GTNF 2024

Advancing Responsible Innovation

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Altria Client Services

Real World Evidence Tool Kit

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Data Sources

- Population level data
- Observational studies
- Electronic health records (EHR)
- Administrative claims data
- Registries
- Wearables
- Sales and marketplace data

Outcome Measures

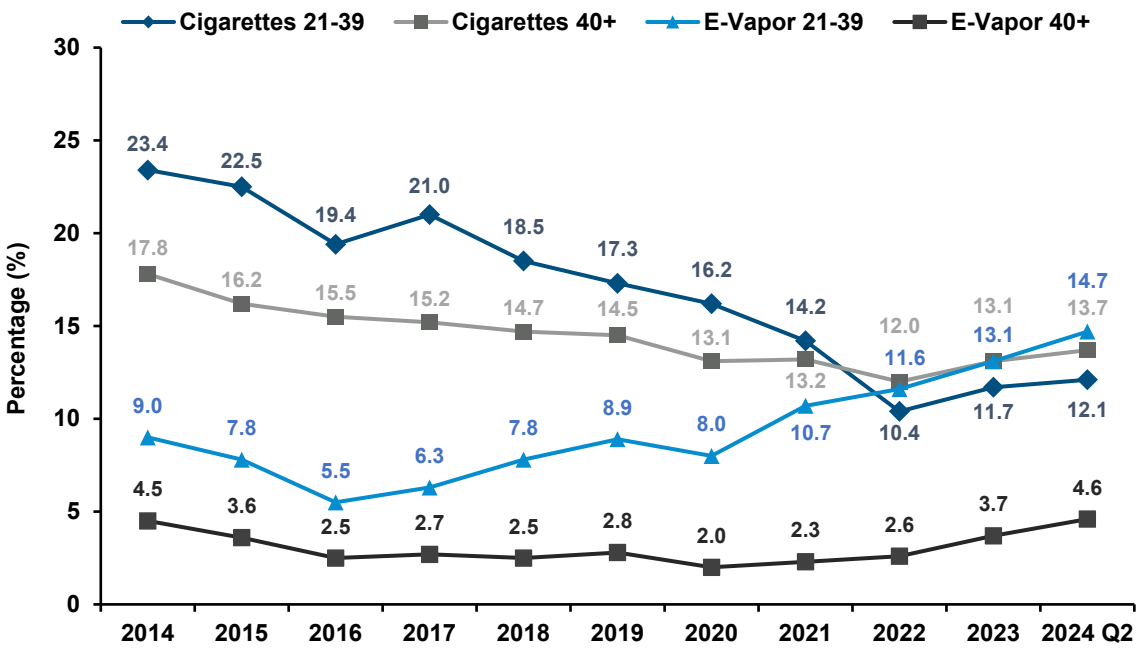
- Trends in prevalence
- Characteristics of user population
- Use behavior/cessation
- Quality of life/wellness
- Biomarkers
- Clinical/disease endpoints
- Healthcare utilization/cost

Sound Science

- Hypothesis-driven
- Study design
- Statistical analysis
- Data interpretations
- Acknowledgment of limitations
- Innovative approaches

Tobacco Landscape is Changing Rapidly

Past 30-Day Tobacco Products Use (21+): Percentages, 2014-Q2 2024



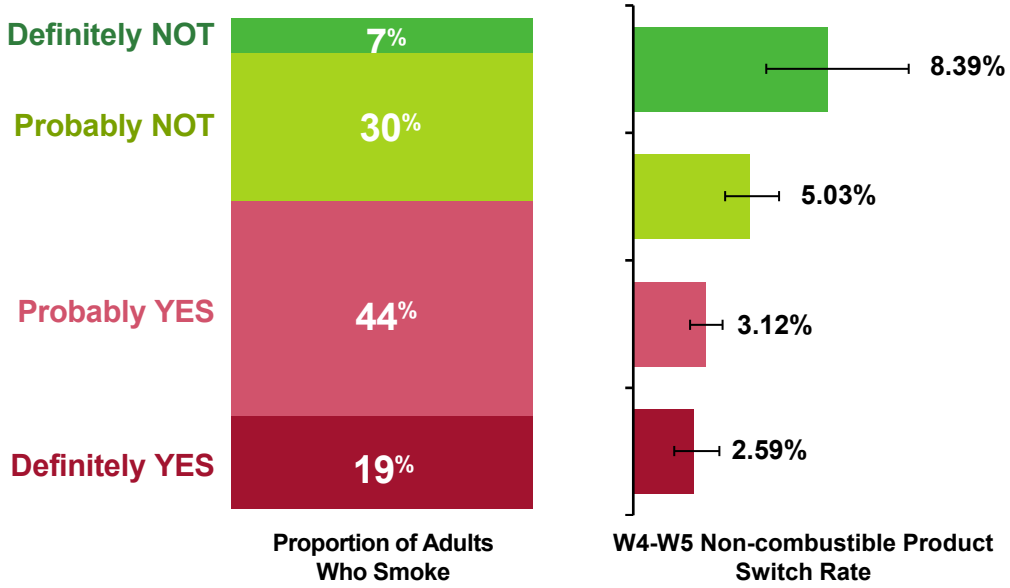
Adults who smoke that are at highest risk of smoking related diseases are continuing to smoke and not adopting E-cigarettes

