TABLE OF CONTENTS

6.3.2 Epidemiological Evidenced of Tobacco use in the US 5
6.3.2.1 Introduction 5
6.3.2.1.1 Background 5
6.3.2.1.2 Objectives 5
6.3.2.1.3 Methods 5
6.3.2.1.3.1 Search strategies 5
6.3.2.1.3.2 Inclusion criteria 6
6.3.2.1.3.3 Exclusion criteria 6
6.3.2.2 Smoking in the United States 6
6.3.2.2.1 Prevalence of cigarette smoking 6
6.3.2.2.1.1 Search strategies 6
6.3.2.2.1.2 Results 6
6.3.2.2.1.3 Discussion 55
6.3.2.2.1.4 Conclusions 55
6.3.2.2.2 Cigarette smoking initiation 56
6.3.2.2.2.1 Search strategies 56
6.3.2.2.2.2 Results 56
6.3.2.2.2.3 Discussion 80
6.3.2.2.2.4 Conclusions 80
6.3.2.2.3 Smoking cessation 81
6.3.2.2.3.1 Search strategies 81
6.3.2.2.3.2 Results 81
6.3.2.2.3.3 Discussion 134
6.3.2.2.3.4 Conclusions 135
6.3.2.2.4 Relapse to smoking 135
6.3.2.2.4.1 Search strategies 135
6.3.2.2.4.2 Results 136
6.3.2.2.4.3 Discussion 140
6.3.2.2.4.4 Conclusions 145
6.3.2.3 Alternative tobacco and nicotine containing products 145
6.3.2.3.1 Electronic cigarettes (e-cigarettes) 145

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.3.1.1 Search strategies 145
6.3.2.3.1.2 Results 145
6.3.2.3.1.3 Discussion 173
6.3.2.3.1.4 Conclusions 176
6.3.2.3.2 Smokeless tobacco 177
6.3.2.3.2.1 Definitions 177
6.3.2.3.2.2 Search strategies 177
6.3.2.3.2.3 Results 177
6.3.2.3.2.4 Conclusions 195
6.3.2.3.3 Dual or poly-tobacco use 195
6.3.2.3.3.1 Search strategies 195
6.3.2.3.3.2 Prevalence of dual or poly-tobacco use 195
6.3.2.3.3.3 Discussion 202
6.3.2.3.3.4 Conclusion 203
6.3.2.4 General discussion 203
6.3.2.5 General conclusions 204
6.3.2.6 References 205

Table of Tables

Table 1. Characteristics of surveys assessing cigarette smoking in adults 7
Table 2. Percentage of adults who were current cigarette smokers,* by selected characteristics – National Health Interview Survey, United States, 2005 and 2014 (Jamal 2015) 14
Table 3. Tobacco Product Use in the Past Month in Adults by Age Category in the NSDUH 2002-2014 (Hedden S 2015) 20
Table 4. State-specific prevalence of current cigarette smoking among adults aged ≥ 18 years, by state/territory –BRFSS, US, 2011-2013 (Nguyen 2015) 21
Table 5. Percentage of persons aged ≥18 years who were 'everyday' or 'some days' cigarette users and selected characteristics – National Adult Tobacco Survey, United States, 2012-2013 (Agaku 2014b) 23
Table 6. Characteristics of surveys assessing cigarette smoking in youth 26
Table 7. Percentage of high school students who ever tried cigarettes smoking* and who smoked a whole cigarette for the first time before age 13 years, by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Surveillance System (2013) (Kann 2014) 32

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 8. Trends in Lifetime, 30-day and Daily Prevalence of Use of Cigarettes for Grades 8, 10 and 12 Combined in the MTF 2015 (Johnston 2016) 35

Table 9. Tobacco Product Use in the Past Month among Youth Aged 12 to 17 years in the NSDUH 2002-2014 (Hedden S 2015) 36

Table 10. Percentage of high school students who ever tried cigarettes smoking* and who smoked a whole cigarette for the first time before age 13 years, by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Surveillance System (2013) (Kann 2014) 39

Table 11. Percentage of high school students who currently smoked cigarettes* and who currently frequently smoked cigarettes, †by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Survey, 2013 (Kann 2014). 40

Table 12. Percentage of high school students who ever smoked cigarettes daily* and who currently smoked cigarettes daily,† by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Survey, 2013 (Kann 2014). 42

Table 13. Ever reported past 30-day cigarette smoking (Waves I-IV), according to Wave I participant sociodemographic characteristics, N (%).[a, b] 2008-2009 Add Health Study(Kaufman 2015) 45

Table 14. Prevalence of cigarette smoking in mental illness populations 46

Table 15. Prevalence of cigarette smoking in military personnel 50

Table 16. Prevalence of cigarette smoking in HIV + populations 52

Table 17. Prevalence of cigarette smoking in sexual minorities 53

Table 18. Prevalence of cigarette smoking initiation 58

Table 19. Determinants of cigarette smoking initiation 66

Table 20. Characteristics of studies reporting cessation rates in adult populations 83

Table 21. Characteristics of studies assessing cessation rates in youth populations 104

Table 22. Characteristics of studies assessing the quit rates in specific populations ... 113

Table 23. Determinants of smoking cessation in different populations 120

Table 24. Characteristics of studies assessing relapse rates in US populations 137

Table 25. Determinants of relapse in the US population 141

Table 26. Characteristics of studies assessing the prevalence of e-cigarette use in adult populations 150

Table 27. Characteristics of studies assessing the prevalence of e-cigarette use in youth populations 156

Table 28. Determinants of e-cigarette use in adult and youth populations in the US .. 163

Table 29. Studies evaluating the probability of initiation of cigarette smoking in e-cigarette users 172

Table 30. Studies evaluating the probability of cigarette smoking cessation in e-cigarette users 174

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 31. Characteristics of studies assessing the prevalence of smokeless tobacco use in adult populations.....179
Table 32. Characteristics of studies assessing the prevalence of smokeless tobacco use in youth populations 183
Table 33. Determinants of smokeless tobacco use in adult and youth populations in the US 187
Table 34. Studies evaluating the probability of initiation of cigarette smoking in smokeless tobacco users 192
Table 35. Studies evaluating the probability of cigarette smoking cessation in smokeless tobacco users.....194
Table 36. Prevalence of dual and poly-tobacco use.....197

Table of Figures

Figure 1. Prevalence of e-cigarette ever use in adults in the US (Schoenborn 2015).....147

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2 Epidemiological Evidenced of Tobacco use in the US

6.3.2.1 Introduction

6.3.2.1.1 Background

The need to assess the impact of candidate Modified Risk Tobacco Products (MRTP) on population harm is clear from the MRTP's Guidance which states that "manufacturers must demonstrate that MRTPs meet a series of rigorous criteria, and will benefit the health of the population as a whole" (FDA (Food and Drug Administration) 2012).

Such an assessment requires investigating multiple factors associated with tobacco use in general and, in this case, a specific candidate MRTP, including the toxicity of the product, the intensity of its use and the prevalence (uptake and continued use) of use (Hatsukami 2012, Stratton 2001). In order to assess the epidemiological impact of marketing THS with respect to the prevalence of tobacco product use in the United States (US), there would be a need to measure the prevalence of use of these products before and after marketing authorization. Therefore the aim of this section is to summarize the epidemiological evidence of the prevalence of use of cigarettes, rates and determinants of initiation, cessation and relapse of cigarette smoking as well as alternative tobacco and nicotine containing products widely used (electronic cigarettes [e-cigarettes] and smokeless tobacco due to being the most commonly used products in American populations) in the US. Additionally, the potential association between cigarette smoking and the use of alternative tobacco and nicotine containing products will be evaluated.

6.3.2.1.2 Objectives

- To understand and summarize what the prevalence of use of the cigarettes, e-cigarettes and smokeless tobacco are overall and by subgroups.
- To gain insight into the prevalence of patterns of dual or multiple product use.

6.3.2.1.3 Methods

Literature searches were conducted to identify publications on the following subjects: the prevalence of cigarette smoking, electronic cigarette (e-cigarette) use and, smokeless tobacco use; the rates of initiation, cessation and relapse as well as their determinants; and the potential association/interrelationships of the use of alternative tobacco or nicotine containing products.

6.3.2.1.3.1 Search strategies

The literature searches were performed in MEDLINE through PubMed (except for prevalence of smoking, see section 6.3.2.2.1.1). The general process of performing a given literature search included: running a search query in PubMed, screening of publication titles and abstracts for content and finally the retrieval of selected full text articles. When it was not obvious if the study should be included in the review after inspection of the abstract (or the abstract is not available), a full copy was requested. Retrieved full text articles were reviewed to decide whether to include them or not according to the inclusion/exclusion criteria. Importantly, there might be an overlap between the studies identified through different searches, and 1 search could identify a publication deemed eligible to be included in another section.

In general terms, the literature searches were limited to publications in English and studying human US-based populations. More details on these specific searches including

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

the search queries, dates when these were performed, etc., can be found in each sub-section within section 6.3.2.

6.3.2.1.3.2 Inclusion criteria

The inclusion criteria were as follows:

- Studies published in English.
- Human subjects and US-based populations.
- Observational (cross sectional and cohort studies), clinical studies (where applicable).
- Inclusion of relevant and quantifiable information on the specific subject.

6.3.2.1.3.3 Exclusion criteria

The exclusion criteria were as follows:

- Letters, commentaries, case reports or case series.
- Diseased populations (except for those considered specific populations)
- Non US-based populations.

6.3.2.2 Smoking in the United States

6.3.2.2.1 Prevalence of cigarette smoking

6.3.2.2.1.1 Search strategies

A search was performed in the Center for Disease Control and Prevention (CDC) database for population-based surveys that reported the prevalence of cigarette smoking (Centers for Disease 2016h). Additionally, any US-based studies found through the literature searches performed as part of this section of the dossier where prevalence of cigarette smoking is reported were included.

6.3.2.2.1.2 Results

6.3.2.2.1.2.1 Smoking in the general adult population

The prevalence of tobacco smoking is usually measured through population-based surveys, relying on self-reported information (Bilal 2014). In the US there are a variety of surveys that evaluate the prevalence of smoking as well as other tobacco related endpoints. The Office on Smoking and Health conducts and supports national and international surveys on tobacco use, smoking cessation, secondhand smoke exposure, and other tobacco-related topics among youth, adults and specific populations (Centers for Disease 2016h). There were in total 10 surveys reported by the CDC. Out of these 10 surveys, 3 reported relevant information for adults (Centers for Disease 2016a, Centers for Disease 2016c, Centers for Disease 2016e) and 1 reported results from both adult and youth populations (Hedden S 2015). A summary of the characteristics of these surveys can be found below in Table 1.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 1. Characteristics of surveys assessing cigarette smoking in adults

Survey	Period	Sampling	Definitions	Summary of findings
National Health and Nutrition Survey (NHIS) (Centers for Disease 2016e)	2005-2014	NHIS is a large-scale household interview survey of a statistically representative sample of the US civilian noninstitutionalized population. Interviewers visit 35,000–40,000 households across the country and collect data about 75,000–100,000 individuals. Data are adjusted for selection and nonresponse, and weighted to provide nationally representative estimates. The 2014 NHIS included 36, 697 respondents aged ≥ 18 years; the response rate was 58.9%.	• Current smokers were respondents who reported smoking ≥ 100 cigarettes during their lifetime and, at the time of interview, reported smoking every day or some days. • Former cigarette smokers were respondents who reported smoking ≥ 100 cigarettes in their lifetime but currently did not smoke.	• The percentage of US adults who smoke cigarettes declined from 20.9% in 2005 to 16.8% in 2014 (10). Among daily cigarette smokers, declines were observed in the percentage who smoked 20-29 cigarettes per day (from 34.9% to 27.4%) or ≥ 30 cigarettes per day (from 12.7% to 6.9%).

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of findings
National Survey on Drug Use and Health (NSDUH) (Hedden S 2015)	2002-2014	NSDUH is a face-to-face household interview survey that is conducted in two phases: the screening and the interview phase. The interviewer conducts a screening of the eligible household with an adult resident (aged 18 or older) in order to determine whether 0, 1, or 2 residents aged 12 or older should be selected for the interview. NSDUH collects data using audio computer-assisted self-interviewing, in which respondents read or listen to the questions on headphones and then enter their answers directly on the NSDUH laptop computer. In 2014, screening was completed at 127,605 addresses, and 67,901 completed interviews were obtained, including 17,046 interviews from adolescents aged 12 to 17 and 50,855 interviews from adults aged 18 or older. Weighted response rates for household screening and for interviewing were 81.9 and 71.2 percent, respectively, for an overall response rate of 58.3 percent for people aged 12 or older. Weighted interview response rates were 80.0 percent for adolescents and 70.3 percent for adults.	• Cigarette use is defined as smoking 'part of a cigarette' in the last 30 days and the data is presented by total tobacco (mixture of products used) and by age strata (12-17 year olds, 18-25 year olds or young adults and aged 26 and above). The NSDUH also reports daily cigarette use and the prevalence of those smoking 1 pack or more a day.	• In 2014, about 27.9 million adults aged 26 or older smoked cigarettes every day, which represents 63.3 percent of the adults aged 26 or older who were current smokers. The percentage of current smokers aged 26 or older in 2014 who smoked cigarettes every day was lower than the percentages in most years from 2002 to 2012.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of findings
Behavioral Probability Factor Surveillance System (BRFSS) (Centers for Disease 2016a)	2011-2013	The Behavioral Probability Factor Surveillance System (BRFSS) is the nation's premier system of health-related telephone surveys that collect state data about US residents regarding their health-related probability behaviors, chronic health conditions, and use of preventive services (8). Established in 1984 with 15 states, BRFSS now collects data in all 50 states as well as the District of Columbia and three US territories. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world. By collecting behavioral health probability data at the state and local level, BRFSS has become a powerful tool for targeting and building health promotion activities. As a result, BRFSS users have increasingly demanded more data and asked for more questions on the survey. Currently, there is a wide sponsorship of the BRFSS survey, including most divisions in the CDC National Center for Chronic Disease Prevention and Health Promotion; other CDC centers; and federal agencies, such as the Health Resources and Services Administration, Administration on Aging, Department of Veterans Affairs, and Substance Abuse and Mental Health Services Administration (8).	• Current cigarette smoking was assessed by two questions: "Have you smoked at least 100 cigarettes in your entire life?" and "Do you now smoke cigarettes every day, some days, or not at all?" Respondents who reported smoking at least 100 cigarettes in their lifetime and who reported currently smoking "every day" or "some days" were classified as current cigarette smokers.	• Current cigarette smoking ranged from 11.8% (Utah) to 29.0% (Kentucky) in 2011 and from 10.3% (Utah) to 27.3% (West Virginia) in 2013 (Table 4). During 2011-2013, current cigarette smoking declined significantly in 26 states.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of findings
National Adult Tobacco Survey (NATS) (Centers for Disease 2016c)	2012-2013	The NATS was created to assess the prevalence of tobacco use, as well as the factors promoting and impeding tobacco use among adults. NATS also establishes a comprehensive framework for evaluating both the national and state-specific tobacco control programs (6). NATS was designed as a stratified, national, landline, and cell phone survey of non-institutionalized adults aged 18 years and older residing in the 50 states or D.C. It was developed to yield data representative and comparable at both national and state levels. The sample design also aims to provide national estimates for subgroups defined by gender, age, and race/ethnicity.	• Cigarette smokers were those who had smoked 100 or more cigarettes in their lifetime and smoked every day or some days.	• During 2012–2013, an estimated 18% of US adults smoked cigarettes every day or some days. By sex, the prevalence of cigarette smoking was higher in men than women (20 % vs 14.5%).
National Health and Nutrition Survey (NHANES) (Centers for Disease 2016d)	N.A.	NHANES is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations (9).	• N.A.	• Only datasets are available but no current report.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of findings
Current Population Survey (CPS) (Census 2016)		The Current Population Survey (CPS) is one of the oldest, largest, and most well-recognized surveys in the United States. It is immensely important, providing information on many of the things that define the US population as individuals and as a society (9). In addition to being the primary source of monthly labor force statistics, the CPS is used to collect data for a variety of other studies that keep the nation informed of the economic and social well-being of its people. This is done by adding a set of supplemental questions to the monthly basic CPS questions. Supplemental inquiries vary month to month and cover a wide variety of topics such as child support, volunteerism, health insurance coverage, and school enrollment. Supplements are usually conducted annually or biannually, but the frequency and recurrence of a supplement depend completely on what best meets the needs of the supplement's sponsor (9).	• N.A.	• Data not relevant for this report

N.A.: Not applicable

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

By far, the National Health Interview Survey (NHIS) (Centers for Disease 2016e) was the most exhaustive survey reporting prevalence by different demographic strata, followed by the National Adult Tobacco Survey (NATS), while the Behavioral Risk Factor Surveillance System (BRFSS) gave detailed information on state-level prevalence.

Summarizing the results briefly, the prevalence of cigarette smoking in adults has declined from 23.9% to 16.8% from 2005 to 2014. Also, most states have seen a decline in smoking rates since 2011, except for Alabama, Arkansas and Tennessee where the prevalence has actually increased, and in Idaho where there has been no change in prevalence rates. In survey-specific results, the NHIS reported an overall prevalence of smoking of 16.8% in 2014, while similar figures were reported by the NATS (18% for 2013) and BRFSS (19% for 2013). The National Survey on Drug Use and Health (NSDUH) (Hedden S 2015), however, reported higher smoking rates (28.4% in those aged 18-25 and 21.5% in those aged 26 or older) for the year 2013. Notably, the definition of smoking in the NHIS, NATS and BRFSS was the same (having at least smoked 100 cigarettes in a lifetime and reporting current daily or occasional smoking) while the NSDUH defined smoking as having smoked a whole or a part of a cigarette in the last 30 days.

Additionally, higher prevalence was reported in the 25-44 year old stratum (both NHIS and NATS reported a prevalence of 20% in this stratum), in populations that were American Indians or Alaskan Natives (NHIS 29.2%), had a GED diploma (NHIS 43.0% and NATS 41.0%), lived below the poverty level (NHIS 26.3% and NATS 26.4%), lived either in the Midwest (NHIS 20.7% and NATS 19.4%) or the South (NHIS 17.2% and NATS 19.5%), were uninsured (NHIS 27.9%) or had Medicaid only (29.1%), reported a disability (NHIS 21.9%), and finally among those identifying themselves as lesbian, gay, bisexual or transgender (NHIS 23.9%).

6.3.2.2.1.2.1.1 Summary of surveys assessing the prevalence of cigarette smoking in the US

National Health Interview Survey (NHIS)

The 2014 NHIS included 36,697 respondents aged ≥ 18 years. Current smokers were respondents who reported smoking ≥ 100 cigarettes during their lifetime and, at the time of interview, reported smoking every day or some days. Former cigarette smokers were respondents who reported smoking ≥ 100 cigarettes in their lifetime but currently did not smoke. Data were adjusted for differences in the probability of selection and nonresponse, and weighted to provide nationally representative estimates. Current smoking was assessed overall and by gender, age, race/ethnicity, education, poverty status, US census region, health insurance coverage, disability/limitation status and sexual orientation.

The percentage of US adults who smoke cigarettes declined from 20.9% in 2005 to 16.8% in 2014 (Jamal 2015). Among daily cigarette smokers, declines were observed in the percentage who smoked 20-29 cigarettes per day (from 34.9% to 27.4%) or ≥ 30 cigarettes per day (from 12.7% to 6.9%). In 2014, prevalence of cigarette smoking was higher among males, adults aged 25-44 years, multiracial and American Indian/Alaska Native populations, persons who have a General Education Development certificate (GED), live below the federal poverty level, live in the Midwest, are insured through Medicaid or are uninsured, have a disability or limitation, or are lesbian, gay, or bisexual

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

(Jamal 2015). A comparison of the prevalence rates from 2005 to 2014 by different strata is provided in Table 2.

National Survey on Drug Use and Health (NSDUH)

In the NSDUH (Hedden S 2015), current cigarette use was defined as smoking 'part of a cigarette' in the last 30 days and the data are presented by total tobacco (mixture of products used) and by age strata (12-17 year olds, 18-25 year olds or young adults, and aged 26 and above). In this section only adults will be discussed.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 2. Percentage of adults who were current cigarette smokers,* by selected characteristics – National Health Interview Survey, United States, 2005 and 2014 (Jamal 2015)

Characteristic	Men			Women			Total		
	2005 (n = 13, 762) Weighted % (95 % CI)	2014 (n = 16, 398) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 17, 666) Weighted % (95 % CI)	2014 (n = 20, 299) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 31, 428) Weighted % (95 % CI)	2014 (n = 36, 697) Weighted % (95 % CI)	% decline from 2005 to 2014
Overall	**23.9 (22.9-24.8)**	**18.8† (18.0-19.7)**	**21.1§**	**18.1 (17.4-18.9)**	**14.8† (14.0-15.7)**	**18.2§**	**20.9 (20.3-21.5)**	**16.8† (16.1-17.4)**	**19.8§**
Age group (years)									
18-24	28.0 (25.0-31.1)	18.5† (15.6-21.3)	34.2§	20.7 (18.3-23.1)	14.8† (10.6-19.1)	28.4	24.4 (22.4-26.4)	16.7† (14.0-19.3)	31.6§
25-44	26.8 (25.4-28.2)	22.9† (21.4-24.4)	14.4§	21.4 (20.2-22.6)	17.2† (16.0-18.5)	19.5§	24.1 (23.1-25.1)	20.0† (19.1-21.0)	16.8§
45-64	25.2 (23.7-26.7)	19.4† (17.8-20.9)	2.32§	18.8 (17.7-20.0)	16.8† (15.5-18.1)	10.9	21.9 (21.0-22.9)	18.0† (17.0-19.1)	17.7§
≥ 65	8.9 (7.6-10.2)	9.8 (8.5-11.0)	(9.5)¶	8.3 (7.3-9.3)	7.5 (6.4-8.5)	9.8	8.6 (7.8-9.3)	8.5 (7.7-9.3)	0.8
Race/Ethnicity									
Caucasian	24.0 (22.8-25.2)	19.3† (18.1-20.4)	19.8§	20.0 (19.1-20.9)	17.2† (16.0-18.5)	13.7§	21.9 (21.1-22.7)	18.2† (17.3-19.1)	16.9§
African American	26.7 (23.9-29.4)	22.1† (19.8-24.4)	17.1§	17.3 (15.5-19.0)	13.7† (12.1-15.2)	20.9§	21.5 (19.8-23.1)	17.5† (16.1-18.8)	18.6§
Hispanic	21.1 (19.3-23.0)	14.8† (13.2-16.4)	30.0§	11.1 (9.8-12.4)	7.6† (6.5-8.6)	31.7§	16.2 (15.1-17.4)	11.2† (10.2-12.2)	31.2§
AI/AN	37.5 (20.7-54.3)	25.6 (12.5-38.7)	31.7	26.8 (15.6-38.1)	32.5 (17.4-47.5)	(20.9)¶	32.0 (22.2-41.7)	29.2 (19.7-38.7)	8.6
Asian††	20.6 (15.7-25.5)	14.5 (11.1-17.8)	29.8§	6.1 (3.7-8.5)	5.1 (3.5-6.7)	16.5	13.3 (10.4-16.3)	9.5 (7.7-11.2)	29.1§
Multiple race	26.1 (16.3-36.0)	33.4 (23.4-43.3)	(27.7)¶	23.5 (14.8-32.2)	23.2 (15.6-30.8)	1.3	24.8 (17.7-31.8)	27.9 (21.7-34.1)	(12.6)¶

