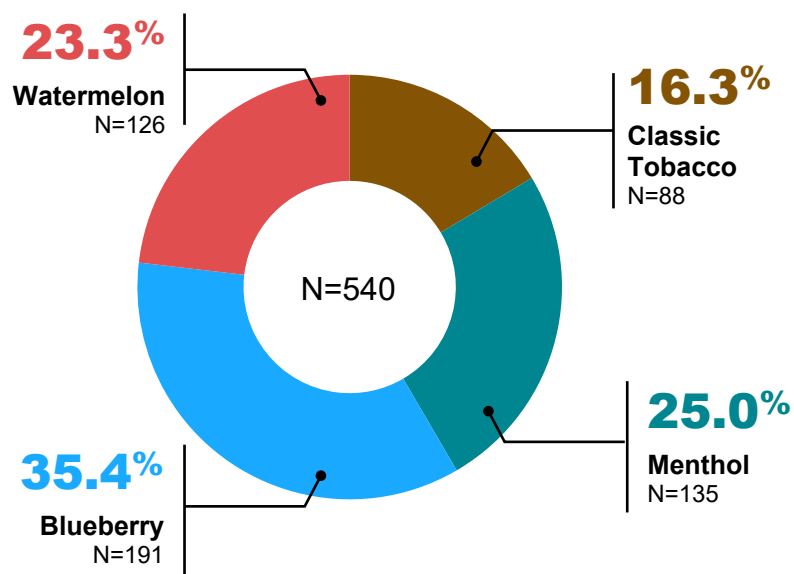
Complete Switching at 3 Months By Initial Flavor Used

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Proportion of Complete Switchers at 3 Months By Initial Flavor Used

(based on those completing the survey at 3 months)



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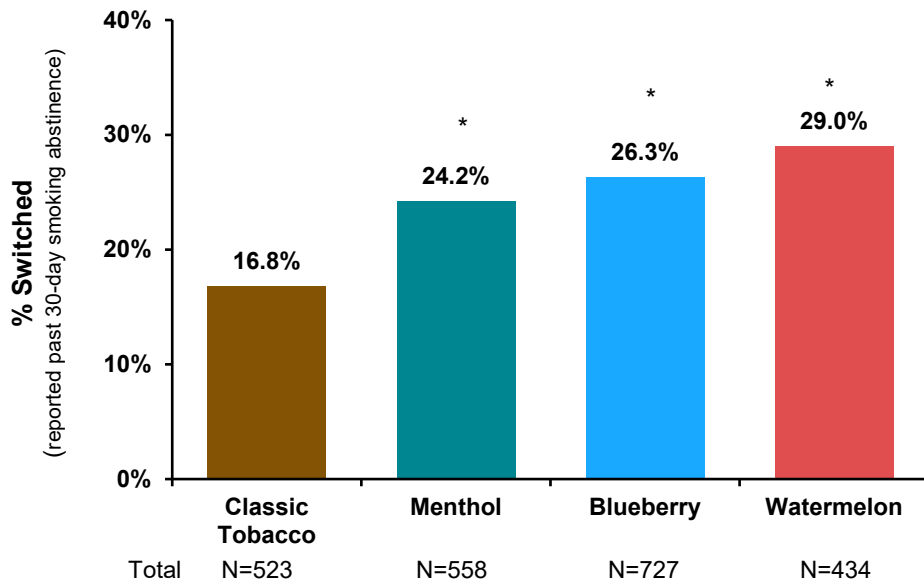