Source: Altria Adult Tobacco Consumer Tracker (ATCT), a nationally representative, mixed-mode tracking survey

Association of Switching and Nicotine Misperception

ADULT SMOKERS WERE ASKED:

Do you believe NICOTINE is the chemical that causes most of the cancer caused by smoking cigarettes?



Nicotine misperception might be a factor preventing adults who smoke from switching to smoke free alternatives

Source: Hannel T, Wie L, Muhmmad-Kah RS, Largo EG and Sarkar M., Harm Reduction J, 21:145 (2024)

Real World Evidence Demonstrates Switching Success with NJOY ACE®

PRIMARY OUTCOMES COHORT

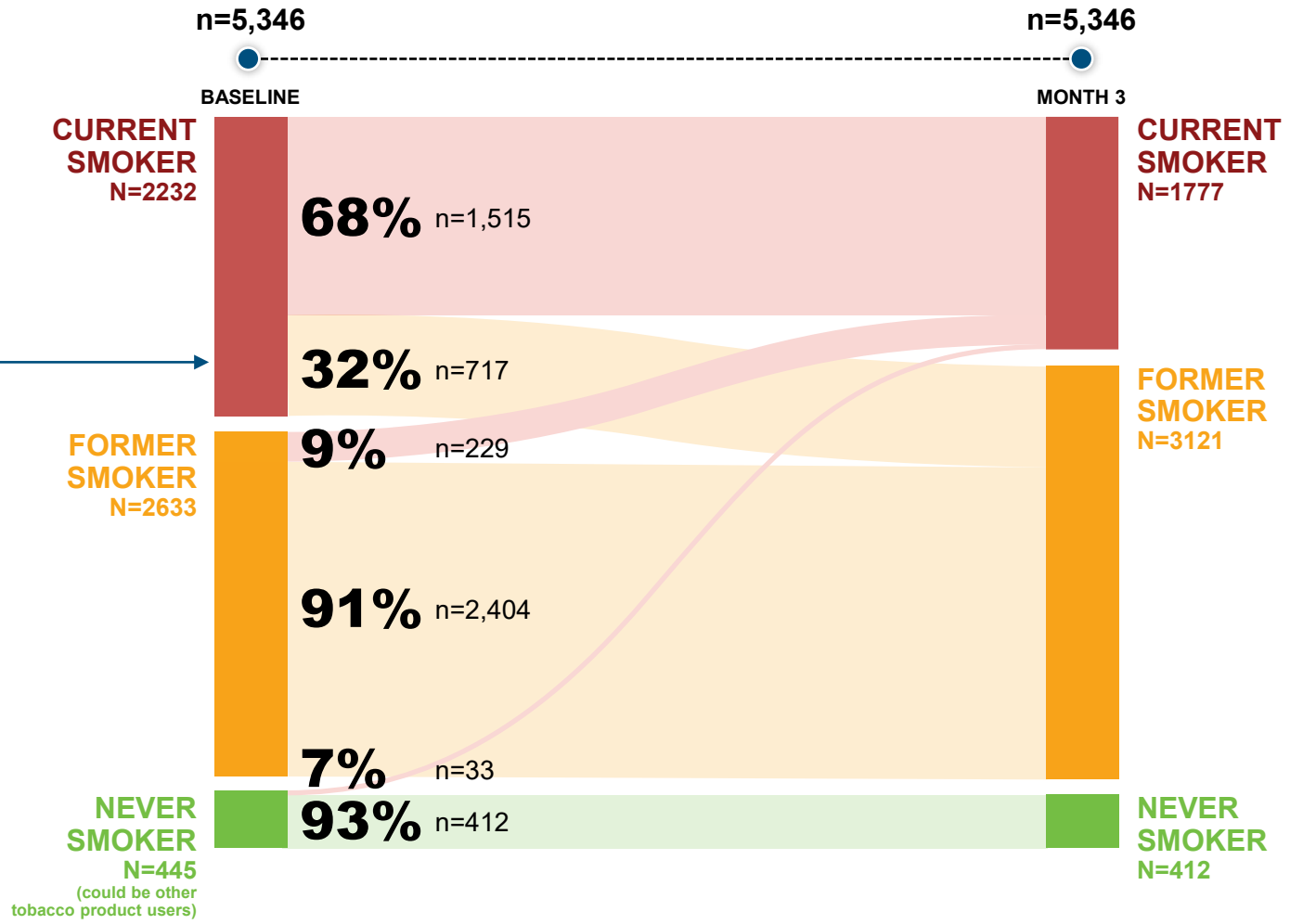
32%

of Adult Smokers

(21+ at Baseline)