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Characteristic	Men			Women			Total		
	2005 (n = 13, 762) Weighted % (95 % CI)	2014 (n = 16, 398) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 17, 666) Weighted % (95 % CI)	2014 (n = 20, 299) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 31, 428) Weighted % (95 % CI)	2014 (n = 36, 697) Weighted % (95 % CI)	% decline from 2005 to 2014
Education level[§§]									
0-12 years (no diploma)	29.5 (27.2-31.8)	26.6 (24.2-29.0)	9.9	21.9 (20.0-23.7)	19.5 (17.5-21.5)	11.0	25.5 (24.0-27.1)	22.9 (21.3-24.5)	10.1
8th grade or less	21.0 (17.7-24.3)	16.4 (13.2-19.6)	21.9	13.4 (11.1-15.6)	11.3 (8.9-13.8)	15.2	17.1 (15.1-19.0)	13.7 (11.6-15.7)	19.7
09th – 11th grade	36.8 (33.3-40.2)	33.3 (29.4-37.3)	9.3	29.0 (26.1-31.8)	25.9 (22.5-29.4)	10.4	32.6 (30.4-34.9)	29.5 (26.9-32.2)	9.5
12th grade (no diploma)	30.2 (23.5-36.9)	29.8 (23.2-36.3)	1.4	22.2 (16.9-27.5)	21.0 (15.1-26.8)	5.4	26.0 (21.8-30.2)	25.7 (21.4-30.1)	1.0
GED	47.5 (41.5-53.6)	46.6 (40.2-53.0)	2.0	38.8 (33.6-44.0)	38.9 (32.9-44.8)	(0.1) [¶]	43.2 (39.1-47.4)	43.0 (38.7-47.4)	0.5
High School graduate	28.8 (27.0-30.7)	24.7 (22.8-26.6)	14.4	20.7 (19.3-22.2)	18.8 (16.8-20.8)	9.4	24.6 (23.4-25.7)	21.7 (20.3-23.0)	11.8
Some college	26.2 (24.0-28.4)	19.8[†] (17.7-21.9)	24.4[§]	21.1 (19.2-22.9)	19.6 (17.6-21.5)	7.2	23.5 (22.1-24.9)	19.7[†] (18.3-21.1)	16.3[§]
Associate degree	26.1 (23.2-28.9)	21.2[†] (16.3-26.1)	18.5	17.1 (15.0-19.3)	13.7 (11.8-15.6)	20.1	20.9 (19.2-22.6)	17.1[†] (14.5-19.6)	18.4[§]
Undergraduate degree	11.0 (10.5-13.3)	9.1[†] (7.7-10.5)	23.6[§]	9.6 (8.3-10.8)	6.9[†] (5.8-8.0)	28.1[§]	10.7 (9.8-11.6)	7.9[†] (7.1-8.8)	26.0[§]
Graduate degree	6.9 (5.3-8.5)	5.8 (4.5-7.1)	16.1	7.4 (5.9-8.8)	5.0 (3.8-6.3)	31.6[§]	7.1 (6.0-8.3)	5.4[†] (4.5-6.3)	24.0[§]
Poverty Status[¶¶]									
At or above poverty level	23.7 (22.6-24.7)	17.5[†] (16.5-18.4)	26.2[§]	17.6 (16.8-18.5)	13.1[†] (12.2-14.0)	25.8[§]	20.6 (19.9-21.3)	15.2[†] (14.6-15.9)	26.1[§]
Below poverty level	34.3 (31.0-37.5)	30.4 (27.5-33.2)	11.3	26.9 (24.5-29.3)	23.3[†] (21.3-25.4)	13.2[§]	29.9 (27.9-31.9)	26.3[†] (24.6-28.1)	11.9[§]
Unspecified	21.2 (19.2-23.2)	14.9[†] (11.8-17.9)	29.8[§]	16.1 (14.8-17.5)	17.7 (12.0-23.3)	(9.6) [¶]	18.4 (17.2-19.6)	16.4 (13.0-19.9)	10.8

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Characteristic	Men			Women			Total		
	2005 (n = 13, 762) Weighted % (95 % CI)	2014 (n = 16, 398) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 17, 666) Weighted % (95 % CI)	2014 (n = 20, 299) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 31, 428) Weighted % (95 % CI)	2014 (n = 36, 697) Weighted % (95 % CI)	% decline from 2005 to 2014
US Census region* **									
Northeast	20.7 (18.6-22.9)	17.1† (14.9-19.3)	17.5	17.9 (16.4-19.5)	13.6† (11.8-15.3)	24.3§	19.2 (17.8-20.6)	15.3† (13.9-16.7)	20.5§
Midwest	27.3 (25.3-29.3)	21.7† (19.7-23.7)	20.5§	21.3 (19.8-22.8)	19.7† (17.2-22.2)	7.2	24.2 (23.0-25.3)	20.7† (18.9-22.4)	14.4§
South	25.3 (23.6-27.0)	19.8† (18.5-21.0)	22.0§	18.5 (17.3-19.7)	14.9† (13.6-16.3)	19.2§	21.8 (20.6-23.0)	17.2† (16.3-18.1)	20.9§
West	20.1 (18.3-21.9)	15.8† (14.0-17.5)	21.4§	13.9 (12.6-15.2)	10.6† (9.5-11.7)	24.0§	17.0 (16.0-18.0)	13.1† (12.1-14.2)	22.7§
Health insurance coverage†††									
Medicaid only	38.0 (32.7-43.2)	32.7 (28.5-36.8)	14.0	33.5 (30.2-36.7)	27.1† (24.6-29.5)	19.1§	34.9 (32.1-37.8)	29.1† (27.0-31.2)	16.7§
Medicare only	13.8 (10.9-16.7)	15.5 (13.2-17.8)	(12.6)¶	11.6 (9.4-13.8)	10.1 (8.3-11.9)	12.8	12.5 (10.7-14.3)	12.5 (10.9-14.0)	0.2
Private insurance	19.7 (18.7-20.8)	14.3† (13.3-15.4)	27.4§	15.1 (14.4-15.9)	11.6† (10.5-12.7)	23.3§	17.3 (16.7-18.0)	12.9† (12.2-13.7)	25.4§
Other public insurance	32.8 (27.1-38.4)	26.0 (21.5-30.5)	20.5	24.2 (19.7-28.7)	16.1† (12.3-20.0)	33.4§	28.2 (24.6-31.9)	21.1† (18.3-24.0)	25.1§
Uninsured	38.0 (35.5-40.5)	31.5† (28.8-34.2)	17.1§	27.6 (25.4-29.7)	23.5 (21.2-25.9)	14.6	33.3 (31.5-35.0)	27.9† (26.0-39.7)	16.2§
Disability/Limitation§§§									
Yes	---¶¶¶	25.2 (22.6-27.8)	---¶¶¶	---¶¶¶	19.3 (17.4-21.2)	---¶¶¶	---¶¶¶	21.9 (20.3-23.5)	---¶¶¶
No	---¶¶¶	18.9 (17.8-20.1)	---¶¶¶	---¶¶¶	13.6 (12.5-14.7)	---¶¶¶	---¶¶¶	16.1 (15.2-16.9)	---¶¶¶

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Characteristic	Men			Women			Total		
	2005 (n = 13, 762) Weighted % (95 % CI)	2014 (n = 16, 398) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 17, 666) Weighted % (95 % CI)	2014 (n = 20, 299) Weighted % (95 % CI)	% decline from 2005 to 2014	2005 (n = 31, 428) Weighted % (95 % CI)	2014 (n = 36, 697) Weighted % (95 % CI)	% decline from 2005 to 2014
Sexual Orientation**									
Straight	---¶¶¶	18.7 (17.8-19.6)	---¶¶¶	---¶¶¶	14.6 (13.7-15.6)	---¶¶¶	---¶¶¶	16.6 (15.9-17.3)	---¶¶¶
Gay/Lesbian/Bisexual	---¶¶¶	23.1 (16.4-29.8)	---¶¶¶	---¶¶¶	24.5 (19.1-29.9)	---¶¶¶	---¶¶¶	23.9 (19.8-27.9)	---¶¶¶

Abbreviations: CI = confidence interval; GED = General Education Development certificate. * Persons who reported smoking ≥100 cigarettes during their lifetime and who, at the time of interview, reported smoking every day or some days. Excludes 296 (2005) and 121 (2013) respondents whose smoking status was unknown. † Denotes significant linear trend during 2005–2013 ($p<0.05$), adjusted for sex, age, and race/ethnicity as applicable. § Excludes 45 (2005) and 73 (2013) respondents of unknown race. Unless indicated otherwise, all racial/ethnic groups are non-Hispanic; Hispanics can be of any race. ¶ Does not include Native Hawaiians or Other Pacific Islanders. ** Among persons aged ≥25 years. Excludes 339 (2005) and 155 (2013) persons whose educational level was unknown. †† Family income is reported by the family respondent who might or might not be the same as the sample adult respondent from whom smoking information is collected. 2005 estimates are based on reported family income and 2004 poverty thresholds published by the US Census Bureau, and 2013 estimates are based on reported family income and 2012 poverty thresholds published by the US Census Bureau. §§ *Northeast:* Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont. *Midwest:* Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin. *South:* Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia. *West:* Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming. ¶¶ Disability/limitation was defined based on self-reported presence of selected impairments, including vision, hearing, cognition, and movement. Limitations in performing activities of daily living was defined based on response to the question, "Because of a physical, mental, or emotional problem, does [person] need the help of other persons with personal care needs, such as eating, bathing, dressing, or getting around inside this home?" Limitations in performing instrumental activities of daily living was defined based on response to the question, "Because of a physical, mental, or emotional problem, does [person] need the help of other persons in handling routine needs, such as everyday household chores, doing necessary business, shopping, or getting around for other purposes?" Any disability/limitation was defined as a "yes" response pertaining to at least 1 of the disabilities/limitations listed (i.e., vision, hearing, cognition, movement, activities of daily living, or instrumental activities of daily living). In 2013, the American Community Survey disability questions were asked of a random half of families at the end of the family interview, with proxy reporting permitted for family members not present during the interview. For population estimates, the sample adult weight was doubled to account for the half of respondents for whom the disability questions were not asked. *** Questions for pertaining to disabilities/limitations and sexual orientation were not included in the 2005 National Health Interview Survey. ††† Response option were ''straight, that is, not gay'' for men, ''straight, that is, not gay or lesbian'' for women, ''gay'' for men, ''gay or lesbian'' for women, and "bisexual" for either men or women.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

In 2014, about 4.3 million young adults aged 18 to 25 years were daily cigarette smokers (43% of those who were current cigarette smokers), while 27.9 million adults aged 26 or older smoked cigarettes daily (63.3% of those who reported smoking) (Hedden S 2015). The percentage of young adult current smokers who smoked cigarettes daily in 2014 was lower than the percentages in most years from 2002 to 2010, but no change was seen between 2011 and 2014. While at least half of the young adults who were current smokers in 2002 to 2005 smoked cigarettes every day (ranging from 50.1 to 52.7 percent), about 2 in 5 young adults in 2014 who were current cigarette users smoked cigarettes daily. The percentage of young adult daily smokers who smoked 1 or more packs of cigarettes per day was lower in 2014 (22.5 percent) than in 2002 to 2011.

Despite the decline in every day smoking rates, daily smokers represented nearly two thirds of current smokers in this age group in 2014. More detailed information can be seen in Table 3.

Behavioral Risk Factor Surveillance System (BRFSS)

The BRFSS survey (Centers for Disease 2016a, Nguyen 2015) assessed prevalence of current cigarette smoking and current smokeless tobacco use. Current cigarette smoking was assessed by two questions: “Have you smoked at least 100 cigarettes in your entire life?” and “Do you now smoke cigarettes every day, some days, or not at all?” Respondents who reported smoking at least 100 cigarettes in their lifetime and who reported currently smoking “every day” or “some days” were classified as current cigarette smokers.

State-specific point prevalence for current cigarette smoking and current smokeless tobacco use was calculated for all 50 US States and the District of Columbia. Estimates were weighted to adjust for differences in the probability of selection and nonresponse. The relative percent change (RPC) in the prevalence during 2011–2013 was also calculated. Logistic regression was used to assess trends over time adjusting for sex, age, and race/ethnicity; the Wald test was used to determine statistical significance ($p<0.05$). The analysis was restricted to 2011–2013 because of a change in the weighting methodology and the addition of cell phone samples beginning in 2011. Detailed results can be found in Table 4.

Current cigarette smoking ranged from 11.8% (Utah) to 29.0% (Kentucky) in 2011 and from 10.3% (Utah) to 27.3% (West Virginia) in 2013 (Table 5). During 2011–2013, cur-rent cigarette smoking declined in 26 states: Arizona, Florida, Georgia, Hawaii, Illinois, Indiana, Kansas, Kentucky, Maine, Maryland, Michigan, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Mexico, Oklahoma, Oregon, Rhode Island, South Dakota, Texas, Utah, Vermont, Wisconsin, and Wyoming. No marked changes were observed in any other state (Nguyen 2015).

National Adult Tobacco Survey (NATS)

The last survey assessing the prevalence of cigarette smoking in US adults that will be discussed is the NATS (Centers for Disease 2016c). The survey assessed use of the following tobacco and nicotine containing products: cigarettes, cigars/cigarillos/filtered little cigars, regular pipes, water pipes/hookah, e-cigarettes, chewing tobacco/snuff/dip, snus, and dissolvable tobacco products. In this section, only cigarette smoking will be discussed. Based on documented differences in the patterns of tobacco and nicotine

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

containing products use, NATS assessed varying thresholds of lifetime use to separate established users from experimenters and nonusers. Usage thresholds (to define ever use) for the different tobacco and nicotine containing products were as follows: cigarettes (≥100 times), cigars/cigarillos/filtered little cigars (≥50 times), regular pipes (≥50 times), water pipes/hookahs (≥1 time), chewing tobacco/snuff/dip (≥20 times), e-cigarettes (≥1 time), snus (≥1 time), and dissolvable tobacco products (≥1 time). Respondents who met the respective thresholds were then asked if they now used the product "every day," "some days," or "not at all." A response option of "rarely" was also provided for all tobacco products other than cigarettes based on cognitive testing, suggesting that some users of these other products did not consider "some days" or "not at all" to accurately reflect their use pattern.

Data were weighted to provide nationally representative estimates. Two definitions were used to assess the effect of occasional tobacco use on estimates of current tobacco use: 1) every day or some days, and 2) every day, some days, or rarely.

During 2012–2013, an estimated 18% of US adults smoked cigarettes every day or some days. By sex, the prevalence of cigarette smoking was higher in men than women (20 % vs 14.5%). By age, the prevalence of cigarette smoking was higher in those aged 25-44 (21.8%) and lowest in those aged ≥ 65 years (7.8%). By race and/or ethnicity the prevalence of cigarette smoking was higher in those reporting other race or ethnicity (27.9%) and lowest in Asian non-Hispanics (7.6%) compared to Caucasians (17.2%) and Hispanics (14.6). By US Census region, the prevalence of cigarette smoking was higher in residents of the Midwest and South (19.4% and 19.5% respectively) and lowest in the Northeast (16.0%). Prevalence by education was higher in those who had a GED (41%) as their highest education and lowest among those with a graduate degree (4.9%). Prevalence of cigarette smoking was highest in those with households with an income below 20,000 USD (26.4%) and lowest in those households with an income higher than 100,000 USD (9.3%). Finally, the smoking prevalence was higher in those from the Lesbian, Gay, Bisexual and Transgender (LGBT) community than those who were heterosexual (27.7% vs. 17.3%) (Table 5).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 3. Tobacco Product Use in the Past Month in Adults by Age Category in the NSDUH 2002-2014 (Hedden S 2015)

Substance	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Aged 18-25													
Cigarettes	40.8*	40.2*	39.5*	39.0*	38.5*	36.2*	35.7*	35.8*	34.3*	33.5*	31.8*	30.6*	28.4
	(0.48)	(0.47)	(0.49)	(0.47)	(0.48)	(0.49)	(0.45)	(0.48)	(0.47)	(0.47)	(0.47)	(0.46)	(0.53)
Daily Use	51.8 *	52.7*	51.6*	50.1*	48.8*	49.2*	47.8*	45.3	45.8*	45.3	45.1	43.1	43.0
	(0.72)	(0.69)	(0.72)	(0.73)	(0.77)	(0.76)	(0.81)	(0.80)	(0.80)	(0.86)	(0.88)	(0.83)	(0.91)
Smoked 1+ pack per day[1]	39.1*	37.1*	34.9*	36.9*	34.4*	32.9*	31.6*	29.5*	27.3*	26.1*	25.1	22.3	22.5
	(0.93)	(0.88)	(0.86)	(0.93)	(0.93)	(0.92)	(0.91)	(0.92)	(0.94)	(0.97)	(0.90)	(0.90)	(1.16)
Aged 26+													
Cigarettes	25.2*	24.7*	24.1*	24.3*	24.7*	24.1*	23.8*	23.0*	22.8*	21.9	22.4	21.6	21.5
	(0.42)	(0.41)	(0.39)	(0.39)	(0.40)	(0.40)	(0.41)	(0.39)	(0.38)	(0.39)	(0.40)	(0.38)	(0.32)
Daily Use	68.8*	68.0*	67.8*	68.9*	67.9*	66.3*	67.0*	67.2*	64.8	66.5*	66.0*	64.9	63.3
	(0.87)	(0.86)	(0.80)	(0.79)	(0.74)	(0.83)	(0.86)	(0.84)	(0.86)	(0.88)	(0.85)	(0.88)	(0.72)
Smoked 1+ pack per day[1]	57.1*	58.0*	59.2*	55.1*	54.5*	55.1*	53.0*	49.4*	48.8*	47.4*	45.2	44.7	43.3
	(1.12)	(0.99)	(1.05)	(1.02)	(1.00)	(1.06)	(1.10)	(1.16)	(1.09)	(1.05)	(1.09)	(1.15)	(0.93)

NOTE: Estimates shown are percentages with standard errors included in parentheses.
* Difference between estimate and 2014 estimate is statistically significant at the 0.05 level.
1 Respondents with missing data for number of cigarettes smoked per day were excluded from the analysis.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 4. State-specific prevalence of current cigarette smoking among adults aged ≥ 18 years, by state/territory –BRFSS, US, 2011-2013 (Nguyen 2015)

	Cigarette smoking						
	2011		2012		2013		
State/Territory	%	(95%) CI	%	(95%) CI	%	(95%) CI	RPC[§]
Alabama	24.3	(22.9-25.8)	23.8	(22.4-25.2)	21.5	(19.9-23.1)	11.5
Alaska	22.9	(21.0-25.0)	20.5	(18.9-22.3)	22.6	(20.8-24.4)	-1.3
Arizona	19.3	(17.2-21.3)	17.1	(15.6-18.6)	16.3	(14.4-18.4)	-15.5[¶]
Arkansas	27.0	(24.8-29.2)	25.0	(23.4-26.8)	25.9	(24.1-27.8)	7.1
California	13.7	(12.9-14.40	12.6	(11.8-13.4)	12.5	(11.7-13.5)	-8.8
Colorado	18.3	(17.2-19.4)	17.7	(16.8-18.7)	17.7	(16.8-18.6)	-3.3
Connecticut	17.1	(15.8-18.6)	16.0	(14.9-17.20)	15.5	(14.3-16.8)	-9.4
Delaware	21.8	(19.9-23.6)	19.7	(18.2-21.3)	19.6	(18.0-21.2)	-10.1
District of Columbia	20.8	(18.8–22.9)	19.6	(17.4–22.0)	18.8	(16.9–20.9)	-9.6
Florida	19.3	(18.2–20.5)	17.7	(16.3–19.2)	16.8	(16.0–17.8)	-13.0[¶]
Georgia	21.2	(19.9-22.6)	20.4	(18.9-22.0)	18.8	(17.6-20.1)	-11.3[¶]
Hawaii	16.8	(15.5-18.3)	14..6	(13.3-15.9)	13.3	(12.2-14.5)	-20.8[¶]
Idaho	17.2	(15.6-18.9)	16.4	(14.7-18.3)	17.2	(15.7-18.8)	0.0
Illinois	20.9	(19.2-22.7)	18.6	(17.0-20.3)	18.0	(16.6-19.6)	-13.9[¶]
Indiana	25.6	(24.3-27.0)	24.0	(22.8-25.2)	21.9	(20.8-23.1)	-14.5[¶]
Iowa	20.4	(19.1-21.6)	18.1	(17.0-19.3)	19.5	(18.3-20.7)	-4.4
Kansas	22.0	(21.2-22.8)	19.4	(18.4-20.4)	20.0	(19.3-20.7)	-9.1[¶]
Kentucky	29.0	(27.5-30.5)	28.3	(26.9-29.7)	26.5	(25.1-27.8)	-8.6[¶]
Louisiana	25.7	(24.3-27.2)	24.8	(23.2-26.3)	23.5	(21.5-25.6)	-8.6
Maine	22.8	(21.7-23.9)	20.3	(19.2-21.4)	20.2	(19.0-21.5)	-11.4[¶]
Maryland	19.1	(17.8-20.5)	16.2	(15.0-17.4)	16.4	(15.3-17.5)	-14.1[¶]
Massachusetts	18.2	(17.3-19.2)	16.4	(15.6-17.2)	16.6	(15.6-17.7)	-8.8
Michigan	23.3	(22.0-24.6)	23.3	(22.1-24.6)	21.4	(20.3-22.5)	-8.2[¶]
Minnesota	19.1	(18.1-20.1)	18.8	(17.8-19.8)	18.0	(16.9-19.3)	-5.8
Mississippi	26.0	(24.6-27.4)	24.0	(22.5-25.5)	24.8	(23.3-26.4)	-4.6[¶]
Missouri	25.0	(23.5-26.6)	23.9	(22.4-25.5)	22.1	(20.6-23.6)	-11.6[¶]
Montana	22.1	(20.8-23.4)	19.7	(18.6-20.9)	19.0	(17.9-20.1)	-14.0[¶]
Nebraska	20.0	(19.3-20.7)	19.7	(18.9-20.6)	18.5	(17.5-19.6)	-7.5[¶]
Nevada	22.9	(21.0- 25.0)	18.1	(16.6-19.8)	19.4	(17.4-21.5)	-15.3[¶]

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

	Cigarette smoking						
	2011		2012		2013		
State/Territory	%	(95%) CI	%	(95%) CI	%	(95%) CI	RPC[§]
New Hampshire	19.4	(18.0-20.9)	17.2	(15.8-18.6)	16.2	(15.0-17.6)	-16.57.6)
New Jersey	16.8	(15.9-17.8)	17.3	(16.4-18.3)	15.7	(14.7-16.7)	-6.5[¶]
New Mexico	21.5	(20.3-22.7)	19.3	(18.2-20.5)	19.1	(17.9-20.3)	-11.2[¶]
New York	18.1	(16.9-19.4)	16.2	(14.9-17.6)	16.6	(15.5-17.8)	-8.3
North Carolina	21.8	(20.5-23.1)	20.9	(19.9-21.9)	20.3	(19.1-21.5)	-6.9
North Dakota	21.9	(20.3-26.4)	21.2	(19.6-22.9)	21.2	(19.8-22.7)	-3.2
Ohio	25.1	(23.8-26.4)	23.3	(22.2-24.4)	23.4	(22.2-24.6)	-6.8
Oklahoma	26.1	(24.7-27.6)	23.3	(22.0-24.6)	23.7	(22.4-25.0)	-9.2[¶]
Oregon	19.7	(18.3-21.2)	17.9	(16.4-19.4)	17.3	(15.9-18.8)	-12.2[¶]
Pennsylvania	22.4	(21.3-23.6)	21.4	(20.4-22.3)	21.0	(19.9-22.0)	-6.2
Rhode Island	20.0	(18.6-21.5)	17.4	(16.0-18.9)	17.4	(16.1-18.8)	-13.0[¶]
South Carolina	23.1	(21.9-24.4)	22.5	(21.4-23.7)	22.0	(20.8-23.2)	-4.8
South Dakota	23.0	(21.2-25.0)	22.0	(20.5-23.5)	19.6	(18.1-21.2)	-14.8[¶]
Tennessee	23.0	(20.7-25.5)	24.9	(23.4-26.4)	24.3	(22.6-26.1)	5.7
Texas	19.2	(18.0-20.4)	18.2	(17.0-19.4)	15.9	(14.8-17.0)	-17.2[¶]
Utah	11.8	(11.0-12.7)	10.6	(9.8-11.4)	10.3	(9.6-11.1)	-12.7[¶]
Vermont	19.1	(17.7-20.5)	16.5	(15.2-17.9)	16.6	(15.4-17.9)	-13.1[¶]
Virginia	20.9	(19.4-22.5)	19.0	(17.7-20.3)	19.0	(17.9-20.2)	-9.1
Washington	17.5	(16.4-18.7)	17.2	(16.3-18.1)	16.1	(15.1-17.1)	-8.0
West Virginia	28.6	(27.0-30.3)	28.2	(26.7-29.7)	27.3	(25.9-28.7)	-4.5
Wisconsin	20.9	(19.2-22.7)	20.4	(18.7-22.1)	18.7	(17.2-20.3)	-10.5[¶]
Wyoming	23.0	(21.5-24.6)	21.8	(19.9-23.7)	20.6	(19.1-22.2)	-10.4[¶]
Median prevalence**	**21.2**		**19.6**		**19.0**		**-10.4[¶]**

Abbreviations: CI = confidence interval; RPC = relative percent change (see below).

