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# Switching Away From Smoking and Reduction in Cigarette Consumption among US Adult Purchasers of the JUUL System across 24 Months Including Diverse Subpopulations Disproportionately Affected by Cigarette Smoking

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## Abstract

**Objectives:** Electronic nicotine delivery systems (ENDS) can reduce tobacco-related risks for adults who smoke cigarettes (AWS) by facilitating complete switching away from combustible cigarettes. However, little is known about ENDS use and switching among subpopulations that have been disproportionately affected by smoking, which could contribute to reducing tobacco-related disparities.

**Methods:** AWS (age $\geq$ 21 years) were recruited following their first purchase of a JUUL Starter Kit in 2018. Participants self-reported switching (no past-30-day cigarette smoking) at 1-, 2-, 3-, 6-, 9-, 12-, 15-, 18-, 21-, and 24-months follow-up assessments. Percent switched and percent with a substantial smoking reduction from baseline ( $\geq$ 50% decrease in cigarettes/day among those who continued smoking) were analyzed. Analyses focused on racial/ethnic minorities, persons with low income and education levels, sexual minorities, and those with mental and physical health conditions.

**Results:** Overall rates of switching away from cigarettes increased across follow-ups to 51.2% at Month 12 and 58.6% at Month 24. Among those who continued to smoke, 45.4% reported a substantial smoking reduction in Month 24. Rates of switching and substantial smoking reduction were similar between subgroups disproportionately affected by cigarette smoking and their referent counterparts, except for lower switch rates in individuals with physical health conditions.

**Conclusions:** AWS demonstrated progressively increasing switching rates over two years after purchasing JUUL products. A similar trend was also observed across populations disproportionately affected by smoking. ENDS products such as JUUL may provide an opportunity to benefit population health and reduce tobacco-related disparities among AWS.

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## Introduction

Cigarette smoking remains a leading cause of preventable morbidity and mortality in the United States and worldwide.<sup>[1][2]</sup> While cigarette smoking prevalence has declined considerably in the US,<sup>[1]</sup> disparities continue to exist in the prevalence of cigarette smoking and rates of smoking cessation: adults who smoke (AWS) who belong to certain racial/ethnic minority groups, are socioeconomically disadvantaged, are members of sexual minorities, and those with mental health conditions have a higher prevalence of smoking and experience more difficulty quitting smoking—leading to substantial tobacco-related disparities in the US population.<sup>[3][4][5][6][7]</sup>

Regulatory agencies and public health experts recognize that nicotine-delivery products exist on a continuum of risk, with combustible cigarettes and nicotine replacement therapy (NRT) presenting the most and the least harm and noncombustible products such as electronic nicotine delivery systems (ENDS) at the lower end of the risk spectrum.<sup>[8][9][10][11]</sup> Hence, AWS who would not otherwise quit are likely to improve their individual health if they switch completely to ENDS, and widespread switching is likely to benefit population health. Moreover, evidence indicates that, even if it is short of complete switching, substantial reductions in cigarette consumption (50% or more) are associated with substantial reductions in exposure to smoking-related toxicants,<sup>[12][13][14]</sup> and are likely to reduce the AWS' risk.<sup>[15][16]</sup>

Evidence from randomized clinical trials and real-world observational studies demonstrate that many AWS who adopt ENDS are able to switch completely away from smoking.<sup>[17][18][19][20][21]</sup> However, recent evidence suggests that certain subgroups of AWS such as racial/ethnic minorities and AWS in low socioeconomic status may experience additional challenges in switching completely away from cigarettes with ENDS,<sup>[22][23][24]</sup> paralleling previously-reported differences in smoking cessation.<sup>[25][26]</sup> Thus, the potential benefits of switching to ENDS may not reach these populations and could further increase tobacco-related disparities.

While ENDS are still relatively new, currently available products in the US market are highly heterogeneous in their features and specifications.. The fourth and latest generation ENDS have been reported to be more satisfying and effective in facilitating complete switching.<sup>[27][28]</sup> For example, JUUL is a widely-used closed-system brand of ENDS with a nicotine salt-based formulation whose purchasers have reported a substantial rate of switching.<sup>[29][30][31]</sup> In addition, observational and experimental studies have also suggested that JUUL could facilitate comparably high rates of switching among groups with disproportionate rates of cigarette smoking.<sup>[32][33][34]</sup> However, questions remain on how ENDS such as JUUL affect smoking and switching behaviors of AWS, especially those disproportionately affected by smoking.