transitioned to Former Smokers

by the primary outcomes time point*

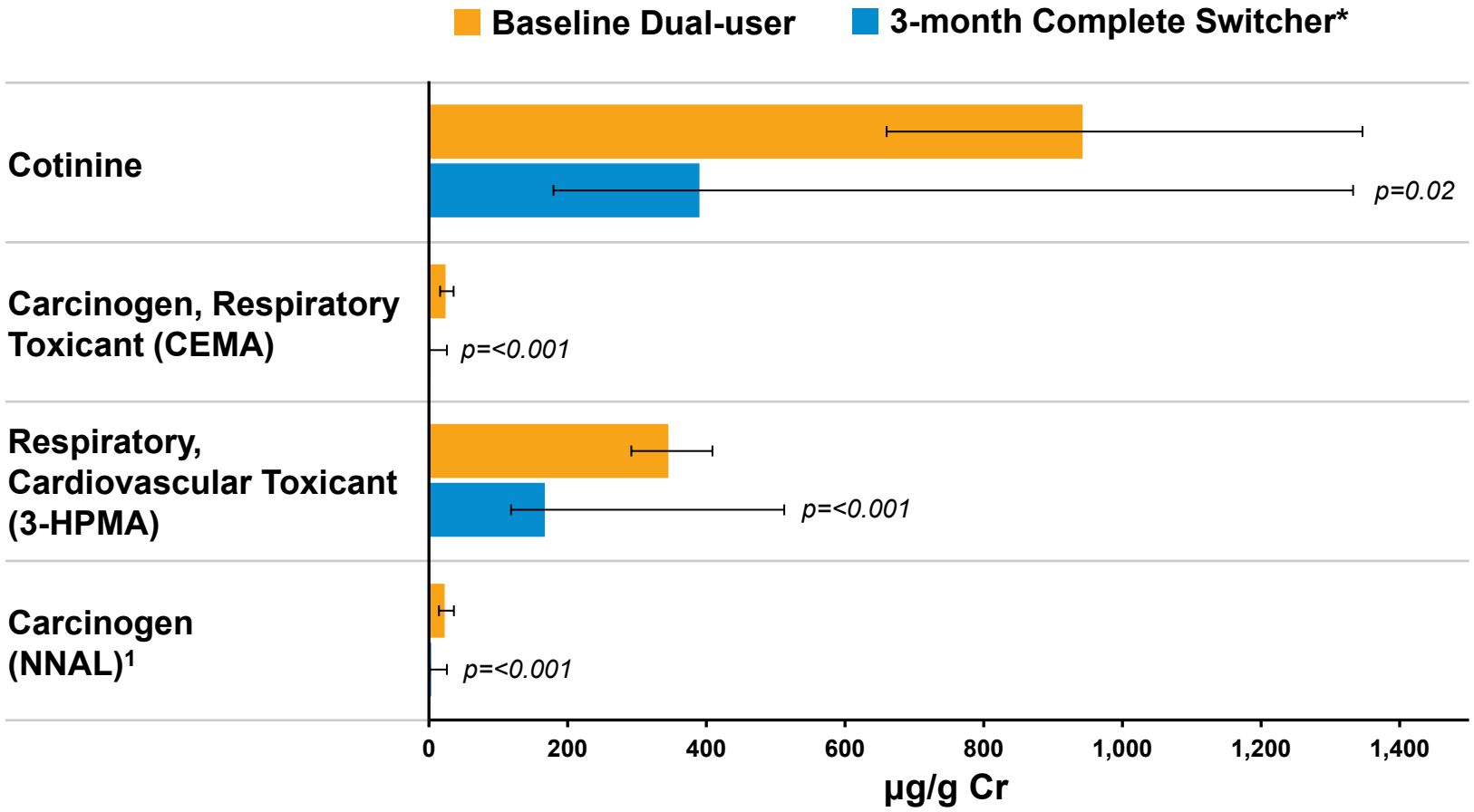


* Indicates that switching rate calculated based on the number of participants initially using NJOY ACE at baseline and completing survey at three months (per protocol population).
Source: Prospective Longitudinal Cohort Study Figure 7-1. N=36 did not answer the smoking frequency question at the Primary Outcomes time point and are not included on this figure.

Real World Evidence Show Significant Reduction in Biomarkers of Exposure Among Switchers

> …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 + 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

Real World Evidence Challenges to Assess Long Term Health Effects of e-Vapor

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NEJM Evidence

Published July 23, 2024
NEJM Evid 2024; 3 (8)
DOI: 10.1056/EVIDe2400220

EXCHANGE

An Exchange about "Population-Based Disease Odds for E-Cigarettes and Dual Use versus Cigarettes"

> **We challenge the validity of the authors' conclusions, which we believe are premature and reflect a serious misinterpretation of the epidemiologic evidence.**

> Because e-cigarettes are a **relatively new product category** mostly used by people 40 years of age or younger, it is hard to see how reliable predictions can be made of health outcomes that are more common in older people.

> **The time needed to see disease outcomes** and reliably predict future health risks in the short term is challenging, and perhaps the best that can be done in the absence of long-term epidemiologic studies is to assess exposure and effect biomarkers.

Response to Glantz et al paper published in NEJM

Rodu et al: Cross-sectional e-cigarette studies are unreliable without timing of exposure and disease diagnosis
Hajat et al - Analysis of common methodological flaws in the highest cited e-cigarette epidemiology research
Shahab - Modelling the impact of vaping: what we need to know and which methods to use
Emphasis added to quotes above

Leveraging Real World Data to Assess Impact of e-Vapor in COPD Patients

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Therapeutic Advances in Chronic Disease — *Original Research*

COPD smokers who switched to e-cigarettes: health outcomes at 5-year follow up