* Persons aged ≥18 years who reported having smoked ≥100 cigarettes during their lifetime and smoke every day or some days at the time of survey.

† Persons aged ≥18 years who reported currently using chewing tobacco, snuff, or snus (a small pouch of smokeless tobacco) every day or some days at the time of survey.

§ RPC was calculated by dividing the difference between the 2013 and 2011 estimates by the 2011 estimates, and expressed as a percentage.

¶ $p<0.05$ for trend (2011–2013) in multivariate logistic regression model adjusted for sex, age, and race/ethnicity.

** Median prevalence across all 50 US states and the District of Columbia.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 5. Percentage of persons aged ≥18 years who were 'everyday' or 'some days' cigarette users and selected characteristics – National Adult Tobacco Survey, United States, 2012-2013 (Agaku 2014b)

	Cigarette Smoking[§]	
Characteristic	**%**	**(95% CI)**
Overall	18.0	(17.5-18.5)
Sex		
Men	20.0	(19.8-21.4)
Women	14.5	(13.9-15.1)
Age group (yrs.)		
18-24	18.5	(16.9-20.0)
25-44	21.8	(20.9-22.8)
45-64	19.2	(18.5-19.9)
≥ 65	7.8	(7.3-8.3)
Race/Ethnicity		
Caucasian, Non-Hispanic	17.2	(16.6-17.7)
African American, Non-Hispanic	19.7	(18.0-21.4)
Asian, Non-Hispanic	7.6	(5.3-10.0)
Other, Non-Hispanic	27.9	(25.7-30.0)
Hispanic	14.6	(13.2-15.9)
US Census region[†††]		
Northeast	16.0	(16.0-17.9)
Midwest	19.4	(18.3-20.5)
South	19.5	(18.6-20.3)
West	16.4	(18.8-21.1)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Characteristic	Cigarette Smoking[§] %	(95% CI)
Education		
0-12 years (no diploma)	25.6	(23.7-27.4)
GED	41.0	(36.7-45.3)
High School diploma	20.2	(19.2-21.2)
Some college, no diploma	20.0	(18.8-21.1)
Associate degree	18.0	(16.8-19.1)
Undergraduate degree	8.2	(7.6-8,8)
Graduate degree	4.9	(4.3-5.4)
Annual household income (USD)		
< 20,000	26.4	(24.7-28.1)
20,000-49,999	22.6	(21.6-23.6)
50,000-99,999	15.7	(14.8-16.6)
≥100,000	9.3	(8.5-10.1)
Unspecified	18.0	(16.9-19.1)
Sexual Orientation		
Heterosexual/straight	17.3	(16.8-17.8)
LGBT	27.7	(24.7-30.7)
Unspecified	20.4	(18.9-22.0)

Abbreviations: CI = confidence interval; GED = General Education Development certificate; USD = US dollars; LGBT = lesbian, gay, bisexual, or transgender. § Reported smoking at least 100 cigarettes during their lifetime and now smoked "every day" or "some days. ††† *Northeast*: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont. *Midwest*: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin. *South*: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia. *West*: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.1.2.2 Smoking in youth populations

Out of the 10 CDC surveys, 4 reported relevant information for youth populations (Centers for Disease 2016f, Centers for Disease 2016i, Centers for Disease 2016j, Johnston 2014) and 1 reported results from both adult and youth populations (Hedden S 2015). Additionally, 1 other survey was identified through the literature searches (Kaufman 2015). A summary of the characteristics of these surveys can be found below in Table 6. The prevalence of smoking has declined from 20.7% in 1991(Johnston 2014) to 13.0-17.7% in 2002 (Hedden S 2015, Johnston 2014) to 4.9-7.0% in 2014 (Hedden S 2015, Johnston 2014). In survey-specific findings, the Young Risk Behavior Surveillance System (YRBSS) was by far the most informative of the surveys as it reported prevalence using different definitions of smoking, age groups (defined as grades) and race/ethnicity (Table 7). As was the case for adults, males were more commonly smokers (National Youth Tobacco Survey [NYTS], 10.6% defined as past 30-day smokers). For youth, however, Caucasians were more likely to be smokers compared to other races/ethnicities (NYTS 10.8% in high school students and 18.6% identified as current smokers in the YRBSS). For middle school students, on the other hand, Hispanics were more prone to be smokers (3.7% in the NYTS) compared to Caucasians (2.2%) and African Americans (1.7%). The Monitoring the Future study (MTF) (2015) (Johnston 2016) found that youth from the 8^{th} to 12^{th} grade had a lifetime smoking rate of 21.1%, a 30-day prevalence of 9.6% and a daily use prevalence of 4.7%. The NYTS (2013) study reported a prevalence of smoking (as smoking at least 1 cigarette during the past 30 days) of 2.5% in middle school students (grades 6 to 8) and 9.2% in high school students (grades 9 to 12). The YRBSS (2011) reported the prevalence of current smoking (in the last 30 days) to be 15.7% in high school students, while ever smoking was reported by 41.1%. Add Health (2014) (Kaufman 2015) reported smoking (any use in the past 30 days) as 48.8% in high school students, while finally the NSDUH (Hedden S 2015) reported a prevalence of cigarette use (in the last 30 days) of 4.9% in those aged 12-17 years. Out of the 4.9% who reported ever use, 24.1% were daily users. Detailed results from each survey are found below.

Monitoring the Future Surveys (MTF)

In 2015 about 44,900 students in 382 secondary schools participated in the study, with sample sizes in 8th, 10th, and 12th grades of about 15,000, 16,100, and 13,700, respectively. The main finding reported by the MTF is that cigarette smoking has continued its long decline and is now at the lowest level in the history of the survey.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 6. Characteristics of surveys assessing cigarette smoking in youth

Survey	Period	Sampling	Definitions	Summary of Results
Monitoring the Future (MTF) (Centers for Disease 2016b)	1976-2015	The MTF s an ongoing study of the behaviors, attitudes, and values of American secondary school students, college students, and young adults. Each year, a total of approximately 50,000 8th, 10th and 12th grade students are surveyed (12th graders since 1975, and 8th and 10th graders since 1991) (7). In addition, annual follow-up questionnaires are mailed to a sample of each graduating class for a number of years after their initial participation. The Monitoring the Future Study has been funded under a series of investigator-initiated competing research grants from the National Institute on Drug Abuse, a part of the National Institutes of Health. This longitudinal survey is conducted at the Survey Research Center in the Institute for Social Research at the University of Michigan.	• Current use was defined as 30-day prevalence of cigarette.	• Cigarette smoking has continued their long declines and is now at the lowest levels in the history of the survey. Additionally, the new product of e-cigarettes, which has made rapid inroads among adolescents in recent years, has a 30-day prevalence higher than the prevalence of tobacco cigarette smoking, though its prevalence did not rise further in 2015. • One important new finding in 2015 is that very few of the students using electronic vaporizers are using to help them quit smoking regular cigarettes; only 5%, 7%, and 10% of the users in the three grades indicate this as one of the reasons for their use. More than half say they wanted "to experiment—see what it's like" and around one-third gave the reason "because it tastes good." (Johnston 2014)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of Results
National Survey on Drug Use and Health (NSDUH) (Hedden S 2015)	2002-2014	NSDUH is a face-to-face household interview survey that is conducted in two phases: the screening and the interview phase. The interviewer conducts a screening of the eligible household with an adult resident (aged 18 or older) in order to determine whether 0, 1, or 2 residents aged 12 or older should be selected for the interview. NSDUH collects data using audio computer-assisted self-interviewing, in which respondents read or listen to the questions on headphones and then enter their answers directly on the NSDUH laptop computer. In 2014, screening was completed at 127,605 addresses, and 67,901 completed interviews were obtained, including 17,046 interviews from adolescents aged 12 to 17 and 50,855 interviews from adults aged 18 or older. Weighted response rates for household screening and for interviewing were 81.9 and 71.2 percent, respectively, for an overall response rate of 58.3 percent for people aged 12 or older. Weighted interview response rates were 80.0 percent for adolescents and 70.3 percent for adults.	• Cigarette use is defined as smoking 'part of a cigarette' in the last 30 days and the data is presented by total tobacco (mixture of products used) and by age strata (12-17 year olds, 18-25 year olds or young adults and aged 26 and above). The NSDUH also reports daily cigarette use and the prevalence of those smoking 1 pack or more a day.	• Among adolescents aged 12 to 17 in 2014, 1.7 million used tobacco products in the past month, including 1.2 million current cigarette smokers. These 2014 numbers represent 7.0 percent of adolescents who were current tobacco users and 4.9 percent who were current cigarette smokers.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of Results
National Youth Tobacco Survey (NYTS) (Centers for Disease 2016f)	2013	The survey was designed to provide national data on long-term, intermediate, and short-term indicators key to the design, implementation, and evaluation of comprehensive tobacco prevention and control programs. The NYTS also serves as a baseline for comparing progress toward meeting selected Healthy People 2020 goals for reducing tobacco use among youth. The NYTS provides nationally representative data about middle and high school youth's tobacco-related beliefs, attitudes, behaviors, exposure to pro- and anti-tobacco influences. This Survey datasets are available for public use, so that researchers and public health managers can explore the data in detail. In addition, states can compare their estimates of prevalence of youth tobacco use with national data (5). The latest dataset available is the one for 2014. Data from this survey will be presented in this report.	• Current use of each tobacco product was (including cigarettes) was defined as using a product ≥ 1 day during the past 30 days.	• In 2013, more than 1 in 5 high school students (22.9%) and more than 1 in 20 middle school students (6.5%) reported using a tobacco product on 1 or more days during the past 30 days. In addition, nearly half of high school students (46.0%) and almost 1 in 5 of middle school students (17.7%) had ever used tobacco.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of Results
Youth Tobacco Survey (YTS) (Centers for Disease 2016j)	2011	The YTS collects data from students in grades 6 through 12. Individual State Departments of Health plan and implement the survey with assistance from the CDC staff. The YTS is intended to enhance the capacity of state agencies and organizations to design, implement, and evaluate tobacco prevention and control programs for the purposes of preventing young people from using tobacco and helping current users quit (Centers for Disease 2016j).	• N.A.	• No current report is available.
Young Probability Behavior Surveillance System (YRBSS) (Centers for Disease 2016i)	2013	The YRBSS monitors six types of health-probability behaviors that contribute to the leading causes of death and disability among youth in high school ages (9th to 12th grades). YRBSS also measures the prevalence of obesity and asthma among youth and young adults and it includes a national school-based survey conducted by CDC and state, territorial, tribal, and local surveys conducted by state, territorial, and local education and health agencies and tribal governments (Centers for Disease 2016i)	• Smoking is defined as ever smoking (smoking a whole cigarette before age 13 years), current cigarette use (had smoked on at least 1 day during the 30 days before the survey), current frequent use of cigarettes (smoking 20 or more days during the 30 days before the survey), current frequent use of cigarettes (smoking 20 or more days during the 30 days before the survey), smoking more than 10 cigarettes a day, ever daily smoking (ever smoking cigarettes daily for 30 continuous days) and current daily smoking (smoking cigarettes on all 30 days during the 30 days before the survey).	• Results from the 2013 national YRBS indicated that 41.1% of students had ever tried cigarette smoking (even on or two puffs). The prevalence of having ever smoked cigarettes was higher among male (42.5%) than female (39.6%) students.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of Results
Add Health (Kaufman 2015)	2008-2009	Add Health is a study of adolescent health-related behaviors (Kaufman 2015). The nationally based sampling frame involved the selection of a random sample of 80 high schools (public, private, and parochial) and 54 associated feeder schools throughout the US and is representative of US schools with respect to region, urbanicity, school size, school type, and ethnic distribution. All students were eligible for selection into the core in-home sample (University of North Carolina and Carolina Population Center). Data were collected in participants' homes. A computer-assisted interview was conducted by a trained interviewer. For sensitive topics, participants responded via audio computer-assisted self-interview. A sample of 20,774 male and female adolescents in grades 7 through 12 were selected to participate in the initial in-home survey conducted between April and December 1995 (Wave I). Participants were interviewed at Wave II (n = 14,738) approximately 1 year later (April–August 1996), at Wave III (n = 15,197) approximately 6 years later (August 2001–April 2002), and at Wave IV (n = 15,701) approximately 13 years later (January 2008–February 2009). Wave II surveyed those from the Wave I in-home interviews, but excluded those who were in the 12th grade at	• Participants were asked questions regarding the use of smokeless tobacco, cigarette smoking (during the past 30 days, on how many days did you smoke cigarettes?" and the responses were dichotomized to indicate use –yes or no- for each wave).	• 48% of the population reported using cigarettes within 30 days during at least 1 wave and women were more likely to report smoking cigarettes (51.9% vs. 45.7%).

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Sampling	Definitions	Summary of Results
		Wave I who were not part of the genetic sample, and those who were only in the Wave I disabled sample. Wave III and Wave IV samples consist of Wave I respondents who could be located and re-interviewed.		

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 7. Percentage of high school students who ever tried cigarettes smoking* and who smoked a whole cigarette for the first time before age 13 years, by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Surveillance System (2013) (Kann 2014)

	Ever smoked cigarettes						Smoked a whole cigarette before age 13					
	Female		Male		Total		Female		Male		Total	
Category	**%**	**CI†**	**%**	**CI**	**%**	**CI**	**%**	**CI**	**%**	**CI**	**%**	**CI**
Race/Ethnicity												
Caucasian§	4.9	(38.1-45.8)	43.9	(40.7-47.2)	**42.9**	**(39.8-46.1)**	8.6	(6.5-11.3)	11.6	(8.9-15.0)	**10.1**	**(8.0-12.8)**
African American§	31.7	(26.7-37.2)	36.5	(31.3-42.1)	**34.0**	**(29.6-38.8)**	4.1	(3.1-5.3)	9.6	(7.0-12.9)	**6.7**	**(5.3-8.4)**
Hispanic	41.4	(35.3-47.7)	45.1	(40.7-49.5)	**43.2**	**(38.7-47.8)**	7.6	(6.0-9.7)	10.9	(8.7-13.5)	**9.2**	**(7.6-11.1)**
Grade												
9	30.3	(26.8-34.0)	33.1	(29.6-36.9)	**31.7**	**(28.7-34.8)**	8.7	(6.5-11.7)	10.4	(8.7-12.3)	**9.5**	**(7.8-11.6)**
10	37.7	(33.3-42.2)	40.2	(35.8-44.7)	**39.0**	**(35.2-42.9)**	8.2	(6.0-11.0)	10.2	(8.3-12.4)	**9.2**	**(7.7-10.9)**
11	45.2	(39.6-50.8)	49.1	(44.4-53.8)	**47.0**	**(42.4-51.7)**	8.3	(5.9-11.4)	13.7	(10.0-18.5)	**10.9**	**(8.3-14.3)**
12	46.5	(41.7-51.4)	49.7	(45.4-53.9)	**48.1**	**(44.4-51.8)**	5.5	(4.1-7.5)	9.1	(7.1-11.7)	**7.3**	**(5.8-9.2)**
Total	**39.6**	**(36.3-43.1)**	**42.5**	**(39.9-45.2)**	**41.1**	**(38.4-43.8)**	**7.8**	**(6.1-9.9)**	**10.8**	**(9.1-12.8)**	**9.3**	**(7.8-11.1)**

* Even 1 or 2 puffs. † 95% confidence interval. § Non-Hispanic.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Among 12th graders, 30-day prevalence of smoking reached a peak in 1976 at 39%. (The authors report that the peak likely occurred earlier at lower grade levels as these same class cohorts passed through them in previous years; however, data on grades 8 and 10 were not gathered until 1991) (Johnston 2016). After about a one-quarter drop in 12th grade 30-day prevalence between 1976 and 1981, the rate remained stable until 1992 (28%). In the 1990s, smoking began to rise sharply, after 1991 among 8th and 10th graders and 1992 among 12th graders. Over the next four to five years (1993-1998), smoking rates increased by about one half in the lower two grades and by almost one third in grade 12. Smoking peaked in 1996 for 8th and 10th graders and in 1997 for 12th graders before beginning a fairly steady and substantial decline that continued through 2004 for 8th and 10th graders. Between the peak levels in the mid-1990s and 2004, 30-day prevalence of smoking declined by 56% in the 8th grade, 47% in the 10th, and 32% in the 12th (Table 8). This important decline in adolescent smoking decelerated after about 2002. Still, by 2015, 30 day prevalence levels had fallen from peak levels by 83%, 79%, and 69% in grades 8, 10, and 12, respectively. Smoking initiation by 8th graders declined by nearly three quarters, from a peak of 49% in 1996 to just 13% by 2015. The authors also suggested that the fact that fewer young people now initiate cigarette smoking is an important reason for the large declines in current use. They reported that the proportion of students who have ever tried cigarettes has fallen from peak levels reached in 1996 or 1997 by roughly three-quarters, two-thirds, and one-half in the three grades, respectively (Johnston 2016).

NSDUH

In 2014, screening was completed with 127,605 addresses, and 67,901 completed interviews were obtained, including 17,046 interviews from adolescents aged 12 to 17. Adults are also included in this survey, but in this section we will cover only results for those aged 12-17, as the adult results were reported previously. Tobacco use and cigarette use were lower in 2014 than in most years from 2002 to 2013 across all age groups. For example, about 1 in 8 adolescents aged 12 to 17 (13.0%) were current cigarette smokers in 2002. By 2014, about 1 in 20 adolescents (4.9%) were current smokers (defined as any cigarette use within the last 30-days) (Hedden S 2015).

Among total US adolescents aged 12 to 17 in 2014, it was estimated that 1.7 million used tobacco products in the past month, including 1.2 million current cigarette smokers (projected figures). These 2014 numbers represent 7.0 percent of adolescents who were current tobacco users and 4.9 percent who were current cigarette smokers. From 2002 to 2014, the percentage of adolescents who were past month tobacco users declined roughly by half, from 15.2% to 7.0%. Similarly, the percentage of adolescents who were current cigarette smokers in 2014 was lower than the percentages in 2002 to 2013. Detailed findings can be seen in Table 9.

National Youth Tobacco Survey (NYTS)

The NYTS determined the prevalence and trends of current (past 30-day) use of different tobacco products including cigarettes among US middle (grades 6-8) and high school (grades 9-12) students (Arrazola 2015). The most current report includes data from 4 years (2011–2014). Of 258 schools selected for the 2014 NYTS, 207 (80.2%) participated, with a sample of 22,007 (91.4%) among 24,084 eligible students yielding an overall response rate of 73.3%. Sample sizes and overall response rates for 2011, 2012,

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

and 2013 were 18,866 (72.7%), 24,658 (73.6%), and 18,406 (67.8%), respectively. Participants were asked about current (past 30-day) use of cigarettes, cigars (defined as cigars, cigarillos, or little cigars), smokeless tobacco (defined as chewing tobacco, snuff, or dip), e-cigarettes, hookahs, tobacco pipes (pipes), snus, dissolvable tobacco (dissolvables), and bidis. Current use for each product was defined as using a product on ≥1 day during the past 30 days. Data were weighted to account for the complex survey design and adjusted for nonresponse. National prevalence estimates were computed.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 8. Trends in Lifetime, 30-day and Daily Prevalence of Use of Cigarettes for Grades 8, 10 and 12 Combined in the MTF 2015 (Johnston 2016)

Cigarette Smoking	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2014-2015 Difference
Lifetime Prevalence	53.5	53.0	54.0	54.6	55.8	57.8	57.4	56.0	54.5	51.8	49.1	44.2	40.8	39.6	37.4	35.0	33.3	31.3	31.2	30.9	28.7	27.0	25.6	22.9	21.1	-1.8 ss
30-day Prevalence	20.7	21.2	23.4	24.7	26.6	28.3	28.3	27.0	25.2	22.6	20.2	17.7	16.6	16.1	15.3	14.4	13.6	12.6	12.7	12.8	11.7	10.6	9.6	8.0	7.0	-1.0 ss
Daily Prevalence	12.4	11.9	13.5	14.0	15.5	16.8	16.9	15.4	15.0	13.4	11.6	10.2	9.3	9.0	8.0	7.6	7.1	6.4	6.4	6.4	5.7	5.2	4.7	3.6	3.2	-0.4

Source. The Monitoring the Future study, the University of Michigan.
Level of significance of difference between classes: s = .05, ss = .01, sss = .001.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 9. Tobacco Product Use in the Past Month among Youth Aged 12 to 17 years in the NSDUH 2002-2014 (Hedden S 2015)

Substance	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Aged 12-17													
Cigarettes	13.0*	12.2*	11.9*	10.8*	10.4*	9.9*	9.2*	9.0*	8.4*	7.8*	6.6*	5.6*	4.9*
	(0.30)	(0.29)	(0.30)	(0.28)	(0.26)	(0.27)	(0.25)	(0.26)	(0.26)	(0.24)	(0.22)	(0.20)	(0.21)
Daily Use	31.8*	29.7*	27.6	25.8	26.5	26.4	22.3	23.0	22.5	22.7	22.0	19.4*	24.1
	(1.03)	(1.06)	(1.13)	(1.12)	(1.19)	(1.16)	(1.11)	(1.17)	(1.29)	(1.28)	(1.33)	(1.35)	(1.89)
Smoked 1+ pack per day[1]	21.8*	22.0*	19.4*	20.1*	17.9	18.7*	18.4*	17.9	16.7	14.8	10.8	11.9	11.9
	(1.61)	(1.68)	(1.80)	(1.87)	(1.94)	(1.94)	(2.08)	(2.12)	(2.24)	(1.97)	(1.88)	(2.47)	(2.52)

NOTE: Estimates shown are percentages with standard errors included in parentheses.
* Difference between estimate and 2014 estimate is statistically significant at the 0.05 level.
1 Respondents with missing data for number of cigarettes smoked per day were excluded from the analysis.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

In 2014, a total of 24.6% of high school students reported current use of a tobacco product. The prevalence of cigarette use among all high school students was 9.2% (Table 10). From 2011 to 2014, statistically significant linear decreases were observed among high school students for current cigarette smoking (15.8% to 9.2%). Among those participants in high school, the prevalence of 30-day cigarette smoking was higher in males than females (10.6% vs 7.9%) and in Caucasians (10.8%). Among those in middle school, the prevalence of cigarette smoking was higher in males than females (3.0% vs. 2.0%) and in Hispanics (3.7%). More details can be seen in Table 10.

Youth Risk Behavior Surveillance System (YRBSS)

The Youth Risk Behavior Surveillance System (YRBSS) monitors various categories of important health-risk behaviors among youth and young adults including tobacco use (Kann 2014). The survey reports ever smoking, smoking a whole cigarette before age 13 years, current cigarette use (had smoked on at least 1 day during the 30 days before the survey), current frequent use of cigarettes (smoking 20 or more days during the 30 days before the survey), smoking more than 10 cigarettes per day, ever daily smoking (ever smoking cigarettes daily for 30 continuous days) and current daily smoking (smoking cigarettes on all 30 days during the 30 days before the survey). The sampling frame for the 2013 national YRBSS consisted of all regular public and private schools with students in at least 1of grades 9–12 in the 50 states and the District of Columbia. In the first sampling stage, schools with any of grades 9–12 were sampled with probability proportional to school enrollment size in 40 states and four large urban school districts; all schools with any of grades 9–12 were invited to participate in two states and 17 large urban school districts. In the second sampling stage, intact classes from either a required subject (e.g., English or social studies) or a required period (e.g., homeroom or second period) were sampled randomly in 41 states and 20 large urban school districts, and all students in the sampled classes were eligible to participate. In 1 state and 1 large urban school district, all students in sampled schools were eligible to participate.