The current analyses follow a cohort of US AWS who purchased a JUUL Starter Kit in 2018 for 24 months, extending the

12-month follow-up of the previous analyses.<sup>[29][30][34]</sup> To elucidate ENDS use and smoking behaviors among those disproportionately affected by smoking, the following objectives were identified: (1) assess trajectories of cigarette smoking and ENDS use over a 24-month follow-up period; (2) evaluate rates of substantial reduction in cigarette consumption among AWS who continued at 24 months; (3) examine differences in switching and substantial smoking reduction among subgroups of AWS that are particularly susceptible to smoking risk and harm (i.e., racial/ethnic minorities, low socioeconomic status, those identifying as a sexual minority, individuals with a history of smoking-related illness, and AWS living with mental health conditions).

## Methods

### Participants and Procedure

Adults (age  $\geq 21$  years) were invited to participate in the Adult JUUL Switching and Smoking Trajectories (ADJUSST) Study upon purchasing a JUUL Starter Kit (JSK) for the first time in a retail store or online between June and October, 2018 in the US. A total of 22,905 AWS (smoked some days or every day in the past 30 days and smoked  $\geq 100$  cigarettes in a lifetime)<sup>[35]</sup> completed the baseline assessment. Following the initial baseline assessment, participants were invited by email to complete 1-, 2-, 3-, 6-, 9-, 12-, 15-, 18-, 21-, and 24-month follow-up assessments. Those who completed the baseline survey were invited to all subsequent follow-up surveys, regardless of baseline characteristics, reported smoking or JUUL use, or completion of previous survey(s). The Advarra® Institutional Review Board approved the study and all participants provided written informed consent and were compensated \$30 for each survey completed.

The final analytic sample consisted of AWS who provided data for switching at  $\geq 1$  follow-up assessment (N=18,420, 80.4% of those who completed baseline). Across the 10 follow-up assessments, participants completed an average of 6.5 surveys with more than 70% responding to  $\geq 5$  follow-ups. The ADJUSST study methodology and further analyses of participants lost to follow-up have been detailed in the previous publication.<sup>[36]</sup>

### Measures

#### *Outcomes: Switching and Substantial Reduction in Cigarette Consumption*

Switching, defined as reporting no cigarette smoking in the past 30 days (“even one or two puffs”), regardless of ENDS use, was assessed at every follow-up survey. Substantial reduction was defined as a reduction in daily cigarette consumption  $\geq 50\%$  relative to baseline cigarette consumption,<sup>[30]</sup> and was analyzed among participants who reported past-30-day smoking at the 24-month follow-up. For the overall trajectory across 24 months, past-30-day smoking and ENDS use (JUUL and/or other brands) were combined to create four statuses: (1) “Dual use,”; (2) “Smoking only,”; (3) “ENDS only,”; and (4) “No Smoking/No ENDS”.

#### *Sociodemographic Characteristics and Study Subgroups*

At baseline, sociodemographic characteristics including race/ethnicity, household income, age, gender, educational attainment, marital status, sexual minority status, and were assessed with items adapted from national surveys, specifically the Population Assessment of Tobacco and Health (PATH) Study. Participants also reported their smoking history and profile: average cigarettes smoked per day (CPD), number of days smoked in the past 30 days, number of years smoked regularly, plans to quit smoking within 30 days, and cigarette dependence.

AWS subgroups that have been disproportionately affected by smoking were identified and analyzed against referent groups. Specifically, racial/ethnic minorities (i.e., non-Hispanic Black, Hispanic, non-Hispanic Asian, non-Hispanic other race or multi-racial) were compared to non-Hispanic White participants. Three income levels anchoring on the federal poverty level (FPL) were defined based on household income relative to the number of people in the household; low income (FPL <150%) were compared with FPL 150-400% and FPL >400%. Those with a high school degree or less education were compared with associate degree holders and those with a bachelor's degree or more education.

Sexual minorities (gay/lesbian/bisexual/something else) were compared with straight participants. Participants were first asked about the level of sexual attraction to both opposite and same sex, or if they have never been sexually attracted to anyone at all. Those endorsing an option other than exclusive heterosexuality ("Only to [opposite sex], never to [same sex]") were followed up with a question on sexual orientation. Options included "Straight, that is not gay" (male), "Straight, that is, not Lesbian or gay" (female), "Gay" (male), "Lesbian or gay" (female), "Bisexual," or "Something else." Participants who self-identified as "Gay" (male), "Lesbian or gay" (female), "Bisexual," or "Something else" were defined as sexual minority individuals, in contrast to those who endorsed exclusive heterosexuality or those who opted for the option "Straight."