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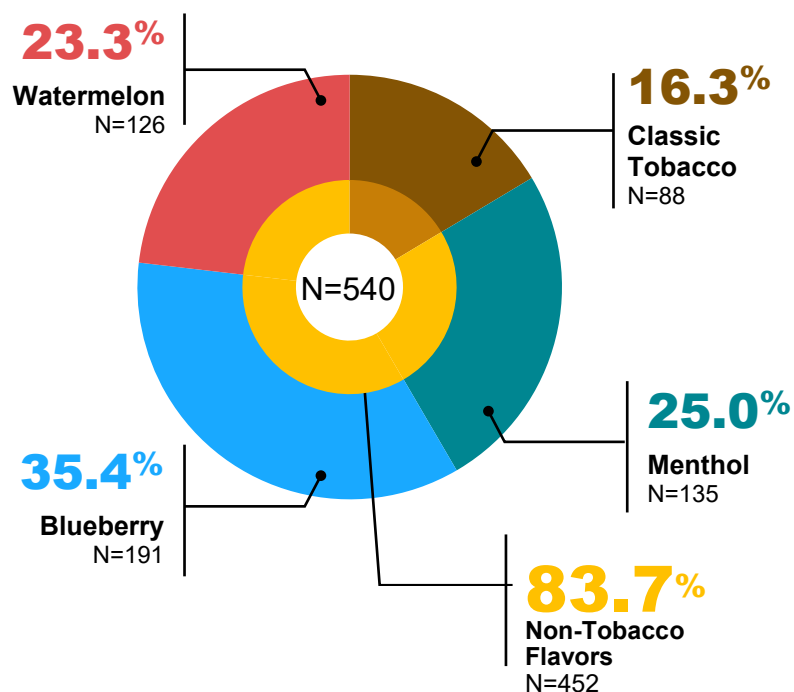
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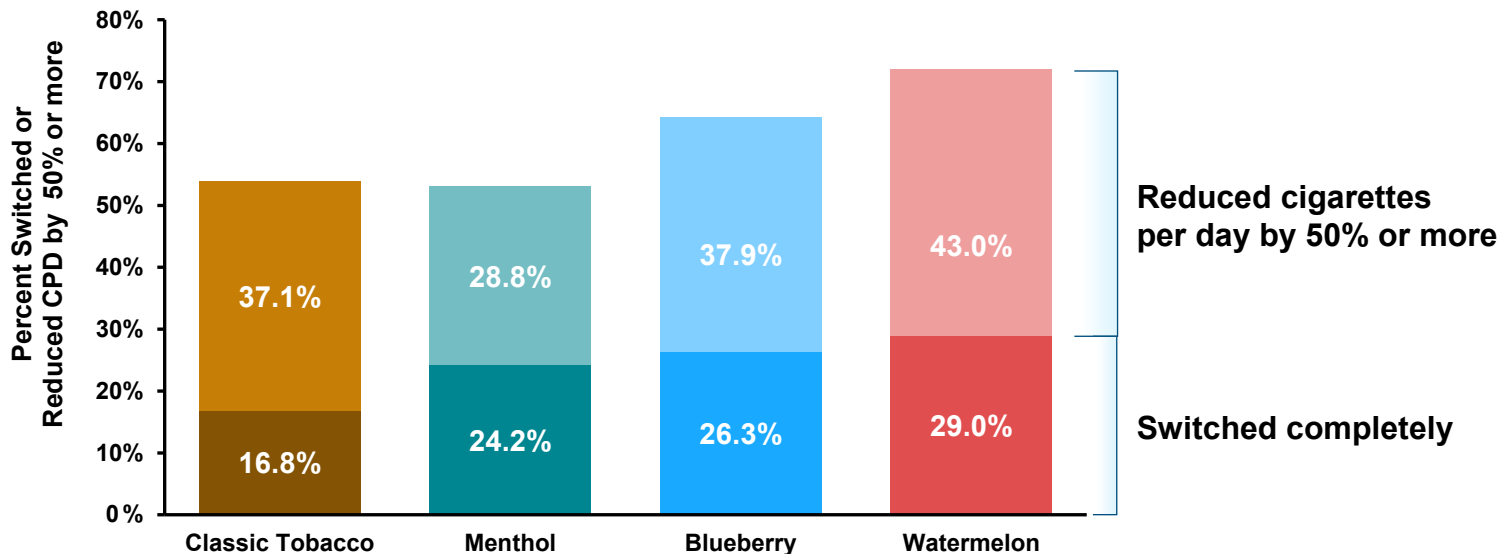


Complete Switching and CPD Reduction at Three Months



POPULATION HARM REDUCTION

Complete Switching and CPD 50% Reduction
by Initially Used Flavor



CPD=cigarettes per day

Source: Aggregated results include PP30dayPPA complete switch for Initial Flavor Used at 3mth timepoint, and CPD \geq 50% reduction for Initial Flavor Used at the 3mth timepoint; NJOY ACE User Survey 6mth Report.