Results from the 2013 national YRBSS indicated that 41.1% of students (aged 10-24 years) had ever tried cigarette smoking (even 1 or 2 puffs). The prevalence of having ever smoked cigarettes was higher among male (42.5%) than female (39.6%) students. The prevalence of having ever smoked cigarettes was higher among Caucasian (42.9%) and Hispanic (43.2%) than African American (34.0%) students, higher among Caucasian female (41.9%) and Hispanic female (41.4%) than African American female (31.7%) students, and higher among Caucasian male (43.9%) and Hispanic male (45.1%) than African American male (36.5%) students. More details can be seen in Table 10. Nationwide 9.3% of students had smoked a whole cigarette for the first time before age 13 years (Table 7).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

The prevalence of having smoked a whole cigarette before age 13 years was higher among Caucasian (10.1%) and Hispanic (9.2%) than African American (6.7%) students and higher among Caucasian female (8.6%) and Hispanic female (7.6%) than African American female (4.1%) students (Table 10). The prevalence of having smoked a whole cigarette before age 13 years was higher among 9th-grade (9.5%) and 11th-grade (10.9%) than 12th-grade (7.3%) students, higher among 9th-grade female (8.7%) than 12th-grade female (5.5%) students, and higher among 11th-grade male (13.7%) than 12th-grade male (9.1%) students. During 1991–2013, a significant decrease occurred overall in the prevalence of having smoked a whole cigarette before age 13 years (23.8%–9.3%). A significant quadratic trend was identified in that the prevalence of having smoked a whole cigarette before age 13 years did not change significantly from 1991–1999 (23.8%–24.7%) and then decreased from 1999-2013 (24.7%–9.3%). The prevalence of having smoked a whole cigarette before age 13 years did not change significantly from 2011 (10.3%) to 2013 (9.3%) (Kann 2014). The prevalence of current cigarette use was 15.7% nationwide among students (Table 11).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 10. Percentage of high school students who ever tried cigarettes smoking* and who smoked a whole cigarette for the first time before age 13 years, by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Surveillance System (2013) (Kann 2014)

	Ever smoked cigarettes						Smoked a whole cigarette before age 13					
	Female		Male		Total		Female		Male		Total	
Category	%	CI†	%	CI	%	CI	%	CI	%	CI	%	CI
Race/Ethnicity												
Caucasian§	4.9	(38.1-45.8)	43.9	(40.7-47.2)	**42.9**	**(39.8-46.1)**	8.6	(6.5-11.3)	11.6	(8.9-15.0)	**10.1**	**(8.0-12.8)**
African American§	31.7	(26.7-37.2)	36.5	(31.3-42.1)	**34.0**	**(29.6-38.8)**	4.1	(3.1-5.3)	9.6	(7.0-12.9)	**6.7**	**(5.3-8.4)**
Hispanic	41.4	(35.3-47.7)	45.1	(40.7-49.5)	**43.2**	**(38.7-47.8)**	7.6	(6.0-9.7)	10.9	(8.7-13.5)	**9.2**	**(7.6-11.1)**
Grade												
9	30.3	(26.8-34.0)	33.1	(29.6-36.9)	**31.7**	**(28.7-34.8)**	8.7	(6.5-11.7)	10.4	(8.7-12.3)	**9.5**	**(7.8-11.6)**
10	37.7	(33.3-42.2)	40.2	(35.8-44.7)	**39.0**	**(35.2-42.9)**	8.2	(6.0-11.0)	10.2	(8.3-12.4)	**9.2**	**(7.7-10.9)**
11	45.2	(39.6-50.8)	49.1	(44.4-53.8)	**47.0**	**(42.4-51.7)**	8.3	(5.9-11.4)	13.7	(10.0-18.5)	**10.9**	**(8.3-14.3)**
12	46.5	(41.7-51.4)	49.7	(45.4-53.9)	**48.1**	**(44.4-51.8)**	5.5	(4.1-7.5)	9.1	(7.1-11.7)	**7.3**	**(5.8-9.2)**
Total	**39.6**	**(36.3-43.1)**	**42.5**	**(39.9-45.2)**	**41.1**	**(38.4-43.8)**	**7.8**	**(6.1-9.9)**	**10.8**	**(9.1-12.8)**	**9.3**	**(7.8-11.1)**

* Even 1 or 2 puffs. † 95% confidence interval. § Non-Hispanic.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 11. Percentage of high school students who currently smoked cigarettes* and who currently frequently smoked cigarettes, †by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Survey, 2013 (Kann 2014).

	Current cigarette use						Current frequent cigarette use					
	Female		Male		Total		Female		Male		Total	
Category	**%**	**CI†**	**%**	**CI**	**%**	**CI**	**%**	**CI**	**%**	**CI**	**%**	**CI**
Race/Ethnicity												
Caucasian¶	18.1	(14.8-21.9)	19.1	(16.2-22.4)	**18.6**	**(15.7-21.9)**	7.7	(5.5-10.6)	7.6	(6.1-9.5)	**7.6**	**(6.0-9.7)**
African American¶	6.2	(4.3-8.9)	10.5	(8.0-13.6)	**8.2**	**(6.3-10.7)**	2.0	(1.2-3.2)	3.6	(2.3-5.4)	**2.7**	**(1.9-4.0)**
Hispanic	13.1	(9.9-17.1)	15.0	(11.9-18.6)	**14.0**	**(11.2-17.4)**	2.4	(1.5-3.7)	3.4	(2.3-5.1)	**2.9**	**(2.3-3.7)**
Grade												
9	10.0	(8.0-12.6)	10.3	(8.3-12.6)	**10.2**	**(8.5-12.2)**	2.5	(1.4-4.3)	3.2	(2.3-4.6)	**2.9**	**(2.1-3.9)**
10	12.6	(10.1-15.7)	13.6	(11.1-16.7)	**13.2**	**(11.2-15.4)**	4.2	(2.6-6.6)	3.8	(2.6-5.7)	**4.0**	**(2.8-5.6)**
11	18.9	(13.9-25.1)	23.4	(19.2-28.1)	**21.1**	**(16.7-26.2)**	6.8	(4.1-11.1)	8.4	(6.4-11.0)	**7.6**	**(5.5-10.3)**
12	18.7	(15.5-22.5)	19.6	(16.1-23.6)	**19.2**	**(16.4-22.2)**	8.2	(6.3-10.6)	8.6	(6.8-10.8)	**8.4**	**(6.8-10.3)**
Total	**15.0**	**(12.5-17.8)**	**16.4**	**(14.3-18.7)**	**15.7**	**(13.5-18.1)**	**5.4**	**(3.9-7.5)**	**5.8**	**(4.7-7.1)**	**5.6**	**(4.4-7.1)**

* On at least 1 day during the 30 days before the survey. † On 20 or more days during the 30 days before the survey. § 95% confidence interval. ¶ Non-Hispanic.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

The prevalence of current cigarette use was higher among Caucasian (18.6%) than African American (8.2%) and Hispanic (14.0%) students, higher among Hispanic (14.0%) than African American (8.2%) students, higher among Caucasian female (18.1%) than African American female (6.2%) and Hispanic female (13.1%) students, higher among Hispanic female (13.1%) than African American female (6.2%) students, and higher among Caucasian male (19.1%) and Hispanic male (15.0%) than African American male (10.5%) students. During 1991–2013, a significant decrease occurred overall in the prevalence of current cigarette use (27.5%–15.7%). A significant quadratic trend was identified in that the prevalence of current cigarette use increased from 1991–1997 (27.5%–36.4%) and then decreased from 1997–2013 (36.4%– 15.7%). The prevalence of current cigarette use did not change significantly from 2011 (18.1%) to 2013 (15.7%) (Kann 2014).

The prevalence of current frequent cigarette use was 5.6% nationwide (Table 11). Current frequent cigarette use was higher among African American male (3.6%) than African American female (2.0%) students. The prevalence of current frequent cigarette use was higher among Caucasian (7.6%) than African American (2.7%) and Hispanic (2.9%) students, higher among Caucasian female (7.7%) than African American female (2.0%) and Hispanic female (2.4%) students, and higher among Caucasian male (7.6%) than African American male (3.6%) and Hispanic male (3.4%) students. During 1991–2013, a significant decrease occurred overall in the prevalence of current frequent cigarette use (12.7%–5.6%). A significant quadratic trend was identified in that the prevalence of current frequent cigarette use increased from 1991–1997 (12.7%–16.7%) and then decreased from 1997–2013 (16.7%–5.6%). The prevalence of current frequent cigarette use did not change significantly from 2011 (6.4%) to 2013 (5.6%) (Kann 2014).

The prevalence of current daily smoking was 4% (Table 12). Currently daily cigarette smoking was higher among Caucasian (5.6%) than African American (1.7%) and Hispanic (1.9%) students, higher among Caucasian female (5.5%) than African American female (1.3%) and Hispanic female (1.2%) students, and higher among Caucasian male (5.7%) than African American male (2.2%) and Hispanic male (2.5%) students. The prevalence of having currently smoked cigarettes daily was higher among 11th-grade (5.1%) and 12th-grade (6.1%) than 9th-grade (2.2%) and 10th-grade (2.9%) students, higher among 11th-grade female (4.4%) than 9th-grade female (1.8%) students, higher among 12th-grade female (6.3%) than 9th-grade (1.8%) and 10th-grade female (2.7%) students, and higher among 11th-grade male (6.0%) and 12th-grade male (5.9%) than 9th-grade male (2.5%) and 10th-grade male (3.1%) students. During 1991–2013, a significant decrease occurred overall in the prevalence of having currently smoked cigarettes daily (9.8%-4.0%). A significant quadratic trend was identified in that the prevalence of having currently smoked cigarettes daily increased from 1991–1999 (9.8%–12.8%) and then decreased from 1999–2013 (12.8%–4.0%). The prevalence of having currently smoked cigarettes daily did not change significantly from 2011 (4.8%) to 2013 (4.0%).

Add Health

Add Health is a study of adolescent health-related behaviors (Kaufman 2015). The nationally based sampling frame involved the selection of a random sample of 80 high schools (public, private, and parochial) and 54 associated feeder schools throughout the US and is representative of US schools with respect to region, urbanicity, school size, school type, and ethnic distribution.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 12. Percentage of high school students who ever smoked cigarettes daily* and who currently smoked cigarettes daily,† by sex, race/ethnicity, and grade – United States, Youth Probability Behavior Survey, 2013 (Kann 2014).

	Ever daily smoking						Current daily smoking					
	Female		Male		Total		Female		Male		Total	
Category	**%**	**CI§**	**%**	**CI**	**%**	**CI**	**%**	**CI**	**%**	**CI**	**%**	**CI**
Race/Ethnicity												
Caucasian¶	11.7	(8.6-15.6)	10.9	(8.9-13.3)	**11.3**	**(9.0-14.1)**	5.5	(3.7-8.1)	5.7	(4.4-7.3)	**5.6**	**(4.2-7.4)**
African American¶	3.1	(2.0-4.6)	5.5	(4.3-7.1)	**4.3**	**(3.3-5.5)**	1.3	(0.7-2.6)	2.2	(1.3-3.6)	**1.7**	**(1.0-2.8)**
Hispanic	5.2	(4.0-6.8)	7.0	(5.0-9.9)	**6.1**	**(5.1-7.4)**	1.2	(0.8-1.9)	2.5	(1.5-4.1)	**1.9**	**(1.4-2.5)**
Grade												
9	4.7	(3.5-7.0)	5.4	(4.0-7.3)	**5.1**	**(3.9-6.5)**	1.8	(0.9-3.7)	2.5	(1.7-3.8)	**2.2**	**(1.5-3.2)**
10	7.1	(5.3-9.5)	6.7	(5.0-8.9)	**6.9**	**(5.4-8.7)**	2.7	(1.5-4.6)	3.1	(2.0-3.8)	**2.9**	**(2.0-4.2)**
11	11.9	(8.2-17.0)	11.5	(8.8-14.9)	**11.7**	**(8.8-15.4)**	4.4	(2.6-7.3)	6.0	(4.2-8.5)	**5.1**	**(3.6-7.4)**
12	11.5	(8.4-15.5)	13.0	(10.6-15.7)	**12.2**	**(10.0-14.9)**	6.3	(4.4-9.1)	5.9	(4.5-7.6)	**6.1**	**(4.7-8.0)**
Total	**8.7**	**(6.5-11.5)**	9.0	**(7.4-10.7)**	**8.8**	**(7.2-10.8)**	**3.8**	**(2.5-5.6)**	**4.2**	**(3.3-5.4)**	**4.0**	**(3.0-5.3)**

* Ever smoked at least 1 cigarette every day for 30 days. † Smoked cigarettes on all 30 days during the 30 days before the survey. § 95% confidence interval. ¶ Non-Hispanic.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Their latest data shows results from 2008-2009. Among the total population (N = 20,774), 48.8% of the adolescents in grades 7-12 reported using cigarettes within 30 days during at least 1 follow-up wave of the study (cumulative prevalence) (Table 13). Males were more likely than females to report using cigarettes (51.9% vs. 45.7%). Caucasians (54.8%) were more likely to report using cigarettes more than Native Americans (49.8%) and African Americans (35.8%). Midwest residents (56.3%) were more likely to report smoking cigarettes than those living in the Northeast (51.8%), in the South (46.0%) and in the West (43.7%) (Kaufman 2015).

6.3.2.2.1.2.3 Prevalence of cigarette smoking in specific populations

Publications that reported the prevalence of smoking in certain specific populations were identified through our literature searches, these publications were extracted as a result of the PubMed searches as explained in the appropriate sections of this part of the document. The results from these studies are described below. Briefly, individuals with a mental disorder (Dickerson 2013, Glasheen 2014, Hickman 2010, Husky 2008), HIV positive (Mamary 2002, Mdodo 2015) or part of the LGBT community (Fallin 2015, Gamarel 2016, Jamal 2015) had a higher prevalence of cigarette smoking than in the general population. A similar increase was seen among military personnel who had been deployed compared to those non-deployed (Harte 2014).

Additionally, even though there were no dedicated surveys assessing the prevalence of cigarette smoking in populations of low economic status, it is important to mention that the major population-based survey (NHIS) as well as other studies report that the prevalence of cigarette smoking is higher in those below the poverty level (26.3%) compared to those at or above the poverty level (15.2%) (Jamal 2014) as well as in those with a high-school education level or lower (21.7%-43%) compared to those some college education or higher (5.4%-19.7%).

Populations with mental illnesses

Six studies assessing the prevalence of cigarette smoking in populations with psychiatric disorders were identified. Details on the study design and characteristics as well as the prevalence rates by diagnosis can be found in Table 14. Four of these studies (Dickerson 2013, Glasheen 2014, Hickman 2010, Husky 2008) included a non-diseased population as well. Glasheen et al. (Glasheen 2014) found that past monthly smoking was higher in individuals with any mental illness (33.1%) and with serious mental illness (43.3%) than those without mental illness (22.1%).Dickerson et al. (Dickerson 2013) found that those who had schizophrenia (64%) or bipolar disorder (44%) were more likely to be current smokers compared to those with no mental illness (19%). Hickman et al. (Hickman 2010) reported that compared to those with no mental illness (23.1%), those with panic disorder (43.5%) were more likely to be smokers among all the mental disorders reported. Finally, the study by Husky et al. (Husky 2008) reported that compared to those with no major depression (19%), subjects with current major depression were more likely to be current daily smokers (34.6%). The same was seen among those reporting lifetime major depression (24.9%).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Military personnel

There were 3 studies assessing the prevalence of cigarette smoking in military populations. Details of these studies can be found in Table 15. The study by Little et al. (Little 2016) reported low prevalence rates of regular use of cigarettes in US Air Force recruits (females 9.9% and males 11.5%). The study by Horton et al. (Horton 2014) found that Marine recruits had a prevalence of current smoking of 27.1% at entry to the study which declined to 22.0% from 2001 to 2010. Finally, the study by Harte et al. (Harte 2014) found statistically significant differences in the prevalence of smoking between deployed military personnel (48.9%) vs. non-deployed military personnel (44.0%).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 13. Ever reported past 30-day cigarette smoking (Waves I-IV), according to Wave I participant sociodemographic characteristics, N (%).[a, b] 2008-2009 Add Health Study(Kaufman 2015)

	Total	Male	Female	Caucasian	African American	Native American	Asian	US Region: West	US Region: Midwest	US Region: South	US Region: North East
Ever reported cigarette use											
No	10,646 (51.2%)	4,941 (48.1%)	5,705 (54.3%)	6,100 (45.2%)	3,095 (64.2%)	205 (50.2%)	937 (60.9%)	2,766 (56.3%)	2,086 (43.8%)	4,120 (54.0%)	1,424 (48.2%)
Yes	10, 128 (48.8%)	5,326 (51.9%)	4,802 (45.7%)	7,381 (54.8%)	1,723 (35.8%)	203 (49.8%)	602 (39.1%)	2,151 (39.1%)	2,682 (56.3%)	3,513 (46.0%)	1,533 (51.8%)

[a]Race excludes 528 (2.4%) with missing Wave I race information. Race was constructed by the Add Health research team according to 22 coding steps based on participant and parent reported race at Wave I.
[b]Region excludes 499 (2.4%) with missing Wave I region information.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 14. Prevalence of cigarette smoking in mental illness populations

Author	Population & study characteristics	Summary of Findings	Prevalence by Diagnosis
Glasheen et al (Glasheen 2014)	Data from NSDUH 2008-2012 which is an annual cross-sectional survey of the civilian, noninstitutionalized US population (men and women) aged 12 or older. NSDUH sampling uses an independent multistage area probability sample within each state and the District of Columbia.	Adults with SMI were more likely than adults with any mental illness (AMI) but not SMI and adults without mental illness to engage in smoking behaviors. Adults with AMI but not SMI were more likely to engage in all smoking behaviors compared with adults without mental illness. The past month quit ratio was significantly lower among adults with SMI and among adults with AMI but not SMI than among adults without mental illness. Adults with SMI comprised 6.9% of past month smokers but consumed 8.7% of all cigarettes.	**Past monthly smoking:** No mental illness: 44.5% Any mental illness: 46.7% Serious mental illness: 30.5% **Past month heavy smoking:** No mental illness: 13.5% Any mental illness: 21.0% Serious mental illness: 53.7%
Peiper et al (Peiper 2013)	Data from the NSDUH 2005-2008 including a total of 133,221 men and women participants aged 18 and above.	Statistically significant sex differences in past-year psychological distress, major depressive episode and anxiety disorder were found for current tobacco use ($p<0.001$). Both male and female smokers were significantly more likely to have serious psychological distress and anxiety disorder compared to never users, while only female smokers were more likely to have major depressive episode. The strongest associations were found for anxiety disorder among all adults as well as both sexes.	**Lifetime User (adults):** Serious psychological distress: 8.2% Major depressive episode: 6.0% Any anxiety disorder: 4.0%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study characteristics	Summary of Findings	Prevalence by Diagnosis
Dickerson et al (Dickerson 2013)	991 adult men and women with schizophrenia or bipolar disorder as well as those not diagnosed with a psychiatric disorder were enrolled in the period January 1999 to December 2011 in the cohort.	There were marked differences in the prevalence of smoking and in the quantity of cigarettes consumed among the diagnostic groups. Overall, 64% of individuals with schizophrenia, 44% with bipolar disorder, and 19% without psychiatric illness reported that they were current smokers. These group differences remained fairly constant over the observation period, and there were no statistically significant time trends in smoking or cigarette consumption after adjustment for demographic covariates. Within the psychiatric illness groups, smoking and cigarette consumption were significantly associated with less education, a history of substance abuse, longer illness duration, Caucasian race, and schizophrenia diagnosis but not with psychiatric symptom severity.	**Current cigarette smoking:** No mental illness: 19% Schizophrenia: 64% Bipolar disorder: 44%
Kotov et al (Kotov 2010)	A cohort of 542 inpatients, including men and women aged 15 and above, with psychosis was followed for 10 years after first hospitalization, completing 5 face-to-face interviews. Assessments included ratings of specific symptoms (psychotic, negative, disorganized, and depressive), Global Assessment of Functioning, and a categorical measure of cigarette consumption. All participants were assigned longitudinal consensus diagnoses by study psychiatrists, and 229 were diagnosed with schizophrenia spectrum disorders. Smoking was defined as any usage of cigarettes.	At baseline, 52.4% of participants were current smokers and 69.3% were lifetime smokers. Smoking rates did not differ among the diagnostic groups (schizophrenia spectrum, major depressive, bipolar, or other psychotic disorder) at any assessment point. Smokers were more severely ill than nonsmokers but did not differ in specific symptoms either cross-sectionally or longitudinally. Among smokers, changes in cigarette consumption were linked only with changes in depression.	**Lifetime smoking:** Schizophrenia: 67.4% Bipolar disorder: 69.2% Major depression: 73.1% Other psychoses: 70.5%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study characteristics	Summary of Findings	Prevalence by Diagnosis
Hickman et al (Hickman 2010)	A cross-sectional study analyzing nationally representative data from 3,411 adult African Americans participating in the 2001–2003 National Survey of American Life. Smoking prevalence and quit rates according to lifetime and past year Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition mental disorders were assessed by a modified version of the Composite International Diagnostic Interview.	Compared with those without mental illness, respondents with a lifetime, past year, or past month mental illness had a higher smoking prevalence (20.6%, 35.6%, 36.0%, and 45.4%, respectively) and lower quit rate (40.5%, 31.2%, and 26.2%, respectively). The odds of being a current smoker among African Americans with mental illness in their lifetime, past year, and past month, after adjusting for age, gender, education, poverty, and marital status were 1.76 (95% CI = 1.39–2.22), 1.57 (95% CI = 1.22–2.03), and 2.20 (95% CI = 1.56–3.12), respectively. Mental illness also was associated with heavier smoking. African Americans with past year mental illness represented 18.1% of the sample, yet consumed 23.9% of cigarettes smoked by African Americans smokers. Past year (odds ratio [OR] = 0.72, 95% CI = 0.53–0.97) and past month (OR = 0.54, 95% CI = 0.29–0.98) mental illness were associated with a lower odds of quitting for at least 1 year.	**Current Smoking:** No mental illness: 23.1% Major depressive disorder: 34.4% Dysthymia: 32.3% Bipolar I disorder: 71.2% Panic disorder: 43.5% Generalized anxiety disorder: 40.8% Posttraumatic stress disorder: 36.6% Agoraphobia: 35.1% Social phobia: 32.0%
Husky et al (Husky 2008)	Data were derived from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Wave 1, 2001-2002, n = 42,565) which included African Americans, Hispanics and young adults aged 18-24 years. Relationships between smoking status (daily, occasional, prior) and DSM-IV major depression (current or lifetime) by gender were assessed.	Current (daily, occasional) and prior smoking significantly increased odds of having current or prior major depression. These associations varied as a function of gender. Women with prior smoking were at significantly higher probability of current and past depression than men (OR: 1.53 vs 1.36; 1.72 vs 1.36), as was true for current occasional (OR: 1.92 vs 1.39; 1.90 vs 1.30) and daily smoking (OR: 2.52 vs 1.95; 1.84 vs 1.48).	**Current Daily Smoking:** Current major depression: 34.6% Lifetime major depression: 24.9% No lifetime major depression: 19%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study characteristics	Summary of Findings	Prevalence by Diagnosis
Vanable et al (Vanable 2003)	Cross sectional study of 2,906 consecutive outpatients of psychiatric clinics in Syracuse, New York. The sample was comprised of 1,482 women and 1,292 men with a mean age of 39 years (± 11.4).	A total of 61% of patients smoked daily, and that 18% smoked heavily (more than 1 pack per day). Current smoking was related to psychiatric diagnosis and illness severity. Diagnoses of bipolar disorder, schizoaffective disorder, and schizophrenia were independently related to smoking status, an association that was most pronounced among persons treated at clinics serving more impaired patients.	**Current Smoking:** Adjustment disorder 51% Anxiety disorder: 56% Depression: 60% Bipolar: 66% Schizoaffective: 67% Schizophrenia: 63% Other: 61%

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 15. Prevalence of cigarette smoking in military personnel

Author	Population & study methods	Summary of Findings	Prevalence by Diagnosis
Little et al (Little 2016)	Cohort study including 13,685 men and women in the US Air Force. The average participant was male with a mean age of 20.5 years. The prevalence of tobacco and nicotine containing products was assessed by asking participants how often they used these products prior to enlistment. Regular use was defined as at least monthly use of the product.	Over a quarter (26.9%) of Airmen reported regular use of a tobacco or nicotine containing product. The two most prevalent products were cigarettes (11.2%) and hookah (10.5%). Among correlates of use, Airmen that regularly use TNCPs were more likely to be male, younger, non-Hispanic Caucasian, and single with a high school degree or General Education Development. Hookah was the most endorsed for intentions to use, and along with e-cigarettes, had the lowest perception of harm. While prevalence of most products remained constant across entering cohorts, the prevalence of e-cigarettes showed significant linear increase.	**Regular use:** Female: 9.9% Male: 11.5%
Horton et al (Horton 2014)	Repeated cross sectional study including 131,961 male Marine recruits with a mean age of 19.8 years. Cigarette smoking was assessed by asking if they had smoked more than 100 cigarettes in their lifetime and also whether they smoked 'some days' or 'every day'. These were classified as current cigarette smokers.	Cigarette smoking decreased in early years, began to increase from 2005 to 2009, and dipped down to 22% in 2010.	**Current smoker:** At entry: 27.1% At end of follow up: 22.0%
Harte et al (Harte 2014)	Cohort study of 1,082 US Army soldiers who had or had not been deployed to Iraq. Smoking was assessed by asking "in the past month, on average, how many cigarettes did you smoke per day?" Those who endorsed any cigarette smoking (irrespective of intensity) were categorized as smokers	Approximately 48 % of participants smoked at both time points, with 6 % initiating smoking and 6 % quitting. Smoking initiation was associated with warzone stress exposure; female gender and high military unit support predicted cessation. Military rank and alcohol use were associated with both smoking initiation and cessation.	**Past month smoker:** **At time 1:** Deployed: 49.2% Not-deployed: 44.0% **At time 2:** Deployed: 48.9% Not-deployed: 45.0%

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

HIV positive individuals

There were 2 studies assessing the prevalence of cigarette smoking in HIV positive populations. Details of these studies can be found in Table 16. Both studies report that the prevalence of current smoking was higher in HIV positive populations when compared to the general population. For instance, the study by Mdodo et al. (Mdodo 2015) reports a prevalence of current smoking in HIV positive subjects of 37.6% while that of the general population was 20.6%. An even higher prevalence was reported by Mamary et al. (Mamary 2002) where the HIV positive group had a prevalence of current smoking of 54.0% compared to 18.0% in the general population.