Participants were also asked about medical history, specifically the diagnoses of certain health conditions made by a healthcare professional. Smoking-related illness (SRI) was defined by one or more diagnoses of chronic obstructive pulmonary disease, emphysema, congestive heart failure, a stroke, a heart attack, or a need for bypass surgery by a healthcare provider. For mental health conditions, participants were asked about the diagnosis of major depression, anxiety, bipolar disorder, mood disorder, schizoaffective disorder, schizophrenia, or other mental health conditions made by a healthcare professional. As the number of participants who reported diagnoses of mental health conditions other than depression and anxiety was very small, AWS reporting the diagnosis of depression and/or anxiety were identified and compared with those who have never been diagnosed with any of the mental health conditions.

## Statistical Analysis

Repeated-measures logistic regression tested associations of interindividual factors with switching across the 10 follow-ups. Simultaneous regressors included the following factors: time-invariant baseline sociodemographic factors, smoking characteristics and time (a continuous measure of months since baseline, including consideration of quadratic departures from linearity). Additionally, interaction terms were tested to determine if the pattern of change in switching over time significantly differed between subgroups. A separate logistic regression model evaluated the substantial reduction in daily cigarette consumption among participants who reported smoking at the 24-month follow-up using the same regressors. All

analyses were conducted in R (version 4.0.2) with alpha set to .05;<sup>[37]</sup> the repeated-measures model was conducted using generalized estimating equations (GEE) with the “geepack” package (version 1.3-2).<sup>[38]</sup>

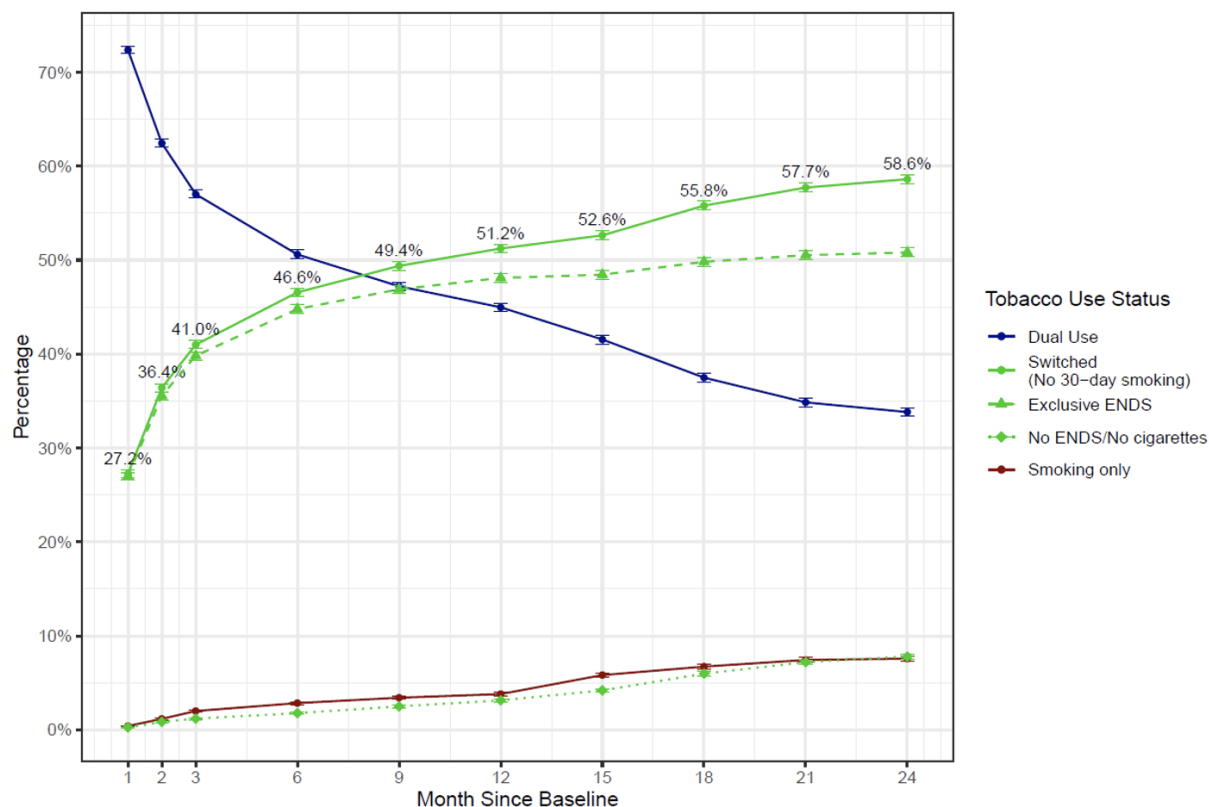
## Results

### Sample Characteristics

Participants were majority non-Hispanic White (78.4%), male (55.1%), and never married (57.5%). The average age was 32.6 ( $SD=10.8$ ). Members of sexual minorities accounted for 15.4% of participants. Depression or anxiety was reported by 40.1%, and SRI by 3.3%. At baseline, participants smoked an average of 11.1 CPD ( $SD=8.2$ ) and had smoked regularly for 12.4 years ( $SD=10.7$ ). The majority (56.7%) reported not planning to quit smoking in the next 30 days (Supplementary Table 1). See Supplementary Tables 2, 3 and 4 for baseline characteristics of subpopulations disproportionately affected by smoking.