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NJOY ACE® ENDS Youth Prevalence is Rare



POPULATION HARM REDUCTION

NJOY Brand Detection Trends in NYTS

NYTS	NJOY Usual Brand Used Among Middle and High School E-Cigarette Users	Past 30-Day ENDS Use % (95% CI)
2021	NA ^a	7.6 (6.6-8.7)
2022	NA ^a	9.4 (8.0-11.1)
2023	NA ^a	7.7 (6.8–8.6)
2024	NA ^a	5.9 (5.3-6.6)

^aData not reported because responses were too low to determine statistically reliable estimates

NYTS=National Youth Tobacco Survey; CI=confidence interval; ENDS=electronic nicotine delivery system; NA=not applicable.

Sources: MMWR Park-Lee et al., 2021; Cooper et al., 2022; Birdsey et al., 2023; Park-Lee et al., 2024



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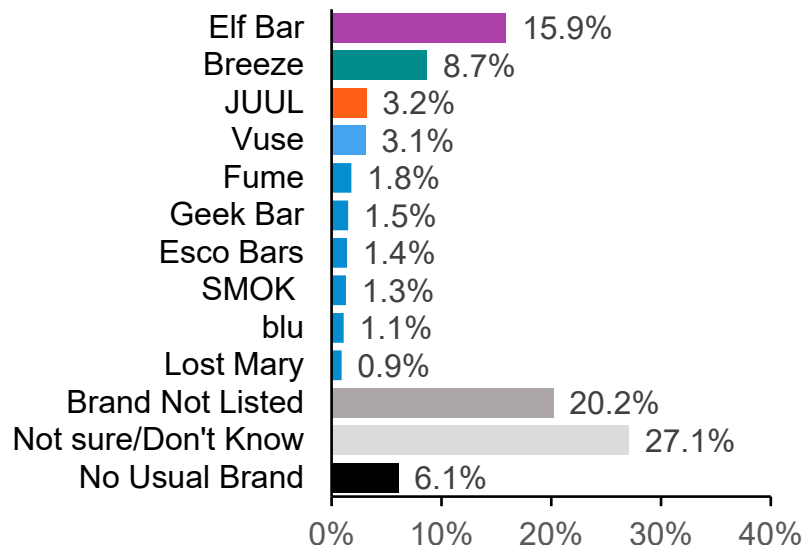
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2024 Usual Brand Used Among Middle and High School Current E-Cigarette Users



NYTS=National Youth Tobacco Survey; CI=confidence interval; ENDS=electronic nicotine delivery system; NA=not applicable.

Sources: MMWR Park-Lee et al., 2021; Cooper et al., 2022; Birdsey et al., 2023; Park-Lee et al., 2024

National Youth Tobacco Survey, 2024. MMWR Morb Mortal Wkly Rep 2024;73:774–778.

DOI: <http://dx.doi.org/10.15585/mmwr.mm7335a3>



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Integration of Multiple Lines of Evidence to Demonstrate APPH*

- ✓ HPHC reduced / eliminated
- ✓ Complete Switching will reduce exposure to most HPHCs which should reduce smoking related disease risks
- ✓ Many AS switch completely or reduce cigs \geq 50%
- ✓ Adults and Youth perceive NJOY ACE products not risk-free
- ✓ Abuse potential lower or comparable to CC
- ✓ Low likelihood of use among nonusers, including youth



Net Population Benefit

APPH

*Appropriate for the Protection of Public Health

NJOY Submitted PMTAs to FDA for NJOY ACE® 2.0 Featuring Bluetooth®-enabled Access Restriction Technology
OUR RESEARCH SHOWS THE

NJOY Bluetooth age-gating restrictions are effective at preventing underage access in virtually all cases



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