Sexual Minorities

There were 4 studies assessing the prevalence of cigarette smoking in sexual minority populations apart from the NHIS study (Jamal 2015). Details of these studies can be found in Table 17. Three studies compared the prevalence of current smoking in sexual minorities vs. heterosexual populations. While Gamarel et al. (Gamarel 2016) found no statistically significant differences in the prevalence of smoking between sexual minority men and heterosexual men, the authors report that sexual minority women did have higher prevalence of smoking than heterosexual women (56.9% vs. 20.7%). Additionally, the study by Fallin et al. (Fallin 2015) reported that the prevalence of current smoking was higher in sexual minority men and women compared to heterosexual men and women. Finally, the NHIS reported that those reporting being gay, lesbian, bisexual or transgender had a higher smoking prevalence than those who reported being heterosexual (23.9% vs. 16.6%).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 16. Prevalence of cigarette smoking in HIV + populations

Author	Population & study methods	Summary of Findings	Prevalence by Diagnosis
Mdodo et al (Mdodo 2015)	Cross sectional study of 4,217 adults with HIV who participated in the Medical Monitoring Project and 27,731 US adults who participated in the NHIS in 2009. The population was 18 years or older. Subjects were asked if they had smoked 100 or more cigarettes in their lifetime. The NHIS sample was asked "Do you now smoke cigarettes every day, some days or not at all?" and the MMP sample was asked 'How often do you smoke cigarettes now?".	Compared with the US adult population, in which an estimated 20.6% of adults smoked cigarettes in 2009, adults with HIV were more likely to smoke, but were less likely to quit smoking. Among adults with HIV, factors independently associated with greater smoking prevalence were older age, non-Hispanic Caucasian or African American race, lower educational level, poverty, homelessness, incarceration, substance use, binge alcohol use, depression and not achieving a suppressed HIV viral load.	**Current smoking:** HIV +: 37.6% General population: 20.6%
Mamary et al (Mamary 2002)	Cross sectional study 228 HIV + subjects (men and women) with an average age of 40 years. Subjects were classified as smokers if they identified themselves as smokers and they were also asked about the frequency of smoking.	Study results revealed a high percentage of smokers among our sample of individuals living with HIV compared to the percentage of smokers found in the general adult population. A total of 123 individuals (54%) reported that they smoked cigarettes. Men were more than twice as likely to have made previous attempts at smoking cessation as were woman.	**Current smoking:** All sample: 54.0% General population in San Francisco: 18.0%

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 17. Prevalence of cigarette smoking in sexual minorities

Author	Population & study methods	Summary of Findings	Prevalence by Diagnosis
Gamarel et al (Gamarel 2016)	Data were drawn from the 2003–2012 National Health and Nutrition Examination Surveys, which assessed 14,972 men and women ages 20 to 59 years for sexual orientation, current smoking status, and household smoking. Cigarette smoking was assessed with two questions: "Have you smoked 100 cigarettes in your lifetime?" and "Do you now smoke?" A current smoker was defined as someone who had smoked at least 100 cigarettes in their life and reported yes to smoking now.	The main effects of identifying as a sexual minority, Sex (male), and living with a household smoker were all associated with a significantly higher odds of being a current smoker.	**Current smoking:** Heterosexual males: 70.1% Sexual minority males: 63.3% Heterosexual women: 20.7% Sexual minority females: 56.9%
Fallin et al (Fallin 2015)	Data were drawn from the CDC's 2009-2010 NATS including 118,590 adult men and women. Current smoking was assessed based on two questions: "Have you smoked at least 100 cigarettes in your entire life?" and "Do you now smoke cigarettes every day, some days, or not at all?" A current smoker was defined as someone who had smoked at least 100 cigarettes in their life and reported smoking "every day" or "some days."	Controlling for age, race, socioeconomic status and geographic region, identifying as a female bisexual was associated with fewer past quit attempts, lower age at first cigarette, and higher nicotine dependence when compared to heterosexual women. There were no differences in desire to quit between male or female sexual minorities and their heterosexual counterparts.	**Current smoking:** **Women:** Lesbian: 22.4% Bisexual: 31.9% Heterosexual: 13.2% **Men:** Gay: 25.9% Bisexual: 33.7% Heterosexual: 15.9%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Summary of Findings	Prevalence by Diagnosis
Tamí-Maury et al (Tami-Maury 2015)	Cross sectional study using convenience sample of 99 LGBT individuals 18 years or older examining tobacco use, sexual orientation, and other socio-demographic factors through survey participation. Participants who responded "Yes" to the question "Have you ever smoked at least 100 cigarettes in your entire life?" and "Do you now smoke every day or some days?" were classified as current smokers.	Findings showed a high prevalence of tobacco and electronic cigarettes use. Caucasian LGBT individuals had greater odds of using any type of tobacco product.	**Current smoking:** Gay: 36.8% Lesbian: 42.1% Bisexual: 15.8%
Matthews et al (Matthews 2014)	Cross sectional analysis of the sexual minority women's health study which included 138 women with a mean age of 37.9 years. To assess smoking status, respondents were asked "Do you currently smoke cigarettes?"	The majority (84.9%) of Wave 1 smokers were also smoking at Wave 2. Among demographic variables, level of education was inversely associated with continued smoking. With respect to substance use, hazardous drinking and cocaine/heroin use were significantly associated with continued smoking. None of the victimization or health variables predicted smoking status.	**Current smoking:** Sexual minority women: 21.5%

LGBT: Lesbian, gay, bisexual and transgender

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.1.3 Discussion

There were four surveys reporting the prevalence of smoking in US adults. Three of these surveys reported a prevalence ranging from 16.8% (NHIS) to 19% (NATS) while the NSDUH reported a smoking prevalence of 28.4%.This is most likely due to the different definitions of 'current cigarette smoker' used in the NSDUH. While the NHIS, NATS and BRFSS considered a current smoker someone who "had smoked 100 or more cigarettes in their lifetime and who at the time of the survey were either daily or occasional smokers", the NSDUH defined cigarette use as smoking 'part of a cigarette' in the last 30 days.

A similar effect was seen in youth populations. Those surveys reporting a 30-day prevalence of smoking from 2014 onwards reported values below 10% for high school students and a prevalence of 2.5% for middle school students. The NSDUH reported a prevalence of 4.9% probably due to the fact that it included both middle and high school students (aged 12-17) and the prevalence of smoking in middle school has been shown to be lower than in high school students (Arrazola 2015). The YRBSS study reported a prevalence of 15.7%, and Add Health reported a prevalence of 48.8% (any past 30-day cigarette smoking) which is triple the prevalence reported by the other studies. The reason for this high prevalence could be due to the fact that this was a cohort study, and the data presented are aggregated from waves I to IV, meaning that any participant reporting last 30-day cigarette smoking during any of the four waves was considered a current smoker at the end of the study. (The authors state, "among the cohort (N = 20,774), 48.8% reported using cigarettes … in at least 1 wave.")

The fact that the prevalence of smoking is higher in certain populations is well known. For instance, patients suffering from serious mental illness have been shown to have higher use of cigarettes compared to the general population, and even as efforts have been made to reduce cigarette smoking in the general population, mental health patients have been ignored, perhaps due to the inattention of health care providers as well as the relative isolation of these patients (Dickerson 2013). Similarly, HIV positive subjects have higher rates of smoking. There has been speculation that this group might lack motivation to quit, because of a pessimistic view of the likelihood of long-term survival (Mamary 2002). Moreover, clinicians who hold similarly unhopeful views might be less likely to recommend smoking cessation to their patients living with HIV (Mamary 2002). Lastly, sexual minorities have been shown to smoke at higher rates than heterosexuals in spite of similar rates in desire to quit (Fallin 2015). The study by Fallin et al. (Fallin 2015) found that this increased prevalence could be due (at least in bisexual individuals) to unique internal and external stressors that these individuals face day to day.

6.3.2.2.1.4 Conclusions

The prevalence of cigarette smoking in adults as well as in youth populations has decreased over the last decade. This decline in smoking has been seen in all demographic strata and in most states. There are still certain sectors of the US population where the prevalence has remained elevated in comparison to overall values, for instance in those living under the poverty level, some racial minorities (American Indians/Alaskan Natives) and those living with disabilities. Higher rates of smoking are also seen in specific populations such as those living with HIV, sexual minorities and mental health patients.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.2 Cigarette smoking initiation

6.3.2.2.2.1 Search strategies

The search for articles on smoking initiation was performed on March 11, 2016, and resulted in 1,617 articles being identified using the following query: (("smoking"[MeSH Terms] OR "smoking"[All Fields]) AND initiation [All Fields]) AND ("united states"[MeSH Terms] OR ("united"[All Fields] AND "states"[All Fields]) OR "united states"[All Fields]). The review of titles and abstracts resulted in 346 articles being extracted and fully reviewed. The relevant articles will be discussed in this section.

6.3.2.2.2.2 Results

6.3.2.2.2.2.1 Smoking initiation rates

Eighteen studies reporting smoking initiation rates in both young adults (Bernat 2012, Boyko 2015, Kiefe 2001, Reed 2010, Staten 2007, Tercyak 2007) and youth populations (Bohnert 2009, Carvajal 2006, Choi 2003, Jackson 2007, Jackson 2006, Mahabee-Gittens 2011, Mahabee-Gittens 2012, Mahabee-Gittens 2013, Song 2009, Tucker 2012, Voorhees 2011, Weiss 2011) were identified through the literature search. Details of the studies can be found in Table 18. Initiation rates varied with the definition of initiation. For instance, those who defined initiation as ever trying cigarettes (even a puff or two) reported the highest initiation rates ranging from 12% (Jackson 2006), to 45.6% among youth populations (Bohnert 2009) and 34% in those aged 18 or older (Staten 2007). Restricted to those who had ever smoked a whole cigarette (used only in the adult population studies), the rates ranged from 20.4% (in women (Bernat 2012) and overall as reported by Song et al. (Song 2009)) to 30% in men (Staten 2007). When any use in the past 30 days was considered, the rates ranged from 12.0% in girls (Voorhees 2011) to 13.8% in all adolescents (Tucker 2012). Finally, when the most restrictive definition was used (initiators were current smokers or had smoked at least 5 cigarettes a week in the last 3 months), the initiation rate dropped to 3.5% in Caucasian women (Kiefe 2001) and 9% in men (Reed 2010). This last definition was found only in studies performed in adult populations. Initiation rates also varied by race/ethnicity as seen in the study by Kiefe et al. (Kiefe 2001) where African Americans were more likely to initiate smoking than Caucasians (rates from 7.1-13.2% in African Americans vs. 3.5-5.1% in Caucasians), while the study by Bohnert et al. (Bohnert 2009) showed the opposite (rate in Caucasians was 20.5% and in African Americans it was 19.0%). Similar rates were reported by Mahabee-Gittens et al. (Mahabee-Gittens 2011). Initiation rates also varied by age within teen groups as shown by Mahabee-Gittens et al. (Mahabee-Gittens 2013), who report that initiation rates (ever smokers) were negligible at age 10 but rose steadily from age 11 and reached a peak at age 17. Finally, initiation rates also varied by sex (Kiefe 2001), as women were shown to have lower initiation rates regardless of the definition of initiation and ages of the population (Bernat 2012, Boyko 2015, Kiefe 2001, Reed 2010, Voorhees 2011).

6.3.2.2.2.2.2 Smoking Initiation in Specific populations

Only 1 study assessing smoking initiation in specific populations was found through the literature search (Jordan 2014). This study assessed smoking initiation in adolescents aged 14-18 years who identified themselves as a sexual minority (referred to as Lesbian, Gay, Bisexual, Queer and Questioning: LGBQ) and those who did not. Overall, LGBQ youth were significantly more likely to have smoked at least 100 cigarettes in their lives.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

However, when examined by age, the general population youth aged 14-17 were more likely than their LGBQ counterparts to have smoked at least 100 cigarettes. The percentage of youth initiating smoking at each age showed a similar pattern for LGBQ and the general population youth, with a slight delay in initiation for LGBQ youth. At age 14, the percentage of current smokers was similar for the 2 groups (LGBQ: 0.8%; general population: 2.5%). For ages 15, 16 and 17, the percentage of current smokers was higher among the general population youth. Then at age 18, the percentage of current smokers among LGBQ youth (47.7%) was nearly double that of youth from the general population (24.2%).

6.3.2.2.2.2.3 Determinants of initiation

The literature search identified 37 studies assessing the determinants of smoking initiation. Out of the 38 studies, 23 evaluated youth populations (Abar 2014, Albers 2008, Bohnert 2009, Carvajal 2006, Choi 2003, Dalton 2009, Distefan 1998, Farrelly 2012, Flay 1994, Fletcher 2012, Gilman 2009, Goldade 2012, Jackson 2007, Jackson 2006, Jackson 1997, Mahabee-Gittens 2011, Mahabee-Gittens 2012, Mahabee-Gittens 2013, Rajesh 2015, Titus-Ernstoff 2008, Tucker 2012, Voorhees 2011, Weiss 2011), 10 evaluated adult populations (aged 18 or above) (Bernat 2012, Doran 2013, Goodwin 2013, Green 2008, Kiefe 2001, Lipkus 1994, Reed 2010, Reed 2007, Staten 2007, Tercyak 2007) and 4 evaluated mixed populations (Dal Cin 2013, Kravitz-Wirtz 2016, Mathur 2014, Spillane 2012).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 18. Prevalence of cigarette smoking initiation

Author	Population & study methods	Initiation rate	Incidence	Progression rate
Boyko et al 2015 (Boyko 2015)	Data from 2 panels of participants taking part of the Millenium Cohort Study were never-smokers were followed up for 3 to 6 years for smoking initiation. This study included 68,472 adult military personnel. Smoking was investigated in those who reported not having smoked 100 or more cigarettes in their lifetime. Smoking initiation was defined as never smokers reporting current use of cigarettes on any follow-up.	**Panel 1** Male: 6.6% Female: 4.8% **Panel 2** Male: 7.3% Female: 6.2%	**Per 100 persons-year (95%CI)** **Panel 1** Male: 1.4 (1.3-1.4) Female: 1.0 (0.9-1.1) **Per 100 persons-year (95%CI)** **Panel 2** Male: 2.7 (2.5-3.0) Female: 2.2 (2.0-2.5)	N.A.
Jordan et al 2014 (Jordan 2014)	Data from 2 surveys. The first one was the Missouri Youth Tobacco Survey from 2011 and included data from 1,547 adolescents from the general population. The second survey was the Out, Proud and Healthy Survey from 2012 and included 410 sexual minority teens aged 14-18 years.	**At age 14:** LGBQ: 0.8% General population: 2.5% **At age 18:** LGBQ youth 47.7% General population : 24.2%.	N.A.	N.A.
Mahabee-Gittens et al 2013 (Mahabee-Gittens 2013)	Longitudinal data from the National Survey of Parents and Youth of 8 nationally representative age cohorts (including boys and girls aged 9-16 years) of never-smokers in the US The sample included 5,705 dyads at baseline. Smoking initiation rates were those of never-smokers at T1 reporting smoking at T2. Smoking Initiators: included both ever smokers (defined as someone who smoked some or regularly but not in the last 30 days) and current smokers (defined as someone who reported any smoking in the last 30 days).	**By age:** 10 years: 1.39% 11 years: 4.1% 12 years: 7.6% 13 years: 10.7% 14 years: 14.5% 15 years: 20.3% 16 years: 22.9% 17 years: 23.8%	N.A.	N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Initiation rate	Incidence	Progression rate
Mahabee-Gittens et al 2012 (Mahabee-Gittens 2012)	Longitudinal data from the National Survey of Parents and Youth cohort (including boys and girls aged 9-16 years) of never-smokers in the US The sample included 3,473 dyads at baseline. Smoking initiation rates were those of never-smokers at T1 reporting smoking at T2. Smoking initiators combined both ever - smokers and current smokers.	**By race:** Caucasians: 20.5% African Americans: 19.0% Hispanics: 21.6%	N.A.	N.A.
Bernat et al 2012 (Bernat 2012)	Participants included youth who were part of the Minnesota Adolescent Community Cohort Study and had not smoked a whole cigarette prior to age 18 (n=2,034). Initiation was defined as having smoked a whole cigarette or more between age 18 and 21.	**By Sex:** Male: 30% Female:20.4%	N.A.	N.A.
Tucker et al 2012 (Tucker 2012)	Longitudinal survey including 4,612 never-smokers to evaluate initiation and 2.837 smokers to evaluate progression. Participants were in grades 7th to 11th. Never-smokers were on average 14.8 years old and smokers were 15.0 years old. Initiation was assessed through the question 'Have you ever tried smoking, even just 1 or 2 puffs?' and 'Have you ever smoked regularly, that is at least 1 cigarette every day for 30 days?'	**Overall:** 13.8%	N.A.	**Overall:** 9.7%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Initiation rate	Incidence	Progression rate
Voorhees et al 2011 (Voorhees 2011)	Participants were 12-17 year old adolescents taking part in a school-based cross sectional study. Respondents were asked if they currently used: cigarettes, pipes, cigars, bidis, kreteks, smokeless cigarettes and flavored cigarettes. New smokers were those who had initiated smoking during the past year and meeting the criteria of smoking 1+ days in the past 30 days.	**By Sex:** Male: 12.5% Female: 12.0% **By Race:** Caucasian: 13.3% African American: 11.0% Hispanic: 16.4% American Indian: 11.5% Asian: 6.3% Native Hawaiian/Pacific Islander: 17.3%	N.A.	N.A.
Mahabee-Gittens et al 2011 (Mahabee-Gittens 2011)	Data from Add Health study from 1995-1996. Participants were aged 11-17 years at wave 1. Included in the analysis were 4,061 dyads Each adolescent in the study sample was categorized as a nonsmoker at Wave 1 or Wave 2 if they reported "no" to the question: "Have you ever tried smoking, even 1 or 2 puffs?" They were categorized as a smoker at Wave 2 if they reported "yes". Thus, experimenters who may have only tried smoking 1 or 2 puffs were considered smokers.	**By age and race:** African Americans 12-14 years old: 18.4% African Americans 15-17 years old: 13.8% Hispanics 12-14 years old: 22.8% Hispanics 15-17 years old: 22.2% Caucasians 12-14 years old: 19.8% Caucasians 15-17 years old: 16.3%	N.A.	N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Initiation rate	Incidence	Progression rate
Weiss et al 2011 (Weiss 2011)	Longitudinal school-based experimental trial of smoking prevention in Southern California. Included 3,358 students from 6th to 8th grade. Initiation was defined as those who had reported not smoking at baseline and then answered to have ever tried cigarette smoking, even a few puffs.	**Overall:** 17.8%		
Reed et al 2010 (Reed 2010)	A total of 1,523 undergraduate students with a mean aged of 20.4 (± 1.8) years attending a large urban university in the southwestern United States were invited to participate in an Internet study examining college student lifestyles and behaviors. Never smokers were defined as participants who had never smoked a cigarette in his or her lifetime. Participants who reported starting smoking in the past year were defined as past year initiators (i.e., if chronological age minus age of initiation was ≤1).	**By gender:** Male: 9% Female:8.6% **By Race:** Non-Caucasian: 6.0% Caucasian: 11.1%	N.A.	N.A.
Song et al 2009 (Song 2009)	Longitudinal study performed in 295 high school students beginning at the start of their 9th grade year, who were followed-up every month until the end of 10th grade. Participants were asked whether they had ever ‘‘smoked a whole cigarette.’’ Responses were coded dichotomously (0=no; 1=smoked a whole cigarette).	**Cigarette smoking:** Overall: 20.4% End of grade 9: 7.2% Beginning of grade 10: 6.6% End of grade 10: 6.6%	N.A.	N.A.
Bohnert et al 2009 (Bohnert 2009)	Cohort study of low birth-weight and normal birth-weight children drawn from newborn discharge lists (1983 – 1985) of two major hospitals in southeast Michigan. Assessments occurred at ages 6, 11, and 17 years. The cumulative incidence of smoking initiation was assessed at age 17 using a standard questionnaire about tobacco use and was coded as a binary variable, 0 for never smoked or 1 for smoked at least part of a cigarette.	**By race:** Caucasians: 45.6% African Americans: 35.9%	N.A.	N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Initiation rate	Incidence	Progression rate
Tercyak et al 2007 (Tercyak 2007)	Data from the Georgetown Adolescent Tobacco Research Project and the Adult Longitudinal Outcomes and Health Assessment cohorts of more than 1,100 ninth-grade students gathered from 1999-2003. These were followed up until after 1 year post graduation. Initiation was categorized as all respondents who had ever smoked even a puff off a cigarette in the year after high school. Progression included respondents who smoked more frequently or intensely over time. The average age of the participants was 18.9 years.	**Overall:** 25% after 12th grade	N.A.	N.A.
Staten et al 2007 (Staten 2007)	Cross sectional study including 437 college students aged 18-24 years. Initiators (late initiators) were those who had smoked their first cigarette after the age of 18	**Overall:** 34%	N.A.	N.A.
Jackson et al 2007 (Jackson 2007)	Cross sectional study using audio computer-assisted self-interviews. 732 participants aged 12-14 years drawn from 14 public middle schools. Initiation was defined as ever trying smoking a cigarette, even 1 puff.	**Overall:** Aged 14-16: 30.0% **By race:** Caucasians: 33.7% African Americans: 26.7%	N.A.	
Jackson & Dickinson 2006 (Jackson 2006)	Randomized study of 873 parent-offspring dyads, parents were current smokers and their children had not tried smoking and were in the third grade. The intervention was based on receiving activity guides and parenting tips while the other group was a control. Initiation was defined as first instance of puffing on a cigarette.	**Overall:** 12-19%	N.A.	N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Initiation rate	Incidence	Progression rate
Carvajal & Granillo 2006 (Carvajal 2006)	Longitudinal cross sectional study including 1,137 adolescents aged 11-14. No definition of initiation	**Overall:** 13% By race: Hispanics: 16% Caucasians: 9% Other: 13%	N.A.	N.A.
Choi et al 2003 (Choi 2003)	Participants of the Teenage Attitudes and Practices survey (a longitudinal survey) including 9,965 adolescents aged 12-18 years. Smoking initiation was defined as an adolescent who had experimented with smoking (even a puff).	**Overall:** 28.8%	N.A.	**Overall:** 7%
Kiefe et al 2001 (Kiefe 2001)	Cohort study including a 3,940 African Americans and Caucasians aged 18-30 years who were followed-up for 10 years. Smoking status was ascertained at all years via an interviewer-administered questionnaire. Participants who reported regular cigarette smoking (at least 5 cigarettes per week almost every week for at least 3 months) at the time of a CARDIA examination were classified as regular smokers at that examination.	**10-year initiation by sex and race:** African American women: 7.1% Caucasian women: 3.5% African American men: 13.2% Caucasian men: 5.1%	N.A.	N.A.