### Temporal trends in switching, dual use, and exclusive smoking over 24 months

Rates of switching continued to increase across the second year of follow-up (Figure 1 and Supplementary Table 5), across months 12 (51.2%), 15 (52.6%), 18 (55.8%), 21 (57.7%), and 24 (58.6%). Over the entire 24-month period, switching rates increased significantly (Linear time:  $OR=1.048$  [CI: 1.046-1.050]), with the rate of increase slowing over time (Quadratic time:  $OR=0.997$  [CI: 0.997-0.998]). In the second year, switching significantly increased linearly, with no slowing over time (Linear time:  $OR=1.027$  [CI: 1.023-1.031]; Quadratic time:  $p>.05$ ).



**Figure 1.** ADJUSST participants' trajectory across 24 months

Consistent with the increase in switching, the proportion of dual users decreased over time from 45.0% at Month 12 to 33.8% at Month 24. The quadratic time trend associated with the decrease in dual use between Months 12 and 24 (Linear time: OR=0.960 [CI: 0.956-0.964]; Quadratic time: OR=1.002 [CI: 1.001-1.003]) indicates that the rate of decrease in dual use accelerated over time.

The percentage of participants who were using ENDS and not smoking increased significantly linearly in the second year (from 48.1% in Month 12 to 50.8% in Month 24; see Supplementary Table 5 for linear and quadratic time effects). The proportion of participants who were neither using ENDS nor smoking cigarettes also increased significantly between Months 12 and 24 (from 3.1% to 7.8%), but the rate of increase slowed over time. Some participants returned to exclusive smoking, increasing from 3.8% at Month 12 to 7.6% at Month 24, with a negative quadratic pattern indicating the rate of increase was slowing over time.

At Month 24, the most common behavior reported by participants was exclusive ENDS use (50.8%), followed by dual use (33.8%), no cigarettes/no ENDS (7.8%), and exclusive smoking (7.6%).

### Association between Characteristics of Special Interest and Switching across 24 Months

Factors associated with participants' complete switching across 24 months were summarized in Table 1. In univariate analyses, AWS of Hispanic descent and those in the highest income category were more likely to report switching; those

with associate degrees, sexual minorities, and AWS with SRI, or mental health conditions were less likely to completely switch compared to the respective reference group.

**Table 1.** Associations between switching and subpopulation characteristics disproportionately affected by smoking, across 24 months

		Main effects		Interaction effects with time	
		Univariate <sup>1</sup>	Multivariable	Linear	Quadratic
Time (months, linear)		1.05 (1.05–1.05)	1.05 (1.05–1.06)	-	
Time (months, quadratic)		0.997 (0.997 – 0.998)	0.997 (0.997 – 0.997)		
Race/ethnicity	Non-Hispanic White	Ref.		Ref.	
	Non-Hispanic Black	1.06 (0.92–1.22)	0.97 (0.81–1.16)	0.996 (0.98–1.01)	0.9999 (0.9994–1.0003)
	Non-Hispanic Asian	1.02 (0.92–1.12)	<b>0.87 (0.77–0.98)</b>	0.9997 (0.99–1.01)	1.0001 (0.9998–1.0004)
	Hispanic	<b>1.14 (1.05–1.24)</b>	0.99 (0.90–1.10)	<b>0.99 (0.98–0.998)</b>	<b>0.9997 (0.9994–0.99996)</b>
	Other Race or Multi-Racial	1.05 (0.94–1.17)	0.96 (0.84–1.10)	0.99 (0.98–1.004)	0.9998 (0.9994–1.0002)
Household income	FPL <150%	Ref.		Ref.	
	FPL 150-400%	1.05 (0.99–1.11)	<b>1.08 (1.00–1.15)</b>	<b>1.01 (1.003–1.01)</b>	<b>1.0003 (1.0001–1.0005)</b>
	FPL >400%	<b>1.08 (1.02–1.15)</b>	<b>1.12 (1.03–1.21)</b>	<b>1.01 (1.01–1.02)</b>	<b>1.0004 (1.0002–1.0006)</b>
Educational attainment	High school or lower	Ref.		Ref.	
	Associate degree	<b>0.92 (0.87–0.98)</b>	<b>0.88 (0.82–0.94)</b>	1.003 (0.998–1.01)	1.0002 (0.99998–1.0004)
	Bachelor’s degree or more	1.02 (0.96–1.09)	<b>0.86 (0.79–0.94)</b>	<b>1.01 (1.003–1.01)</b>	<b>1.0003 (1.0001–1.0005)</b>
Sexual minority (Ref: No)	Yes	<b>0.90 (0.84–0.97)</b>	0.93 (0.86–1.01)	0.999 (0.99–1.004)	0.99997 (0.9998–1.0002)
Smoking-related illness (Ref: No)	Yes	<b>0.57 (0.49–0.66)</b>	0.87 (0.71–1.06)	1.001 (0.99–1.01)	1.0001 (0.9996–1.0005)
Depression or Anxiety (Ref: No)	Yes	<b>0.82 (0.78–0.86)</b>	<b>0.85 (0.80–0.91)</b>	<b>1.005 (1.0005–1.01)</b>	<b>1.0002 (1.000003–1.0003)</b>