Ricardo Polosa, Jaymin B Morjaria, Umberto Prosperini, Barbara Busà, Alfio Pennisi, Mario Malerba, Marilena Maglia and Pasquale Caponnetto

Ther Adv Chronic Dis
2020, Vol. 11: 1–15
DOI: 10.1177/2040622320961617
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Retrospective – prospective follow up (EHR)

Improvements across many health outcomes

- Respiratory exacerbations
- Spirometric indices
- Quality of life using the COPD assessment tool (CAT)
- 6-min walk distance (6MWD)
- Conventional cigarette consumption

> **Larger studies will be required** to clarify the role of the e-vapour category for smoking cessation and/or harm reversal in smokers with COPD. Although these findings are preliminary, the evidence presented in our study about the long-term health impacts of vaping on COPD can be considered by health professionals when providing specific advice to their COPD patients who cannot or do not want to quit smoking.
>
> – Polosa *et al.*

Real World Evidence

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CHALLENGES

1 | **Lack of standard terminology**

2 | **Exposure duration and use frequency**

3 | **Association** vs. causation

4 | **Innovation and rapidly changing tobacco landscape** continue to outpace survey methodology

5 | **Real world data** in health care systems significantly lagging behind

OPPORTUNITIES

1 | **Continue to validate biomarkers** predictive of disease end-points

2 | **Enhance documentation** of tobacco use in medical records

3 | **Adopt standard codes** (e.g., ICD) for documenting use of modern smoke-free products

4 | **Leverage AI** to maximize the utilization of unstructured data in EHR

5 | **Use hybrid study design** by combining tobacco use history from consumers and health outcomes from medical records

Real World Evidence Final Remarks

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INFORM

Science-based Regulation/Policies

- Apply learnings across differing regulatory frameworks
- Support a MRTP filing

Harm Reduction Strategy

- Postmarket surveillance
- Pharmacovigilance
- Risk mitigation strategies
- Modeling
- Educations

Future Research Questions

- Health equity
- Vulnerable populations
- Risk among adults who never used combustible products