N.A.: Not available

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Details of the studies assessing the risk of initiation in the US population are found in Table 19.

In general, determinants of smoking can be divided into three major groups: personal determinants, family related determinants and peer-related or social determinants. Personal determinants are those related to the person's own characteristics. The most studied characteristics were age, sex and race. The determinants of smoking initiation are discussed by age of the populations studied.

Determinants of smoking initiation in adult populations

Among the determinants studied, the following were associated with smoking initiation in adults: poverty (Kiefe 2001), alcohol use or dependence (Goodwin 2013, Green 2008, Reed 2010, Reed 2007, Staten 2007, Tercyak 2007), functional meaning (finding that smoking soothes or helps anxiety) (Bernat 2012), living with a smoker (Green 2008), being single (Kiefe 2001), being male (Bernat 2012), showing psychiatric or mental symptoms (Lipkus 1994), positive reinforcement expectations (Doran 2013) and negative urgency (neuroticism, low conscientiousness, and disagreeableness) (Doran 2013). On the other hand good school performance or achievement (Kiefe 2001, Staten 2007, Tercyak 2007) were associated with a decreased probability of smoking initiation among adults.

Conflicting results were found for age (Green 2008, Reed 2007, Staten 2007), race (Bernat 2012, Green 2008, Kiefe 2001, Reed 2010, Reed 2007), prescription drug use (Reed 2010, Reed 2007), illegal drug use (Reed 2010, Reed 2007) and parental education (Bernat 2012, Reed 2007, Staten 2007).

Determinants of smoking initiation in youth populations

Among the determinants studied, the following were identified as being associated with smoking initiation in youth: peer smoking (Albers 2008, Bohnert 2009, Dalton 2009, Distefan 1998, Flay 1994, Jackson 2007, Jackson 2006, Mahabee-Gittens 2012, Mahabee-Gittens 2013, Rajesh 2015, Titus-Ernstoff 2008, Tucker 2012, Voorhees 2011), sibling smoking (Dalton 2009, Fletcher 2012) parental smoking (Abar 2014, Bohnert 2009, Dalton 2009, Gilman 2009, Goldade 2012, Mahabee-Gittens 2013, Rajesh 2015), low grades (Carvajal 2006, Fletcher 2012, Goldade 2012, Jackson 2007, Titus-Ernstoff 2008, Tucker 2012), no smoking ban at home (Albers 2008, Goldade 2012, Jackson 1997, Voorhees 2011), peer approval of smoking (Choi 2003, Distefan 1998), decreased family cohesion (Mahabee-Gittens 2013, Rajesh 2015, Tucker 2012), parental punishment (Mahabee-Gittens 2012), delinquent behavior and trouble at school (Tucker 2012), access to cigarettes at home (Tucker 2012), hostility (Farrelly 2012), being a bully or victim of a bully (Weiss 2011), sensation seeking (Titus-Ernstoff 2008), increased rebelliousness (Titus-Ernstoff 2008) and family conflicts (Rajesh 2015). On the other hand, the following factors were associated with decreased probability of initiation: higher parental education (Abar 2014, Mahabee-Gittens 2012, Mahabee-Gittens 2013), parental monitoring (Bohnert 2009, Titus-Ernstoff 2008), social support (Abar 2014), parental presence (Mahabee-Gittens 2011), self-regulation (Titus-Ernstoff 2008), higher household income (Albers 2008), expected parental awareness and negative consequences (Jackson 1997) and self-esteem (Titus-Ernstoff 2008).

Conflicting results were found for: age (Abar 2014, Albers 2008, Carvajal 2006, Choi 2003, Dalton 2009, Rajesh 2015, Titus-Ernstoff 2008, Voorhees 2011), sex (Albers 2008,

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Carvajal 2006, Choi 2003, Dalton 2009, Goldade 2012, Jackson 2006, Rajesh 2015, Titus-Ernstoff 2008, Weiss 2011), race (Abar 2014, Carvajal 2006, Choi 2003, Fletcher 2012, Goldade 2012, Jackson 2006, Titus-Ernstoff 2008, Voorhees 2011, Weiss 2011), being exposed to smoking or adult content in movies (Dalton 2009, Farrelly 2012, Jackson 1997), parental monitoring (Bohnert 2009, Titus-Ernstoff 2008),and living with a smoker (Albers 2008, Distefan 1998, Jackson 2007, Voorhees 2011).

Determinants of smoking initiation in mixed populations

The determinants associated with smoking initiation in studies which included both adult and youth populations were: peer smoking (Dal Cin 2013, Scherrer 2012), conduct disorder symptoms (Dal Cin 2013), sensation seeking (Dal Cin 2013, Spillane 2012), maternal nicotine dependence (Scherrer 2012), being white (Scherrer 2012) and symptoms of depression (Spillane 2012), while having a home smoking ban (Mathur 2014), being female (Kravitz-Wirtz 2016) and being African-American was associated with less probability of smoking initiation.

Conflicting results were found for sex (Dal Cin 2013, Kravitz-Wirtz 2016), age (Kravitz-Wirtz 2016, Scherrer 2012, Spillane 2012) and socio-economic status (Dal Cin 2013, Kravitz-Wirtz 2016).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 19. Determinants of cigarette smoking initiation

Author	Population & study methods	Analyses performed	Determinants
Youth Populations			
Rajesh et al 2015 (Rajesh 2015)	Cohort study of 1,328 participants aged 11-14 years of Mexican descent. Initiation or 'trying cigarettes after baseline' was assessed at follow-up and based on responses to three measures: (1) "Have you ever smoked a whole cigarette?" (2) "Have you ever tried a cigarette, even a puff?" and (3) the Minnesota Smoking Index.	Chi-square tests were used to examine the relation between the outcome variable, trying cigarettes after baseline and categorical covariates, whereas Student t tests were used to examine associations between trying cigarettes after baseline and the continuous covariates. Logistic regression was used for variables about familiar cohesion	Increased Probability: Sex (male) ($p<0.001$) Age ($p<0.001$) Positive expectations from smoking ($p<0.001$) Peer smoking ($p<0.001$) Parental smoking ($p=0.001$) ↑ Linguistic acculturation ($p=0.03$) ↓ Family cohesion (OR = 3.06; 95%,CI: 1.38-6.73) ↑ Family conflicts (OR =1.87; 95% CI: 1.19-2.94) No Difference: Parental education
Abar et al 2014 (Abar 2014)	Cohort study of 1,023 middle school students (grades 6-8) and their parents. 814 dyads were included in the study and followed-up for 12 months. Initiation was defined as ever puffing a cigarette.	Comparisons were made between covariate/predictor associations with corresponding substance use behaviors (e.g., ever puffed a cigarette or ever smoked a whole cigarette)	Increased Probability: Grade/Age ($p<0.01$) Parental smoking ($p<0.01$) Decreased Probability: ↑ Parental education ($p<0.001$) ↑ Parental income ($p<0.01$) Social support ($p<0.01$) No Difference: Race

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Mahabee-Gittens et al 2013 (Mahabee-Gittens 2013)	Longitudinal data from the National Survey of Parents and Youth of 8 nationally representative age cohorts (including boys and girls aged 9-16 years) of never-smokers in the US The sample included 5,705 dyads at baseline. Smoking initiation rates were those of never-smokers at T1 reporting smoking at T2. Smoking Initiators: included both ever smokers (defined as someone who smoked some or regularly but not in the last 30 days) and current smokers (defined as someone who reported any smoking in the last 30 days).	Analysis involved a series of lagged logistic regression models using a cohort-sequential .design (values not shown)	Increased Probability: Peer smoking Family structure Parental smoking Decreased Probability: ↑ Parental education No Difference: N.A.
Mahabee-Gittens et al 2012(Mahabee-Gittens 2012)	Longitudinal data from the National Survey of Parents and Youth cohort (including boys and girls aged 9-16 years) of never-smokers in the US The sample included 3,473 dyads at baseline. Smoking initiators combined both ever - smokers and current smokers.	Logistic regression.	Increased Probability: Parental punishment in Caucasians (OR=1.26; 95%CI: 1.11-1.43) Peer smoking (OR= 5.41, 95%CI: 3.75-7.79) Parental monitoring (OR= 1.55, 95%CI: 1.21-1.99) Decreased Probability: ↑ Parental education (OR=0.63, 95%CI: 0.42-0.92) No Difference: N.A.
Goldade et al 2012 (Goldade 2012)	Data from the Minnesota Adolescent Community Cohort including 1,953 participants aged 12-13 who were surveyed every 6 months (2000-2006). Initiation was defined as those having smoked a whole cigarette before age 18 and after baseline.	Linear regression was used to analyze predictors and age of initiation among smokers.	Increase Probability: ↓ Parental education (OR= 2.31, 95%CI: 1.62-3.30) Parental smoking (OR=2.41, 95%CI: 1.97-2.95) Smoking allowed at home (OR=1.81, 95%CI: 2.27-3.69) Peer smoking (OR= 2.90, 95%CI: 2.27-3.69) Sibling smoking (OR=3.06, 95%CI: 2.22-4.22) Decreased Probability: Sex (male) (OR= 0.80, 95%CI: 0.66-0.88) No Difference: Race (OR= 1.00, 95%CI: 0.76-1.31) Living area characteristics (Urbanicity) (OR= 0.84, 95%CI: 0.61-1.15)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Tucker et al 2012 (Tucker 2012)	Longitudinal survey including 4,612 never-smokers to evaluate initiation and 2.837 smokers to evaluate progression. Participants were in grades 7th to 11th. Never-smokers were on average 14.8 years old and smokers were 15.0 years old. Initiation was assessed through the question 'Have you ever tried smoking, even just 1 or 2 puffs?' and 'Have you ever smoked regularly, that is at least 1 cigarette every day for 30 days?'	Logistic regression analyses.	Increased Probability: Best friend smoking (OR not shown) Depressive symptoms (OR= 1.34, 95%CI: 1.05-1.72) Delinquent behavior (OR= 5.56, 95%CI: 2.95-10.48) Trouble at school (OR= 1.39, 95%CI: 1.25-1.55) Access to cigarettes at home (OR= 1.62, 95%CI: 1.33-1.97) Decreased Probability: ↑GPA (OR= 0.73, 95%CI: 0.65-0.82) Family bonding (OR= 0.80, 95%CI: 0.69-0.92) No Difference: N.A
Fletcher & Sindelar 2012 (Fletcher 2012)	Longitudinal survey including 16,673 adolescents in grades 8, 10 and 12. Students were considered initiators if they reported smoking a positive number of cigarettes per day after baseline.	Logistic regression analyses (values not shown)	Increased Probability: Stressors Being Caucasian ↑ Older sibling smoking Decreased Probability: ↑ Good grades No Difference: N.A.
Farrelly et al 2012 (Farrelly 2012)	Participants from the New York Longitudinal Youth Tobacco Evaluation Survey including 1,060 subjects aged 13 to 16 years. Initiation was defined as ever smoking (Have you ever tried smoking cigarettes, even 1 or 3 puffs?)	We estimated the relationship between exposure to smoking in the movies and youth transitions using discrete-time survival analysis.	Increased Probability: Exposure to smoking in movies (OR= 1.09, 95%CI: 1.01-1.15) Exposure to adult content in movies (OR= 1.10, 95%CI: 1.04-1.17) Decreased Probability: N.A. No Difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Weiss et al 2011 (Weiss 2011)	Longitudinal school-based experimental trial of smoking prevention in Southern California. Included 3,358 students from 6th to 8th grade. Initiation was defined as those who had reported not smoking at baseline and then answered to have ever tried cigarette smoking, even a few puffs.	Chi-square analyses assessed whether ever smokers and never smokers differed on bully status, bully-victim status, gender, ethnicity, immigration status, acculturative stress, and program exposure in the 6th grade. Bivariate correlations for all independent variables revealed no multicollinearity problems.	Increased Probability: Hostility ($p<0.0001$) Depressive symptoms ($p<0.0001$) Being a bully ($p<0.01$) Being a bully victim ($p<0.01$) Being Hispanic ($p<0.01$) Acculturative stress ($p<0.01$) Decreased Probability: N.A. No Difference: Gender ($p>0.05$) Immigrant status ($p>0.05$)
Voorhees et al 2011 (Voorhees 2011)	Participants were 12-17 year old adolescents taking part in a school-based cross sectional study. Respondents were asked if they currently used: cigarettes, pipes, cigars, bidis, kreteks, smokeless cigarettes and flavored cigarettes. New smokers were those who had initiated smoking during the past year and meeting the criteria of smoking 1+ days in the past 30 days.	Logistic regression analyses.	Increased Probability: Living with a smoker (OR= 2.5, 95%CI: 2.31-2.70) Second-hand smoke exposure (OR= 5.14, 95%CI: 4.68-5.65) Smoking allowed at home (OR=2.54, 95%CI: 2.34-2.76) Peer smoking (OR= 12.20, 95%CI: 11.14-13.35) Decreased Probability: Grade below 12th grade (OR= all ORs significant for each grade) African American race (OR= 0.80, 95%CI: 0.71-0.90) No Difference: N.A.
Bohnert et al 2009 (Bohnert 2009)	Cohort study of low birth-weight and normal birth-weight children drawn from newborn discharge lists (1983 – 1985) of two major hospitals in southeast Michigan. Assessments occurred at ages 6, 11, and 17 years. The cumulative incidence of smoking initiation was assessed at age 17 using a standard questionnaire about tobacco use and was coded as a binary variable, 0 for never smoked or 1 for smoked at least part of a cigarette.	Logistic regression analyses.	Increased Probability: Peer smoking (OR= 1.75, 95%CI: 1.14-2.69) Decreased Probability: Parent monitoring (OR= 0.89, 95%CI: 0.83-0.96 in Caucasians) No Difference: Urbanicity (OR= 1.17, 95%CI: 0.65-2.10) Mother's education (all ORs were not significant) Maternal smoking (OR= 1.61, 95%CI: 0.89-2.90)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Mahabee-Gittens et al 2011(Mahabee-Gittens 2011)	Data from Add Health study from 1995-1996. Participants were aged 11-17 years at wave 1. Included in the analysis were 4,061 dyads. Each adolescent in the study sample was categorized as a nonsmoker at Wave 1 or Wave 2 if they reported "no" to the question: "Have you ever tried smoking, even 1 or 2 puffs?" They were categorized as a smoker at Wave 2 if they reported "yes". Thus, experimenters who may have only tried smoking 1 or 2 puffs were considered smokers.	Chi-square analysis was used for bivariate comparisons of race/ethnicity and parental smoking status to family bonding variables.	Increased Probability: Lack of parental awareness (p=0.001 and 0.0004 in Caucasians) Decreased Probability: Parent-family connectedness (p=0.03 in Caucasians) Parental presence (p=0.0001 in Hispanics) Maternal happiness with adolescent relationship (p=0.004 in African-Americans and p=0.04 in Hispanics) No Difference: Parent adolescent activities (p>0.05) Parental communication (p>0.05)
Gilman et al 2009 (Gilman 2009)	Cohort study of 564 adolescents aged 12-17 years along with their parents. Smoking initiation was defined as ever smoking even 1 puff. Initiation was defined as ever smoking even a puff.	Discrete-time survival analysis.	Increased Probability: Mother's smoking (OR=2.73, 95%CI: 1.50-4.98 in girls and OR= 2.29, 95%CI 1.39-3.77 in boys) Father's smoking (in boys) (OR= 2.39, 95%CI: 1.45-3.92) Any parent smoking (OR= 2.91, 95%CI: 1.78-4.41) Decreased Probability: N.A. No Difference: N.A.
Dalton et al 2009 (Dalton 2009)	Longitudinal cross sectional study of 2,603 students aged 10 to 14 years. Initiation was defined as established smokers who had smoked at least 100 cigarettes.	Generalized linear models with a log link and Poisson errors were used.	Increased Probability: ↑ Movie smoking exposure (OR= 2.30, 95%CI: 1.81-2.93) Fourth vs First quartile Age 13-14 (OR=1.38, 95%CI: 1.13-1.69) Parental smoking (OR=1.88, 95%CI: 1.57-2.24) Peer smoking (OR=1.77, 95%CI: 1.48-2.13) Any sibling smoking (OR= 1.78, 95%CI: 1.38-2.30) Decreased Probability: Sex (female) (OR= 0.82, 95%CI: 0.69-0.97) No Difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Albers et al 2008 (Albers 2008)	Cohort study with 4-year follow-up of a representative sample including 2,791 Massachusetts youths aged 12-17 years. Initiation was defined as experimentation (trying a cigarette or a puff.	Multilevel (hierarchical) logistic regression	Increased Probability: Living with a smoker (not shown) Peer smoking (in those living with a smoker)ORs=1.44-1.63 No Smoking ban ORs=1.53-1.75 Decreased Probability: Household income > 50,000 USD in those with higher perceived prevalence of adult smoking in town (ORs=0.61-0.62) No Difference: Age (Inconsistent ORs depending on age stratification and subgroup analyses) Sex (Inconsistent ORs depending on subgroup analyses)
Titus-Ernstoff et al 2007 (Titus-Ernstoff 2008)	Longitudinal study of 2,499 school students aged 9-12 years. Initiation was defined as any use of cigarettes after baseline.	Logistic regression analyses.	Increased Probability: Sex (female) (OR= 1.41, 95%CI: 1.13-1.77) Age (older than 9 years) (ORs for all ages were significant) Peer smoking (OR= 4.02, 95%CI: 2.97-5.43) Sensation seeking (ORs = 1.98-5.04) ↑ Rebelliousness (ORs = 1.77-3.49) ↓ Grades (OR= 2.92, 95%CI: 2.24-3.80) ↓ Self-regulation (OR= 2.25, 95%CI: 1.64-3.07) ↓ Self-esteem (OR= 3.26, 95%CI: 1.95-5.45) ↑ Maternal responsiveness (OR= 1.69, 95%CI: 1.30-2.19) ↑ Maternal monitoring (OR= 2.58, 95%CI: 1.73-3.86) Decreased Probability: N.A. No Difference: Being any other race other than Caucasian (OR= 1.29, 95%CI: 0.98-1.70)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Jackson et al 2007 (Jackson 2007)	Cross sectional study using audio computer-assisted self-interviews. 732 participants aged 12-14 years drawn from 14 public middle schools. Initiation was defined as ever trying smoking a cigarette, even 1 puff.	Logistic regression analyses.	Increased Probability: Peer smoking (OR=3.49, 95%CI: 1.87-6.51 in Caucasians 3.81, 95%CI: 2.19-6.56 in African-Americans) Watching to R-rated movies (OR=2.67, 95%CI: 1.07-6.55 in Caucasians) Living with a smoker (not shown) ↓ Good relationship with parents (only in African Americans) (OR= 2.89, 95%CI: 1.39-6.00) Decreased Probability: N.A. No Difference: Watching PG-13 rated movies (OR= 1.46, 95%CI:0.65-3.27)
Jackson & Dickinson 2006 (Jackson 2006)	Randomized study of 873 parent-offspring dyads, parents were current smokers and their children aged 7-8 years who had not tried smoking and were in the third grade. The intervention was based on receiving activity guides and parenting tips while the other group was a control. Initiation was defined as first instance of puffing on a cigarette.	Logistic regression analyses.	Increased Probability: Peer Smoking (OR= 2.61, 95%CI: 1.65-4.12) Decreased Probability: N.A. No Difference: Sex (OR= 1.08, 95%CI: 0.71-1.66 for males) Parental race (OR= 1.19, 95%CI: 0.73-1.97) Parental Education (OR= 0.68, 95%CI: 0.44-1.05) Parent cessation status (OR= 1.31, 95%CI: 0.70-2.46)
Carvajal & Granillo 2006 (Carvajal 2006)	Longitudinal cross sectional study including 1,137 adolescents aged 11-14. No definition of initiation	Logistic regression analyses (values not shown)	Increased Probability: School connectedness ($p<0.001$) Maladaptive coping ($p<0.001$) Decreased Probability: ↑ GPA ($p<0.001$) No Difference: Age ($p>0.05$) Sex (male) ($p>0.05$) Being Hispanic ($p>0.05$) Depressive symptoms ($p>0.05$) Global expectancies ($p>0.05$) Academic aspirations ($p>0.05$)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Choi et al 2003 (Choi 2003)	Participants of the Teenage Attitudes and Practices survey (a longitudinal survey) including 9,965 adolescents aged 12-18 years. Smoking initiation was defined as an adolescent who had experimented with smoking (even a puff).	Logistic regression analyses.	Increased Probability: Peers approve of smoking (OR= 2.02, 95%CI: 1.26-3.23) Perceived safety of experimentation (OR= 1.94, 95%CI: 1.06-3.57) Decreased Probability: N.A. No Difference: Age (OR= 0.99, 95%CI: 0.60-1.66) Gender (OR= 1.29, 95%CI: 0.84-1.99 for males) Religiosity (OR= 0.70, 95%CI: 0.44-1.11) Race (OR= 1.69, 95%CI: 0.93-3.05)
Jackson et al 1997 (Jackson 1997)	Cross sectional study including 1,213 third and fifth grade children. Initiation was defined as any use of tobacco (even 1 or 2 puffs) after baseline.	Logistic regression analyses.	Increased Probability: Indoor smoking allowed (OR= 1.5, 95%CI: 1.2-1.8) Disregard antismoking messages (OR= 10.3, 95%CI: 5.5-19.4) Expect parents awareness (OR= 3.9, 95%CI: 2.5-6.3) Expect negative consequences about not smoking (OR=2.9, 95%CI: 1.1-7.6) Talk about not smoking (OR= 2.0, 95%CI: 1.3-3.1) Decreased Probability: N.A. No Difference: N.A.
Distefan et al 1997 (Distefan 1998)	Participants of the Teenage Attitudes and Practices survey (a longitudinal survey) including 4,149 adolescents aged 12-18 years. Initiation was defined as experimentation but had smoked less than 100 cigarettes in their lifetime.	Logistic regression analyses, not all values shown.	Increase Probability: Male best friend smoking(OR= 1.35, 95%CI 1.11-1.63) Decreased Probability: N.A. No Difference: Living with a smoker (p=0.12) Parents approval of smoking (OR= 1.04, 95%CI: 0.85-1.27) Mother smoking (OR= 1.14, 95%CI: 0.94-1.37) Father smoking (OR= 0.98, 95%CI: 0.81-1.17) Peer approval of smoking (OR= 1.20, 95%CI: 0.98-1.47)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Flay et al 1994 (Flay 1994)	Longitudinal survey of 1,402 seventh grade students from California	Structural equation modeling (values not shown)	Increased Probability: Peer smoking (all races) Parental smoking (only in Hispanics) Decreased Probability: N.A. No Difference: N.A.
Adult Populations			
Doran et al 2013 (Doran 2013)	Longitudinal survey of 400 18-19 year old college freshmen who were never-smokers and were followed-up for 15 months. Smoking was assessed at each online follow-up. Participants were asked whether they had smoked cigarettes since their last assessment. Those who responded positively at any of the five follow-ups were classified as initiators.	Structural equation modeling.	Increased Probability: Sensation seeking ($p<0.01$) Negative urgency ($p<0.05$) Positive reinforcement expectancies ($p<0.05$) Decreased Probability: Negative consequences expectancies ($p<0.01$) No Difference: Lack of perspective ($p>0.05$) Lack of pre-meditation ($p>0.05$)
Goodwin et al 2013 (Goodwin 2013)	Data from the first 2 waves of the National Epidemiologic Survey on Alcohol and Related Conditions. The survey is a nationally representative longitudinal survey of 34,653 non-institutionalized adults aged 18 or above. Among non-smokers (past-year) at Wave 1, smoking initiation was considered positive if the respondent reported smoking cigarettes in the time between Waves 1 and 2.	Logistic regression analyses.	Increased Probability: Alcohol dependence symptoms (OR= 1.49, 95%CI: 1.14-1.97) Alcohol abuse (OR= 1.90, 95%CI: 1.24-2.91) Alcohol dependence (OR= 1.78, 95%CI: 1.17-2.72) Decreased Probability: N.A. No Difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Bernat et al 2012 (Bernat 2012)	Participants included youth who were part of the Minnesota Adolescent Community Cohort Study and had not smoked a whole cigarette prior to age 18 (n=2,034). Initiation was defined as having smoked a whole cigarette or more after baseline between age 18 and 21.	Chi-square and T-test analyses as well as logistic regression.	Increased Probability: Functional meaning (OR= 1.15, 95%CI: 1.03-1.28) Sex (male) (OR= 1.68, 95%CI: 1.37-2.07) Decreased Probability: Being Asian (OR= 0.40, 95%CI: 0.16-0.95) No Difference: Parental education (p>0.05) Peer smoking (p=0.35) Parent would be bothered if smoking (p=0.53) Household smoking ban (p=0.08)
Reed et al 2010 (Reed 2010)	A total of 1,523 undergraduate students with a mean aged of 20.4 (± 1.8) years attending a large urban university in the southwestern United States were invited to participate in an Internet study examining college student lifestyles and behaviors. Never smokers were defined as participants who had never smoked a cigarette in his or her lifetime. Participants who reported starting smoking in the past year were defined as past year initiators (i.e., if chronological age minus age of initiation was ≤1).	Logistic regression analyses.	Increased Probability: Alcohol drinking (OR= 4.50, 95%CI: 1.09-18.52) Decreased Probability: N.A. No Difference: Being Caucasian (OR= 0.17-01.83) Illegal drug use (OR= 1.39, 95%CI: 0.58-3.33) Prescription drug use (OR= 1.07, 95%CI: 0.58-1.97)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Reed et al 2007(Reed 2007)	Cross sectional study of 6,150 undergraduate students aged 18-24 years. Survey was administered online. Initiation was defined as experimentation after baseline (ever-smokers who have smoked fewer than 100 lifetime cigarettes).	Logistic regression analyses.	Increased Probability: Illegal drug use (OR= 3.61, 95%CI: 1.51-8.63) Alcohol drinking (OR= 1.23, 95%CI 1.14-1.34) ↑ School performance Sensation seeking Decreased Probability: N.A. No Difference: Race (OR= 1.33, 95%CI: 0.87-2.05) Prescription drug use (OR= 1.59, 95%CI: 0.89-2.84) Greek membership (OR= 1.04, 95%CI: 0.58-1.88) Age (OR= 1.33, 95%CI: 0.87-2.05)
Green et al 2008 (Green 2008)	Cross sectional study including 2,962 air force technical training students aged 18-36 years. Initiation was defined as current smoking (no details were given)	Logistic regression analyses.	Increased Probability: Peer smoking (OR= 1.67, 95%CI: 1.05-2.67) Instructor smoking (OR= 1.69, 95%CI: 1.12-2.56) Roommate smoking (OR= 1.67, 95%CI: 1.09-2.56) Drinking alcohol (OR= 1.89, 95%CI: 1.35-2.28) Decreased Probability: N.A. No Difference: Age (OR= 0.98, 0.90-1.05) Being Caucasian (OR= 1.57, 95%CI: 1.00-2.44) Education level (OR= 0.48, 95%CI: 0.86-5.12) Family history of smoking (OR= 1.28, 95%CI: 0.92-1.79) Religiousness (OR= 1.04, 95%CI: 0.73-1.48)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Tercyak et al 2007 (Tercyak 2007)	Data from the Georgetown Adolescent Tobacco Research Project and the Adult Longitudinal Outcomes and Health Assessment cohorts of more than 1,100 ninth-grade students gathered from 1999-2003. These were followed up until after 1 year post graduation. Initiation was categorized as all respondents who had ever smoked even a puff off a cigarette in the year after high school. Progression included respondents who smoked more frequently or intensely over time. The average age of the participants was 18.9 years.	Logistic regression analyses.	Increased Probability: Drinking alcohol (OR= 1.82, 95%CI: 1.10-3.0) College non-attendance (OR= 1.34, 95%CI: 1.05-3.33) Decreased Probability: N.A. No Difference: Peer smoking (OR= 1.34, 95%CI: 0.73-2.44)
Staten et al 2007 (Staten 2007)	Cross sectional study including 437 college students aged 18-24 years. Initiators (late initiators) were those who had smoked their first cigarette after the age of 18.	Chi-square and T-test analyses as well as logistic regression.	Increased Probability: Age (OR= 1.35, 95%CI: 1.09-1.66) Peer smoking (OR= 1.99, 95%CI: 1.07-3.70) Drinking (OR= 8.59, 95%CI: 4.00-18.46) Decreased Probability: ↑ Parental education (p=0.03) College service organization (OR= 0.29, 95%CI: 0.15-0.55) No Difference: Parental opinion Greek membership (OR=1.63, 95%CI: 0.86-3.08) Living on campus: (OR= 0.67, 95%CI: 0.33-1.33) Sex (female) (OR= 1.33, 95%CI: 0.77-2.28)
Kiefe et al 2001 (Kiefe 2001)	Cohort study including a 3,940 African Americans and Caucasians aged 18-30 years who were followed-up for 10 years. Participants who reported regular cigarette smoking (at least 5 cigarettes per week almost every week for at least 3 months) at the time of a CARDIA examination were classified as regular smokers at that examination.	Logistic regression analyses.	Increased Probability: Being single (OR= 2.56, 95%CI: 1.45-4.68) Poverty (OR= 1.84, 95%CI: 1.09-3.10) Decreased Probability: High education (OR= 0.82, 95%CI: 0.73-0.92) No Difference: Age (OR= 0.99, 95%CI: 0.67-1.95) Being African-American (OR= 1.14, 95%CI: 0.67-1.95) Not fully employed (OR= 1.20, 95%CI: 0.60-2.25) No health insurance (OR= 0.88, 95%CI: 0.53-1.46)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Lipkus et al 1994 (Lipkus 1994)	Cohort study of 4,038 men and 889 women who were enrolled in the University of Carolina Alumni Heart Study during 1987 through 1991 and were aged 18 or older. Initiation was described as never smokers who reported who had reported to start smoking 1 year or more after baseline	Logistic regression analyses.	Increased Probability: Social introversion (OR=1.29, 95%CI: 1.05-1.57) Lying (OR= 1.39, 95%CI: 1.13-1.71) Hypomania (OR= 1.44, 95%CI: 1.18-1.76) Psychopathic deviate (OR= 1.44, 95%CI: 1.19-1.73) Hostility (OR= 1.30, 95%CI: 1.08-1.56) Decreased Probability: N.A. No Difference: N.A.
Mixed Populations			
Kravitz-Wirtz et al 2016 (Kravitz-Wirtz 2016)	Data for this study are drawn from the 1970 to 2011 waves of the Panel Study of Income Dynamics (PSID), produced and distributed by the University of Michigan's Institute for Social Research and funded by the National Institutes of Health and the National Science Foundation. There were 2,121 participants younger than 25 years of age.	Logistic regression analyses.	Increased Probability: Age (OR= 5.46, 95%CI: 3.65-8.17) Decreased Probability: Sex (female) (OR= 0.68, 95%CI: 0.50-0.92) No Difference: Poverty (OR= 1.51, 95%CI: 0.72-3.19) Mother's age at birth (OR= 1.01, 95%CI: 0.98-1.05)
Mathur et al 2014 (Mathur 2014)	Cohort study including 2,629 adolescents aged 16-20 years belonging to the Minnesota Adolescent Community Cohort study which collected data from 2004 to 2006. The authors measured early initiation with a single item: "How old were you when you smoked a whole cigarette the first time?" the response category was age in years. Then they dichotomously recoded those who responded "before age 13" as early initiators and those who responded "age 13 and older" as late initiators.	A likelihood ratio (G^2_Δ) to test the equivalence of both the latent status prevalence at time 1 and the transition probabilities across groups (values not shown).	Increased Probability: Parental smoking Decreased Probability: Smoking ban No Difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Dal Cin et al 2013 (Dal Cin 2013)	Cohort including 2,341 non-smoking US adolescents aged 13-19 years. Smoking initiation was assessed using a single item: "Have you ever tried smoking cigarettes, even just a puff?"	Logistic regression analyses.	Increased Probability: Peer smoking (OR= 2.21, 95%CI: 1.45-3.35) Sensation seeking (OR= 3.40, 95%CI: 2.14-5.41) Conduct disorder symptoms (OR= 1.89-1.23-2.90) Decreased Probability: Sex (female): (OR= 1.34, 95%CI: 1.07-1.69) Being African American (OR= 0.09, 95%CI: 0.01-0.60) No Difference: Socio-economic status (OR= 0.82, 95%CI 0.53-1.26) TV hours per day (OR= 0.91, 95%CI: 0.55-1.49) Adult responsiveness (OR= 0.96, 95%CI: 0.69-1.34) Sibling smoking (OR= 1.12, 95%CI: 0.81-1.56) Adult monitoring (OR= 0.92, 95%CI: 0.60-1.42)
Spillane et al 2012 (Spillane 2012)	Cohort study including 353 males and 411 females aged 13 to 21 years old. Smoking initiation was defined as non-smokers at baseline who initiated daily smoking (classified as daily smoker at least once during follow-up).	Binary logistic regression analyses.	Increased Probability: Sensation seeking (females only) (OR= 1.3 95%CI: 1.0-1.6) Depression symptoms (males only) (OR= 2.1, 95%CI: 1.3-3.2) Decreased Probability: N.A. No Difference: Age (ORs = 0.7-1.0) Alcohol drinking ORs = 1.4-1.5 not significant Delinquent peer values ORs: 0.9-1.5