<sup>1</sup> All univariate analyses were adjusted for time (linear and quadratic) while accounting for repeated-measure of the ADJUSST study with the GEE model.

NS: Not significant

Note: Boldface indicates statistically significant results ( $p < .05$ ). All main effects of the multivariable model were adjusted for age, sex, marital status, and baseline smoking profile (days smoked in the past 30 days, cigarette-per-day, years smoked regularly, cigarette dependence, and plans to quit within the next 30 days). All interaction effects were examined while adjusting for age, sex, marital status, and baseline smoking profile (days smoked in the past 30 days, cigarette-per-day, years smoked regularly, cigarette dependence, and plans to quit within the next 30 days) as well as other

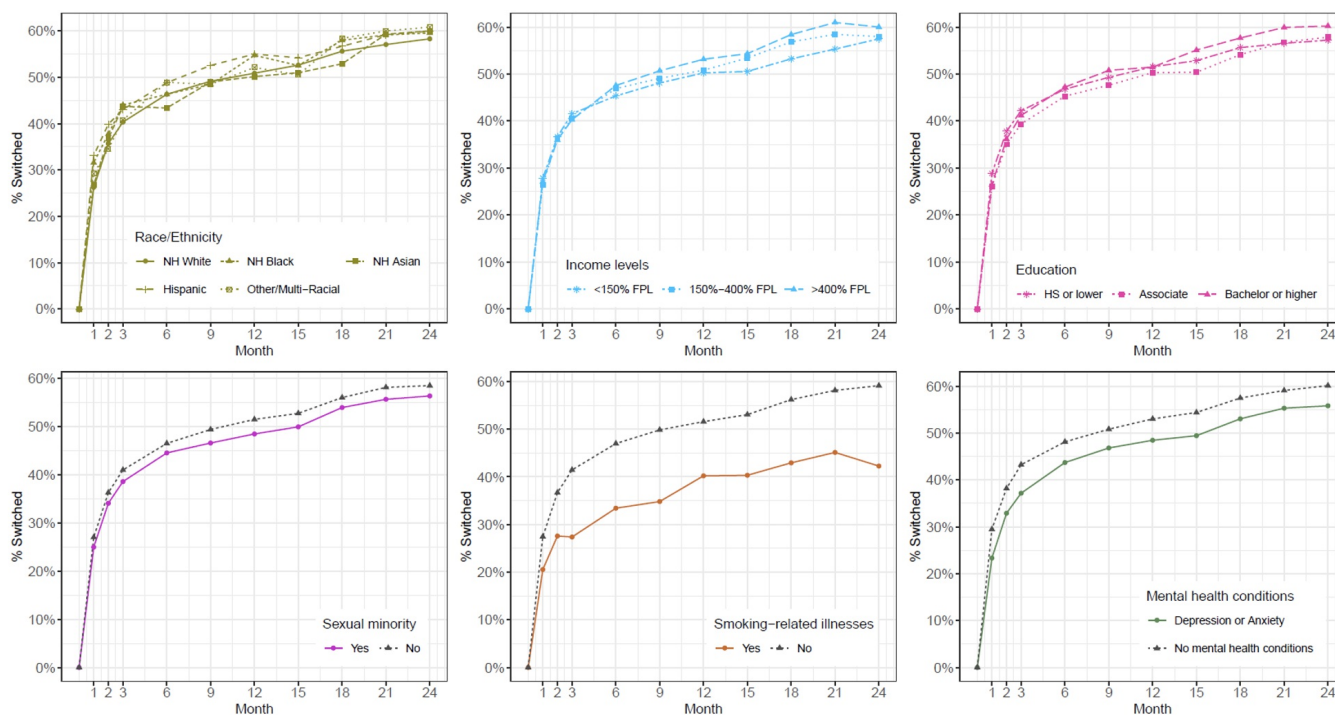


## characteristics of special interest

After adjustment for baseline characteristics and mutual adjustment for the different subgroup memberships, the pattern was different. Among racial/ethnic subgroups, only Asian AWS had significantly lower odds of switching (OR=0.87 [CI: 0.77-0.98]). The odds of switching increased with higher income levels (FPL>400%: OR=1.12 [CI: 1.03-1.21]; FPL 150-400%: OR=1.08 [CI: 1.00-1.15]) but also with low educational attainment (Bachelor or higher: OR=0.86 [CI: 0.79-0.94]; Associate: OR=0.88 [CI: 0.82-0.94], see footnotes).<sup>1</sup> Sexual minority identity and SRI, which were significant in univariate analyses, were no longer related to switching (both  $p>.05$ ). Mental health conditions demonstrated the greatest association with switch rates over the 24-month period, such that the odds of switching were 15% lower in AWS individuals with depression or anxiety (OR=0.85 [CI: 0.80-0.91]), compared to those with no mental health condition.

## Temporal trends in switching across populations disproportionately affected by smoking

As seen in Figure 2, the various subgroups examined showed similar temporal trends: all groups showed increases over time, but with the rate of increase leveling off later in the observation period. Within this consistent pattern, there were some significant variations between groups; however, compared to their respective reference groups, no more than 1% variations were observed in linear or quadratic components of the trend (Table 1, “Interaction effects with time”).



**Figure 2.** Switching rates among subpopulations disproportionately affected by smoking

NH: Non-Hispanic; FPL: Federal Poverty Line; HS: High School