Family Structure: only 1 parent present at home, Functional meaning: smoking lifts the mood, controls weight or calms one down. Greek membership: Being a member of a fraternity or a sorority.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.2.3 Discussion

According to the CDC, tobacco use is started and established primarily during adolescence. Nearly 90% of cigarette smokers first tried smoking by age 18, and 99% first tried smoking by age 26 (Prevention 2015). An individual's path to daily smoking and nicotine dependence has been described in five stages: 1) not susceptible to smoking; 2) susceptible or preparing to smoke; 3) initiation or experimentation (trying the first cigarette); 4) nondaily or irregular smoking; and 5) established or regular smoking (e.g., smoking every day or almost every day) (Patnode 2012). Although children as young as age 10 years may be susceptible to smoking, it can take up to 2 years to progress from early experimentation to established smoking (Vickers 2002). In this section the aim was to summarize the rates and determinants for smoking initiation particularly in adolescents and young adults.

Initiation rates varied by definition of initiation, and the more constrained definitions (considering for instance, current use) had lower rates than broader definitions, such as ever use or experimentation of cigarette smoking. This is because only about one-third to one-half of those who try cigarettes will become smokers (Kessler 1995); therefore, initiating smoking does not provide certainty of becoming a regular smoker (Reidpath 2014). Defining initiation of smoking is not consistent in the literature, which has led to inconsistent findings (White 2002). Initiation rates also varied by sex, although not consistently. It has been reported, however, that even though males are more likely to experiment (Boyko 2015, Kiefe 2001, Reidpath 2014), it is women that are slightly more likely to become heavy smokers, which might be due to the fact that women start smoking earlier than men (White 2002). Interestingly, women are also more likely to stop smoking, probably due to diverse factors such as emotional maturity reached earlier than in males as well as pregnancy (White 2002). Race/ethnicity has also been associated with risk of initiation, but the results are not conclusive as different races are at higher risk for initiation depending on the populations included in different studies. It seems, however, that there is a trend suggesting that initiation is higher in Caucasians (Reidpath 2014), while African Americans have been reported to be more likely to stop initiation at experimentation stages (White 2007).

Among the determinants of smoking initiation, the most consistent associations were with peer smoking, parental smoking, age, sex and race. There is considerable empirical evidence that has identified peer smoking as an influence on smoking initiation particularly in adolescents (Kobus 2003). Kobus (Kobus 2003) reviewed the subject and showed that the mechanism of peer influence appears to be due to decisions reflecting predetermined choices about fitting in, social approval, popularity and autonomy rather than the result of direct or coercive pressures. The second most studied determinant was parental smoking, and this appears to function by moderating the relationship between peer influence and tobacco use (Kobus 2003). Hence parents who smoke tilt the balance towards smoking when peer smoking is present. Kobus (Kobus 2003) reported that peer influence can work towards smoking when peers smoke and towards not smoking when they do not.

6.3.2.2.2.4 Conclusions

Initiation rates vary mostly by definition of what initiation is. These rates also vary by sex and race. Many factors influence initiation, and the most commonly studied factors are peer and parental smoking, sex (being male), age and race (being Caucasian). All these factors are associated with increased risk for initiation.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.3 Smoking cessation

6.3.2.2.3.1 Search strategies

The search for articles on smoking cessation was performed on March 23, 2016 and resulted in 11,749 articles being identified using the following query: ("smoking"[MeSH Terms] OR "smoking"[All Fields]) AND ("cessation"[All Fields] OR "quitting"[All Fields]) AND ("united states"[MeSH Terms] OR ("united"[All Fields] AND "states"[All Fields]) OR "united states"[All Fields]) AND English [lang]. The review of the titles and abstracts resulted in 1 046 articles being extracted and fully reviewed, and the relevant articles are discussed in this section.

6.3.2.2.3.2 Results

There were 57 studies assessing the rates of cessation in diverse populations identified through the literature search. These articles included studies both with or without interventions. Out of these 57 studies, 47 included adult populations while 10 included youth populations.

The search query was not limited to any time period; however, the results presented are from studies published in the last 16 years (from 2000 onwards). Results were also limited to studies which included a minimum sample size of 50 participants.

Cessation rates were provided as point prevalence abstinence (ppa), continuous cessation (from 2 weeks onwards after quit date) as well as according to follow-up treatment administered.

6.3.2.2.3.2.1 Smoking cessation rates in adult populations

Out of the 46 retrieved studies, 38 were interventional and 8 were observational in nature. Detailed characteristics on these studies can be found in Table 20.

From the interventional studies, 18 assessed the effect of various pharmaceutical treatments on smoking cessation. The drugs studied were: varenicline, bupropion, naltrexone, eldepryl, mecamylamine, or combination treatments such as: varenicline plus bupropion, bupropion plus psychotherapy and mecamylamine plus nicotine replacement patch.

Interventional studies

Varenicline and Bupropion

There were 12 studies assessing the impact of varenicline and bupropion treatment on smoking cessation either alone or in combination (Collins 2004, Cox 2012, Croghan 2010, Dale 2001, Ebbert 2014, Gray 2015, Harris 2004, Japuntich 2006, Knight 2010, Nollen 2011, Rose 2014, Schmitz 2007). Varenicline proved to be effective in the treatment of smoking (Nollen 2011). Treatment by varenicline alone resulted in 7-day ppa cessation rates of 44.8% (Gray 2015) measured during treatment to 7-day ppa 3-months post treatment of 23.6% (Nollen 2011). However, the longer the follow-up the lower the cessation rates, as reported by Gray et al. (Gray 2015) who showed that after 4 weeks, the rates had gone down to 22.4%, although Rose and colleagues (Rose 2014) reported slightly better cessation rates of 25.9% for patients receiving varenicline plus placebo of 25.9% after 8-11 weeks of post-quit follow-up. Finally, a study showed 1 year abstinence rates of 27.7% for those who received 24 weeks of varenicline treatment, while those who received only 12 weeks of treatment had an abstinence rate of 22.9% (Knight 2010). The

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

same study reported 1 year abstinence rates of 15.9% for patients who received 12 weeks treatment with bupropion and 9.3% for those who received 12 weeks of placebo treatment.

Monotherapy with bupropion (including both regular bupropion and bupropion sustained release [SR]) yielded 7-day ppa at 7 weeks post treatment of 23.7% (Cox 2012) to 31.2% (Harris 2004) while the 7-day ppa at end of treatment (EOT) was reported to vary by the dosage: 29% with 100 mg, 39% with 150 mg, 44% with 300 mg in comparison to 19% for placebo alone (Dale 2001). Continuous abstinence was reported by 3 studies: the study by Roth et al. (Roth 2005) reported a 6-week abstinence rate assessed at 12-week follow-up of 7.7% in those using bupropion and a 7-day ppa of 15.4%; Bolt et al. (Bolt 2012) reported results of a wide variety of treatments including bupropion monotherapy which resulted in a 8-week abstinence rate of 42%; finally the study by Roth et al. (Roth 2005) reported a 6-month abstinence rate of 16.8%.

Combination treatment with bupropion plus psychotherapy yielded the following results: bupropion plus cognitive behavioral therapy (CBT) showed a higher 7-day ppa at end-of-treatment (EOT) of 44% compared to combination treatment that included bupropion plus supportive therapy (18%) (Schmitz 2007). The ppa decreased as follow-up time increased, and after 1 year follow-up the 7-day ppa was 17% in the bupropion plus CBT group compared to 2% in the bupropion plus supportive therapy group. Similar results were reported by Japuntich et al. (Japuntich 2006) who found that the 7-day ppa for subjects administered bupropion plus comprehensive health enhancement support system at 3 months post treatment was 22.9% decreasing to 15% at 6-months post treatment, while bupropion plus counseling yielded similar rates (20.8% at 3 months and 11.8% at 6 months post treatment). The study by Collins et al. (Collins 2004) reported 8-week continuous cessation rates higher in bupropion plus CBT patients (54.4%) compared to those who received a placebo plus CBT (34.5%). If the subjects received bupropion plus counseling the cessation rate was 32.6% which was higher than the placebo plus counseling group (19.4%).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 20. Characteristics of studies reporting cessation rates in adult populations