**Note.** Smoking-related illnesses=Self-reported lifetime diagnosis of any of the following conditions by a medical professional: chronic obstructive pulmonary disease (COPD), emphysema, asthma, congestive heart failure, stroke, heart attack or a need for bypass surgery. Depression or Anxiety=Self-reported lifetime diagnosis of major depression and/or an anxiety disorder by a medical professional; No mental health conditions=Self-



report that they have never been diagnosed with any of the following mental health conditions by a medical professional: anxiety disorder, bipolar disorder, depression, mood disorder, schizoaffective disorder, schizophrenia, or other mental health condition. See Supplementary Table 1 for switching rates in Months 12 and 24.

### Switch rates at the end of the 24-month observation period

At Month 24, differences in switching rates across subgroups defined by racial/ethnic identity, income, and sexual minority identity were small and non-significant. AWS with higher educational attainment were slightly but significantly ( $p=.045$ ) more likely to be switched at 24 months (57.2%, 57.9%, and 60.2%, from lowest to highest education level). Whereas 55.8% of AWS diagnosed with anxiety or depression were switched at Month 24, it was 60.1% among those with no mental health diagnosis ( $p<.001$ ). The biggest difference was seen between those with and without SRI (42.3% vs. 59.1%,  $p<.001$ ).

### Substantial Reduction in CPD Among Those Reporting Smoking at Month 24, and Associated Factors

At Month 24, 41.4% of the participants (N=4483) reported that they had smoked, even a single puff, in the past 30 days. On average, participants who continued to smoke significantly decreased their CPD between baseline and Month 24 (from 12.5 to 8.3,  $p<.001$ , Supplement Table 6). Reduction in CPD of at least 50% was reported by 45.4% of participants who were still smoking at Month 24 (Table 2); the average CPD reduction among these 'reducers' was 72.8% (from 14.7 at baseline to 4.0 at Month 24,  $p<.001$ ). Those who continued to smoke without substantial reduction maintained cigarette consumption similar to their baseline consumption, with neither significant increase nor decrease (11.7 at baseline vs. 11.8 at Month 24,  $p=.442$ ), which was consistent across most subgroups. Hispanic and other/multi-race AWS without substantial reduction reported a small significant increase in CPD, up to ~1.3 CPD.

**Table 2.** Month-24 smokers' prevalence of and factors associated with substantial reduction (50%+) in cigarette-per-day

		Substantial reduction among M24 AWS	OR (95% CI)
<b>All Month-24 AWS (N=3750)</b>		<b>45.4%</b>	<b>-</b>
Race	Non-Hispanic White	44.7%	Ref.
	Non-Hispanic Black	41.4%	0.74 (0.46–1.19)
	Non-Hispanic Asian	49.0%	1.41 (0.98–2.02)
	Hispanic	46.9%	1.19 (0.89–1.58)
	Other Race or Multi-Racial	47.3%	1.10 (0.76–1.58)
Income	FPL <150%	49.0%	Ref.
	FPL 150–400%	43.1%	0.86 (0.71–1.03)
	FPL >400%	44.0%	0.90 (0.72–1.12)
Education	High school or lower	46.4%	Ref.
	Associate degree	44.9%	1.00 (0.83–1.21)
	Bachelor's degree or more	44.5%	1.02 (0.81–1.29)
Sexual minority	No	46.0%	Ref.
	Yes	44.2%	0.91 (0.73–1.14)
SRI	No	45.2%	Ref.
	Yes	48.6%	1.20 (0.81–1.77)
Depression or Anxiety	No	45.0%	Ref.
	Yes	46.1%	0.91 (0.76–1.07)

*Note: Boldface indicates statistically significant results ( $p < .05$ ). The multivariable model was adjusted for age, sex, marital status, and smoking profile (years smoked regularly, cigarette dependence, and plans to quit within the next 30 days). Days smoked in the past 30 days and cigarette-per-day at Baseline were not included as substantial reduction is defined based on those variables.*

As seen in Table 2, when adjusted for baseline characteristics and mutually adjusted for each other, none of the subgroups of interest differed in the odds of substantial reduction at Month 24 (all  $ps > .05$ ).

## Discussion

In this cohort of US AWS who purchased JUUL products, complete switching continued to increase progressively over the second year of follow-up, reaching 58.6% at 24 months, as the proportion of dual users concomitantly decreased. This continues a pattern seen in the first 12 months of this study,<sup>[29]</sup> wherein switch rates increase over time. This is in contrast to the trends seen in clinical trials of medicinal interventions for smoking cessation, such as NRT and prescription drugs, where abstinence rates decline over time, often steeply.<sup>[39]</sup> Among participants who continued to smoke at Month 24, average cigarette consumption was significantly reduced relative to baseline. Approximately 45% reduced CPD by half or

more from baseline, with the actual decrease exceeding 70%. Studies show that reductions of this magnitude are associated with substantial reductions in exposure to toxicants.<sup>[12][13][14]</sup>

Rates of switching away from smoking were consistently high among groups that have been disproportionately affected by smoking: more than half of AWS who identify as racial/ethnic minorities, were low socioeconomic status, sexual minorities, or have mental health conditions reported switching two years after purchasing a JUUL Starter Kit. Previous studies suggest that some demographically and socioeconomically minoritized groups may experience challenges in complete switching with ENDS.<sup>[23][24]</sup> In contrast, in the current analysis, differences in switch rates at 24 months only ranged between 0.5~3% across several races and ethnicities, income and education levels, and different sexual orientations. This suggests that ENDS such as JUUL can potentially contribute to the mitigation of disparities that affect these vulnerable populations.

More substantial differences were observed with SRI and mental health conditions (16.8% and 4.3%, respectively at Month 24). This is not surprising, considering that AWS with these conditions have lower success with smoking cessation.<sup>[4][5][6]</sup> AWS with mental health conditions may have particular challenges and stresses that make behavior change more difficult. AWS with SRI may represent smokers who have persisted in smoking despite having already suffered serious personal health impacts, and likely after having been directed to stop smoking by healthcare providers, so may have difficulties stopping smoking that were not otherwise captured by measured baseline covariates. Nonetheless, the absolute switching rates of these groups were substantial (42.3% among AWS with SRI; 55.8% among those with mental health conditions at Month 24). These results are supported by previous findings demonstrating that ENDS can facilitate complete switching and substantial reduction in CPD among AWS with physical and mental illnesses,<sup>[33][40][41]</sup> and the positive health effects of switching from combustible to noncombustible products.<sup>[40][42]</sup> Taken together, current findings add to the growing body of literature on the promising potential of ENDS in facilitating switching among AWS who have been disproportionately affected by smoking.

While complete discontinuation of smoking is optimal, a substantial reduction in cigarette consumption is still likely to be beneficial. Multiple studies have shown the amount of toxicant exposure is primarily driven by the amount of cigarettes consumed, with little incremental effects from ENDS use,<sup>[43][44]</sup> indicating dual users who substantially reduce their smoking are still likely to benefit. Furthermore, cigarette reduction is a meaningful step towards complete abstinence from cigarettes.<sup>[45][46]</sup> For those who were not able or not willing to switch completely, rates of cigarette reduction were comparable following ENDS use across groups disproportionately affected by smoking, again suggesting that the outcomes of ENDS use are not substantially affected by disparities. About one-fifth of participants neither switched nor substantially reduced CPD at Month 24, and their cigarette consumption remained unchanged. However, the additional exposures from ENDS use might increase their health risks. These participants may represent a particular group of AWS that may not respond to ENDS. Future research should explore other behavioral and/or pharmacological approaches that may be more effective for them.

The present findings indicate that rates of switching completely away from smoking and substantially reducing cigarette consumption were high. Although the majority of switchers continued to use nicotine through ENDS rather than quitting all

nicotine products altogether, evidence indicates that exclusive ENDS use is likely to be far less harmful than cigarette smoking.<sup>[43][44]</sup> The trends in switching and substantial smoking reduction were broadly comparable across populations disproportionately affected by smoking, suggesting that the use of ENDS could contribute to mitigating disparities in smoking-related harm. However, it is notable that some of the subpopulations studied here have lower rates of adoption of ENDS. For example, racial/ethnic minority AWS or those in low socioeconomic status have significantly lower rates of using ENDS<sup>[47]</sup> and are less likely to have tried to completely switch to ENDS.<sup>[9][22]</sup> Barriers to the adoption of and switching to ENDS, such as risk misperceptions,<sup>[48]</sup> warrant further research and intervention if the benefits of ENDS are to be realized among subpopulations disproportionately affected by smoking as well. Utilization of ENDS could complement other measures of tobacco control and contribute to accelerating the public health goal of reducing smoking-related disparity and curtailing cigarette-related diseases and deaths in the U.S.<sup>[49][50]</sup>

There are several limitations that should be taken into account when interpreting the results of this study. First, ADJUST is a naturalistic, non-interventional study of a cohort of JUUL purchasers. Without a randomized control group to compare to, the observational nature of the study precludes drawing causal conclusions. The study was based on self-reports, and participants' smoking status was not biochemically verified, consistent with practice for large nationally-representative observational studies.<sup>[18][19][20][21]</sup> Second, the recruitment was based on the purchase of JSK. Therefore, the cohort was not meant to be representative of US AWS who use ENDS, let alone all current AWS. However, the sample does represent an important and pragmatic segment: those who purchase and, in a sense, commit to ENDS use. Third, with 10 follow-up surveys being conducted over the course of two years, the study was limited by missing data. However, 72% of the participants responded to 5 or more surveys and previous analyses on loss-to-follow-up demonstrated that the biases from survey nonresponse are limited.<sup>[36]</sup> Nonetheless, there is a possibility of selective loss-to-follow-up. Lastly, participants may also have used other tobacco products that were not assessed in this study.

This study has several strengths as well. ADJUST includes a large number of participants who made the financial commitment of purchasing JSK, and therefore represents a group of AWS who have a serious interest in JUUL. They are likely to differ from the general population of AWS or even the group of AWS who have tried ENDS before, but they are more representative of real-world AWS who have the potential to switch to ENDS and offer more readily applicable insights in the current marketplace. The two-year follow-up provided a long-term perspective on this population of interest. This analysis extends AWS' initial first-year trajectory with cigarettes and JUUL and demonstrates the continuous increase in switching. The cohort included many members of subpopulations disproportionately affected by tobacco use, allowing for analysis of sub-populations.

## Conclusion

Among this sample of AWS who purchased JUUL products, switching rates continued to increase over a 24-month period. Two years after purchasing a JUUL Starter Kit, 58.6% of AWS reported not smoking, and 45.4% of those who continued to smoke had substantially reduced their cigarette consumption. Subgroups that have been disproportionately affected by smoking, such as racial/ethnic minorities, those in low socioeconomic statuses, sexual minorities, and AWS with medical

and psychological conditions, showed comparable rates of switching and substantial smoking reduction. Through facilitating complete switching and smoking reduction, ENDS products such as JUUL could be an effective harm reduction strategy among populations in the US that have been disproportionately affected by cigarette smoking.

## Statements and Declarations

### Funding

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### Declaration of Interests

SK, SS, and AS provide consulting services on tobacco harm reduction on an exclusive basis to Juul Labs, Inc. through PinneyAssociates, Inc. NIG is a full-time employee of Juul Labs, Inc. SS holds a patent for a novel nicotine medication that has not been developed or commercialized.

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### Data Availability Statement

The analyzed data are not publicly available; however, the survey instrument for the current survey is publicly available at: <https://www.juullabs.com/wp-content/uploads/2021/03/ADJUSST-Baseline-and-Follow-Up.pdf>

## Footnotes

<sup>1</sup> At the aggregate level, AWS with bachelor's degree or more had consistently higher switching rates than those with high school or lower education (Figure 2). However, AWS in the highest education but the lowest income category often reported *lower* rates of switching (differences ranging between 2~7%) than AWS with high school or lower levels of education. This discrepancy was not explained by their smoking profile or JUUL use behaviors, indicating effects of other unmeasured factors in this particular high education-low income subgroup of AWS.

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