Survey	Period	Study characteristics	Intervention	Definition	Rates
Gray et al (Gray 2015)	2015	Double-blind double - dummy randomized trial on female smokers aged 18-45 years and averaging ≥ 10 CPD for at least 6 months.	Participants were randomized to receive a 4-week course of (a) varenicline tablets and placebo patches (n=67) or (b) placebo tablets and nicotine patches (n=73). Two brief cessation counseling sessions were provided for all participants.	The outcome of primary clinical interest was 2-week end-of-treatment abstinence. Secondary outcomes included 1- and 4- week end-of treatment abstinence and abstinence at a post-treatment follow-up visit occurring 4 weeks after treatment conclusion. Breath carbon monoxide (≤ 10parts per million) was used to confirm biochemically self-reported abstinence.	• 2-week end of treatment abstinence: o Varenicline = 37.3% o Nicotine patch = 17.8% • 1-week abstinence: o Varenicline = 44.8% o Nicotine patch = 20.6% • 4-week abstinence: o Varenicline = 22.4% o Nicotine patch = 9.6%
Reitzel et al (Reitzel 2015)	2015	Cohort study of 58 smokers aged 18-64 years (65.5% men).	None	Biochemically-verified smoking abstinence on the quit day and at Days 3, 7, 14, 28, and 90 post-quit were assessed.	• Day 3 = 37.3% • Day 7 = 27.5% • Day 14 = 22.4% • Day 28 = 20.0% • Day 90 = 10.3%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Ramo et al (Ramo 2015a)	2015	Interventional study of 79 current smokers aged 18-25 years.	The intervention was based on the US Public Health Service Clinical Practice Guidelines and the Trans-theoretical Model and enrolled participants into study-run 3-month secret Facebook groups matched on readiness to quit smoking	7-day point prevalence abstinence at 12-month follow-up.	• 13%
Abrantes et al (Abrantes 2014)	2014	Randomized Controlled trial including 61 smokers (65.6% female) with a mean age of 47.3 years.	Behavioral exercise intervention for 12 weeks (AE) or a 12-week health education contact control (HEC)	7-day point prevalence of abstinence at 12 weeks 6 and 12-months and continuous abstinence at 8 weeks, 6 and 12-month post quit date.	• 7-day point prevalence: o At 12 weeks: AE = 40%, HEC = 22.6% o At 6-months: AE = 26.7%, HEC = 12.9% o At12-months: AE = 26.7%, HEC = 12.9% • Continuous abstinence: o 8 weeks post quit: AE = 30%, HEC = 25.8% o 6 months post quit: AE = 23.3%, HEC = 9.7% o 12 month post quit: AE = 13.3%, HEC = 3.2%
Rose et al (Rose 2014)	2014	A randomized double-blind, parallel group, adaptive treatment trial identified 222 cigarette smokers showing ≤50% reduction in smoking after 1 week of nicotine patch treatment.	Smokers were randomized to receive 12 weeks of varenicline/bupropion treatment vs. varenicline plus placebo.	Continuous smoking abstinence at weeks 8–11 after the target quit date.	• Combination therapy = 39.8% • Varenicline = 25.9%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Bricker et al (Bricker 2014)	2014	Randomized trial including 121 uninsured South Carolina Quitline callers who smoked ≥ 10 CPD and wanted to quit within the next 30 days.	Participants were randomized to 5 sessions of either ACT or CBT telephone counseling and were offered 2 weeks of NRT.	30-day point prevalence abstinence at 6 months post-randomization.	• ACT = 31% • CBT = 22%
Rojewski et al (Rojewski 2014)	2014	A randomized placebo-controlled trial including 166 smokers with a mean age of 41.3 years for menthol users and 46.2 years for non-menthol smokers.	Participants received placebo or 25 mg naltrexone daily beginning the week before quitting. Additionally, Participants received 21 mg transdermal nicotine patches for 6 weeks, then 14 mg patches for 2 weeks, beginning on their quit date.	7-day point prevalence smoking abstinence rates at 26 weeks post-quit date.	• Naltrexone = 22% • Placebo = 27% • Menthol = 13% • Non-menthol = 30%
Fridberg et al (Fridberg 2014)	2014	A double-blinded, placebo-controlled trial including 315 participants were between 18 and 65 years of age, smoked 10 to 40 cigarettes/d for at least 2 years, had no past year history of DSM-IV Axis I disorders including alcohol or drug dependence (excluding nicotine), no lifetime opioid use disorders, and were generally healthy.	Naltrexone or placebo, both in conjunction with open-label nicotine patch and behavioral therapy	Abstinence at 6- or 12-months. There were categorized into subgroups based upon past 6-month drinking patterns: HDS (n = 69; i.e., averaged ≥2 heavy drinking episodes per month), moderate-to-light drinking smokers, MOD (n = 204, i.e., consumed 1 drink up to a maximum of <2 heavy drinking episodes per month on average), or nondrinking smokers (ND) (n = 42, no alcohol consumed in the past 6 months).	• At 6 months: o Naltrexone HDS = 32% o Placebo HDS = 14% o Naltrexone MOD = 25% o Placebo MOD = 24% o Naltrexone ND = 10% o Placebo ND = 32% • At 12 months : o Naltrexone HDS = 27% o Placebo HDS = 20% o Naltrexone MOD = 22% o Placebo MOD = 19% o Naltrexone ND = 23% o Placebo ND = 15%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Schnoll et al (Schnoll 2015)	2009-2014	Randomized clinical trial of 525 treatment-seeking smokers who smoked ≥ 10 CPD and were aged ≥ 18 years.	Smokers received 12 smoking cessation behavioral counseling sessions and were randomized to 8 (standard), 24, or 52 weeks of nicotine patch treatment.	7-day point prevalence abstinence, confirmed with breath levels of carbon monoxide at 24 weeks	• At 24 weeks: • Standard treatment = 21.7% • Extended and maintenance treatment = 27.2%
Kahler et al (Kahler 2015)	2011-2013	Randomized clinical trial including 66 adults aged ≥ 18 years.	Standard smoking cessation treatment (ST) with smoking cessation treatment that targets positive affect, termed positive psychotherapy for smoking cessation (PPT-S) plus 8-week of NRT.	7-day point-prevalence smoking abstinence was assessed 8, 16 and 26 weeks after quit date verified at all assessments by alveolar carbon monoxide.	• At week 8: o ST = 25.8% o PPT-S = 40.0% • At week 16: o ST = 6.5% o PPT-S = 22.9% • At week 26: o ST = 6.5% o PPT-S = 17.1%
Schlam et al (Schlam 2016)	2010-2013	Randomized trial, including 544 smokers aged ≥ 18 years; smoking ≥ 5 CPD for the previous 6 months	Participants were randomized to 1 of 32 unique experimental conditions. All participants received a standard cessation intervention: 8 weeks of nicotine patch plus nicotine gum and 50 minutes of counseling delivered over four sessions. In addition, they were randomized to receive 1 of 2 levels of each factor: either an 'On' (or more intense) level or an 'Off' (or less intense) level.	7-day point-prevalence smoking abstinence was assessed at 6- and 12-months.	• At 6-months: o 8 weeks of medication = 34% o 26 weeks of medication = 43% • At 12-months: o 8 weeks of medication = 27% o 26 weeks of medication = 34%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Cook et al (Cook 2016)	2010-2013	Randomized controlled trial of 518 adult smokers aged ≥ 18 years where 63.4% were women.	Four factors contrasted intervention components designed to reduce smoking and promote abstinence: (1) nicotine patch versus none; (2) nicotine gum versus none; (3) motivational interviewing (MI) versus none; and (4) behavioral reduction counseling (BR) versus none.	7-day ppa was assessed at 12- and 26-weeks.	• At 12-weeks: o Nicotine patch = 5.7% o Nicotine gum = 8.7% o Motivational interviewing = 8.3% o Behavioral reduction counseling = 10.8% • At 26-weeks: o Nicotine patch = 9.4% o Nicotine gum = 9.1% o Motivational interviewing = 9.1% o Behavioral reduction counseling = 10.8%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Piper et al (Piper 2016)	2010-2013	A fully crossed, six-factor randomized fractional factorial experiment. Including a total of 637 adult smokers (55% women, 88% Caucasian) motivated to quit smoking who visited primary care clinics.	Six intervention components designed to prepare smokers to quit, and achieve and maintain abstinence (i.e. for the preparation, cessation and maintenance phases of smoking treatment): (1) preparation nicotine patch versus none; (2) preparation nicotine gum versus none; (3) preparation counseling versus none; (4) intensive cessation in-person counseling versus minimal; (5) intensive cessation telephone counseling versus minimal; and (6) 16 versus 8-weeks of combination nicotine replacement therapy (nicotine patch plus nicotine gum).	7-day self-reported point-prevalence abstinence at 16 weeks.	• 16-week abstinence rates: o Combination of preparation NRT and cessation counseling = 42.8% o Only one of these components = 29.1% - 31.1% o No therapy = 36%
Ebbert et al (Ebbert 2014)	2009-2013	Randomized, blinded, placebo-controlled multicenter clinical trial of 506 adult smokers aged ≥ 18 years.	Twelve weeks of varenicline /bupropion SR (combination therapy); or varenicline /placebo (monotherapy).	7-day point prevalence abstinence and no smoking from 2 weeks after the target quit date.	• 7-day prevalence at week 12: o Combination therapy = 56.2% o Monotherapy = 48.6% • Prolonged abstinence: o Combination therapy = 53% o Monotherapy = 43.2%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Vickerman et al (Vickerman 2015b)	2012	Longitudinal study that included 715 ≥ 18 years old, tobacco users who enrolled in the Nebraska, North Carolina or Texas state quit line programs.	None	7-day and 30-day point prevalence abstinence rates 7 months after enrollment	• 7-day prevalence abstinence = 27.7% • 30-day prevalence abstinence = 24.5%
Halpern et al (Halpern 2015)	2012	5-group randomized, controlled trial comparing usual care with four incentive programs including 2,538 participants aged ≥ 18 years.	One of the individual-oriented programs and 1 of the group-oriented programs entailed rewards of approximately $800 for smoking cessation; the others entailed refundable deposits of $150 plus $650 in reward payments for successful participants	Sustained abstinence at 6 months, cotinine-verified	• In intention-to-treat analyses, rates of sustained abstinence from smoking through 6 months were higher with each of the four incentive programs (range, 9.4 to 16.0%) than with usual care (6.0%) the superiority of reward-based programs was sustained through 12 months.
Regan et al (Regan 2016)	2010-2012	A randomized controlled trial of a smoking cessation intervention during an admission at Massachusetts General Hospital in Boston which included 402 smokers who were aged ≥ 18 years.	The intervention consisted in offered post-discharge care consisting of 90 days of cessation medication and telephone counseling support to standard care.	7-day point prevalence abstinence verified biochemically verified 3-month and 6-month post discharge.	• 7-day prevalence at 3 months: 26 % • 7-day prevalence at 6 months: 27%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Thomas et al (Thomas 2015)	2010-2012	Randomized trial including 1,217 participants with a mean age of 26.3 years.	Participants were assigned to 1 of 4 study arms to compare the impact of a single Quit and Win contest, with and without Motivation and Problem-Solving Counseling (MAPS) to multiple, concurrent contests (i.e., 3-month long contests) with and without counseling. Assignment was not blinded to staff or participants.	Biochemically verified confirmation of self-reported tobacco abstinence using urine cotinine (cut-point 40 ng/mL) at 6 months post enrollment.	• Quit at 1 month: o No Hookah use = 31.7% o Hookah users = 27.4% • Quit at 4-months: o No Hookah use = 29.7 % o Hookah users = 20.0% • Quit at 6-months: o No Hookah use = 13.9% o Hookah users = 8.9%
Kendzor et al (Kendzor 2014)	2009-2012	Longitudinal observational study including 190 participants aged 18-65 years.	None	7-day ppa at 26 weeks post-quit verified by expired CO level of < 8ppm.	• 7-day ppa = 15.8% • Continuous abstinence = 7.4%
Catley et al (Catley 2016)	2010-2011	Randomized clinical trial including 255 smokers aged ≥ 18 years.	Motivational Interviewing (MI) vs. health education (HE) or a session of brief personalized advice to quit (BI).	Biochemically verified 7-day point prevalence abstinence at 3- and 6-months follow-ups.	• 7-day prevalence at 3-months: • MI = 5% • HE = 8% • BA = 0% • 7-day prevalence at 6-months: • MI = 6% • HE = 15% • BA = 4%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Fu et al (Fu 2014b)	2009-2011	A pragmatic randomized clinical trial involving a population-based registry of current smokers aged 18 to 80 years. A total of 6400 current smokers, identified using the Department of Veterans were included.	Current smokers were randomized to usual care or proactive care. Proactive care combined (1) proactive outreach and (2) offer of choice of smoking cessation services (Telephone or in-person).	7-day ppa and 6-month prolonged smoking abstinence at 1 year.	• 7-day ppa: o Proactive = 15.1% o Usual care = 17.1% • 6-month abstinence o Proactive = 13.5% o Usual care = 10.9%
Bush et al (Bush 2014)	2010	Observational study of US Adult smokers who called 1 of the 5 state quit-lines (Georgia, Louisiana, Maryland, South Carolina, and Texas) which included 595 adults aged ≥ 18 years and smoked ≥ 5 CPD.	None	30 day ppa	• Overweight = 40% • Normal weight and obese = 25%
Nollen et al (Nollen 2011)	2009-2010	Randomized controlled trial including 61 African-American smokers who smoked ≥ 10 CPD (62.5% female) who had a mean age of 46.8 years.	All participants received 3 months of varenicline and a single counseling session focused on making a quit plan. Assigned participants received 5 additional counseling sessions to encourage medication use.	7-day ppa salivary cotinine, and carbon monoxide confirmed at 3months.	• 23.6%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Cox et al (Cox 2012)	2007-2010	A randomized, double-blind placebo-controlled trial including 540 African American participants aged ≥ 18 years who smoked ≥ 10 CPD.	Participants were randomly assigned to receive 300 mg bupropion SR (150 mg once daily for 3 days and then 150 mg twice daily) (n = 270 participants) or placebo (n = 270 participants) for 7 weeks, and up to six sessions of health education counseling. Serum cotinine was measured at baseline (week 0).	The primary outcome was salivary cotinine–verified 7-day point prevalence smoking abstinence at week 7 and 26; a cut point of 15 ng/mL differentiated smokers from non-smokers.	• Abstinence at week 7: • Placebo = 9.6% • Bupropion SR = 23.7% • Abstinence at week 26: • Placebo = 10.0% • Bupropion SR = 13.3%
NHIS 2011 (Frieden 2011)	2001-2010	National representative cross-sectional survey of the US population. The sample included in this report included 27,157 adults aged 25-64 years.	None	Successful recent quitting, no definition of 'recent'	• Recent quitting = 6.2% • 3.2% of those with ≤ 12 years of school education compared with 11.4% of those with an undergraduate degree and 8.1% of those with an associate degree.
Shen et al (Shen 2014)	2004-2010	Data from the New Mexico Pharmaceutical Care Foundation which provided cessation programs. Participants included 1,437 adults aged ≥ 18 years.	None	Point prevalence quit rates at 1-, 3- and 6-months	• At 1-month = 29.3% • At 3-months = 23.3% • At 6-months = 18.0%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Bolt et al (Bolt 2012)	2008	Randomized trial of 1,504 who were randomized into 1 of 6 cessation pharmacotherapies and had a mean age of 44.7 years.	Participants had been randomized into 1 of 6 therapy groups: placebo, nicotine patch, nicotine lozenge, bupropion, nicotine patch + nicotine lozenge, and bupropion + nicotine lozenge.	Biochemically confirmed 8-week abstinence.	• 8-week abstinence rates: o Placebo = 33% o Nicotine patch = 47% o Lozenge = 44% o Bupropion = 42% o Patch plus lozenge = 56% o Bupropion plus lozenge = 52% • Univariate models suggested that the combination treatments produced higher abstinence rates than the monotherapies because of greater suppression of withdrawal, craving, and smoking expectation
Cherrington et al (Cherrington 2015)	2008	Randomized, placebo-controlled trial of 300 African American smokers aged ≥ 19 years.	The intervention consisted of stories DVD plus routine clinical treatment and the control was routine clinical treatment.	Self-reported quit at 2 weeks and continuous quit at 6 months, continued 6 months quit carbon-monoxide verified	• Self-reported quit at 2 weeks: o Intervention = 43.3% o Control = 36.7% • Self-reported continuous quit at 6 months: o Intervention = 33.3% o Control = 26.0% • Verified 6-months quit: o Intervention = 15.3% o Control = 11.3
Kinnunen et al (Kinnunen 2008)	2008	Randomized, placebo-controlled trial of 608 participants aged ≥ 20 years regularly smoking ≥ 5 CPD.	Participants were randomly assigned to 2 or 4 mg nicotine gum or to placebo gum.	12 month abstinence rates verified by expired air carbon monoxide in ppm	• Non-depressed with NRT = 20.1% • Depressed with NRT = 15.1% • Non-depressed without NRT = 9.8% • Depressed without NRT = 5.7%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Gariti et al (Gariti 2009)	2005-2008	A prospective, random assignment experiment that employed a 2 × 2 double blind, double-dummy design for the medication component of the study which included 260 men and women adults who smoked 6-15 CPD.	Participants were randomized to receive 1 of 2 levels of counseling intensity in combination with 1 of 2 pharmacotherapies.	7-day ppa at 1-, 6- and 12-months	• High counseling at 12 weeks = 32.8% • Low counseling at 12 weeks = 21.2%
Buller et al (Buller 2014)	2007-2009	Data from a randomized three-group pretest-posttest trial including 3,094 young adults aged 18-30 years.	NRT	30-day ppa at week 12 and continuous abstinence at week 26	• 30 day ppa: o NRT = 19.4% • 26-week continuous abstinence: o NRT = 8.0% o Non-users = 5.0%
Webb et al (Webb 2010)	2006-2008	Randomized clinical trial of 154 participants aged ≥ 18–65 years and a mean use of 13 CPD	CBT or GHE. Participants in both conditions received 6 sessions of counseling and 8 weeks of transdermal nicotine patches.	7-day point prevalence abstinence, assessed at the end of counseling (2 weeks) and at 3- and 6-month follow-ups. Additionally, 28-day continuous abstinence was measured at 3- and 6-months.	• 7-day ppa EOT: o CBT = 51% o GHE = 27% • 7-day ppa at 3-months: o CBT = 34% o GHE = 20% • 7-day ppa 6-months: o CBT = 31% o GHE = 14
Varghese et al (Varghese 2014)	2005-2008	Interventional study including 6,626 smokers with a mean age of 43.07 years.	Cognitive–behavioral treatment and nicotine patches	Abstinence at EOT, 3 and 6 months after treatment.	• At EOT = 31.9% • 3-months after treatment = 29.3% • 6-month after treatment = 28.6%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Weinberger et al (Weinberger 2010)	2004-2008	8-week randomized, double-blind, placebo-controlled trial including 101 smokers aged of 18-70 who smoked ≥ 15 CPD and reported motivation to quit smoking in the following 30 days.	Participants were randomly assigned to receive either Eldepryl (n=51) or matching placebo (n=50) with gender as a stratification variable in combination with brief (<10 minutes) manualized smoking cessation counseling.	7-day point prevalence abstinence, 4-week continuous abstinence and 7-day point prevalence abstinence at 6 month follow-up at EOT.	• 7-week ppa at EOT: o Eldepryl = 16% o Placebo = 20% • 4-week continuous abstinence: o Eldepryl = 14% o Placebo = 18% • 7-day ppa at 6-months: o Eldepryl = 12% o Placebo = 16%
Smith et al (Smith 2009)	2005-2007	Randomized open-label clinical trial including 1,346 adult patients who smoked ≥ 10 CPD	Patients were randomly assigned to five active pharmacotherapies: three monotherapies (Nicotine Patch, Nicotine Lozenge, and Bupropion SR) and two combination therapies (Patch plus Lozenge and Bupropion plus Lozenge).	Six month abstinence rates	• Bupropion=16.8% • Lozenge=19.9% • Patch=17.7% • Patch plus Lozenge=26.9% • Bupropion plus Lozenge=29.9%.
Knight et al (Knight 2010)	2006	A randomized, double-blind trial including 1,210 aged between 18 and 75 years who smoked ≥ 10 CPD, who had not had an abstinent period of over 3 months in the previous year, and were motivated to quit.	12 plus 12 weeks varenicline therapy, 12 weeks varenicline therapy, bupropion, and placebo.	1-year abstinence	• 12 plus 12 weeks varenicline = 27.7% • 12 weeks varenicline = 22.9% • 12 weeks bupropion = 15.9% • 12 weeks placebo = 9.3%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Schmitz et al (Schmitz 2007)	2007	Randomized, controlled-trial of 154 women aged 30-70 years and smoked ≥ 10 CPD.	Two level factorial design to examine the independent and interactive effects of medication (bupropion 300 mg/day vs. placebo) and CBT vs. supportive therapy [ST]).	Biochemically confirmed 7-day point-prevalence abstinence. During treatment, abstinence was determined at each clinic visit by self-report of no smoking in the past 7 days and a CO level of no more than 10 ppm.	• 7-day ppa at EOT: o Bupropion plus CBT = 44% o Bupropion plus ST = 18% • 7-day ppa at 3-months: o Bupropion plus CBT = 24% o Bupropion plus ST = 1% • 7-day ppa at 6-months: o Bupropion plus CBT = 30% o Bupropion plus ST = 8% • 7-day ppa at 9-months: o Bupropion plus CBT = 23% o Bupropion plus ST = 5% • 7-day ppa at 12-months: o Bupropion plus CBT = 17% o Bupropion plus ST = 2%
Glover et al (Glover 2007)	2007	Randomized, controlled trial including 540 participants aged 19-70 years.	Nicotine transdermal therapy co-administered with the nicotine antagonist, mecamylamine, compared to a nicotine transdermal patch alone (nicotine + 6 mg mecamylamine, nicotine + 3 mg mecamylamine, and nicotine alone).	The primary efficacy parameter was 4-week continuous abstinence after the quit date, confirmed with an expired carbon monoxide of < 10 parts per million.	• Overall 4 week abstinence: o Nicotine patch plus 6 mg mecamylamine = 29% o Nicotine patch plus 3 mg mecamylamine = 29% o Nicotine patch only = 23%
Rafful et al (Rafful 2013)	2001-2005	National Representative Survey on Alcohol and Related Conditions (NESARC) including 43,093 civilian non-institutionalized participants aged ≥ 18 years.	None	Successful quitting from wave 1 to wave 2	• 746 smokers (39.9%) tried to quit and 4.6% of those who tried to quit were successful (total of 1.8% of all smokers).

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Roth et al (Roth 2005)	2005	Interventional study of 198 subjects attending a smoking cessation clinic and had a mean age of 52 years.	Patients received tailored behavioral counseling, educational materials, and drug therapy consisting of sustained-release (SR) bupropion; nicotine patch, inhaler, or nasal spray; or combination therapy	Continuous abstinence at 6 weeks and point prevalence at 12 weeks	• At 6-weeks: o Nicotine patch = 22.9% o Bupropion SR = 7.7% o Combination patch plus inhaler = 25% • At 12-weeks: o Nicotine patch = 18.6% o Bupropion SR = 15.4% o Combination patch plus inhaler = 22.2%
Slopen et al (Slopen 2013)	2004-2005	Cohort study including 4,938 adults aged 25-74 years followed-up for 9-10 years.	None	Quit from baseline	• 6.8%
Collins et al (Collins 2004)	2004	Randomized, placebo-controlled trial including 314 women and 241 men who smoked ≥ 10 CPD and were aged ≥ 18 years.	Behavioral counseling plus 10 weeks of bupropion (300 mg) vs. placebo	Prolonged abstinence and biochemically-verified point prevalence at EOT (8 weeks after quit date) and at 6-month follow-up.	• At EOT: o Intervention = 54.4% o Control = 34.5% • At 6-months: o Intervention = 32.6% o Control = 19.4% • Men were more likely to be abstinent at EOT (51.0% vs. 40.1%)
Harris et al (Harris 2004)	2004	A double-blind placebo-controlled, randomized trial including 535 adult participants.	Bupropion vs. placebo	7-day ppa at 7 weeks	• Overall rate = 31.21%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Lukowski et al (Lukowski 2015)	2002	Interventional study of 4,960 (subset) participants who had called into 6 state quit lines and were aged ≥ 18 years.	Participants received up to 5 coaching sessions and up to 8 weeks of nicotine replacement therapy.	30-day point prevalence abstinence at 3-month and 6-month post-intervention calls in a subset of participants (n = 4,960) for whom follow-up interviews were completed.	• Prevalence of abstinence at 3-months: • Emotional challenged or mental illness = 31% • Control = 34% • Prevalence of abstinence at 6-months: • Emotional challenged or mental illness = 33% • Control = 43%
Japuntich et al (Japuntich 2006)	2001-2002	Randomized clinical trial of 284 adults aged ≥ 18 years who smoked ≥ 10 CPD.	Smokers were randomly assigned to receive either bupropion plus counseling alone, or bupropion and counseling in addition to 12 weeks of access to the Comprehensive Health Enhancement Support System for Smoking Cessation and Relapse Prevention (CHESS SCRP; a Web site which provided information on smoking cessation as well as support).	7-day ppa, biochemically verified using expiratory breath carbon monoxide at 3- and 6-months post quit.	• At 3-month post quit: o CHESS SCRP = 22.9% o Control = 20.8% • At 6-month post quit: o CHESS SCRP = 15.0% o Control = 11.8%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Intervention	Definition	Rates
Dale et al (Dale 2001)	2001	Double-blind, placebo-controlled, dose-response trial including 615 healthy men and women aged ≥ 18 years who were smoking ≥ 15 CPD and were motivated to stop smoking.	Random assignment of patients to placebo or bupropion SR treatment, 100, 150, or 300 mg/d, for 7 weeks (total duration of study was 52 weeks: 7 weeks of treatment and 45 weeks of follow-up).	7-day ppa, biochemically verified at end of follow-up.	• Placebo = 19% • Bupropion 100 mg = 29% • Bupropion 150 mg = 39% • Bupropion 300 mg = 44%

PPA: point prevalence abstinence, GHE= group general health education, CBT = cognitive behavioural therapy

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

There were 2 studies assessing cessation therapy with bupropion plus nicotine lozenges (Bolt 2012, Smith 2009). The study by Bolt et al. (Bolt 2012) reported a 8-week abstinence of 52% compared to 33% in placebo treated patients, 44% in lozenge-only patients and 42% in bupropion-only patients, while the study by Smith et al. (Smith 2009) reported a 6 month abstinence rate of 29.9% compared to 16.8% in bupropion-only and 19.9% in lozenge-only treated patients. Additionally, there was 1 study (Croghan 2010) assessing cessation rates in those administered bupropion plus nicotine inhaler. Successful cessation rates were reported by race/ethnicity and found that the 12-week quit rates were 25% in Asians, 16% in African Americans, 11% in Native Americans and 29% in other race/ethnicity groups including Caucasians.

There were 2 studies assessing abstinence rates in subjects receiving varenicline plus bupropion (Ebbert 2014, Rose 2014). Rose et al. (Rose 2014) reported that 8-11 weeks abstinence rates were 39.8% in the bupropion plus varenicline group, compared to 25.9% in the varenicline plus placebo group. A study by Ebbert et al. (Ebbert 2014) reported a 7-day ppa at 12-weeks post treatment of 56.2% compared to 48.6% of monotherapy (either varenicline or bupropion) and prolonged abstinence at 2 weeks post treatment of 53% in combination treatment compared to 43.2% in the monotherapy group.

Finally, 1 study assessing any pharmaceutical treatment including either varenicline or bupropion (Regan 2016) reported 7-day ppa at 3-months post treatment of 26% and at 6 months of 27%.

Naltrexone

There were 2 studies assessing the effect of naltrexone on smoking cessation (Fridberg 2014, Rojewski 2014). The study by Rojewski et al. (Rojewski 2014) reported 7-day ppa at EOT of 22% in those subjects administered naltrexone while the 7-day ppa was 27% in the placebo group. The study by Fridberg et al. (Fridberg 2014) reported abstinence stratified by alcohol use intensity groups. Among heavy drinkers administered naltrexone the abstinence rate at 6-months was 32% compared to 14% in the placebo group. Naltrexone was shown to significantly increase smoking abstinence rates among heavy drinkers but not in moderate-to-light or nondrinking smokers.

Nicotine replacement therapies (NRT)

There were 13 studies assessing the impact of NRT on smoking cessation (Bolt 2012, Bricker 2014, Buller 2014, Cook 2016, Gray 2015, Kinnunen 2008, Lukowski 2015, Piper 2016, Roth 2005, Schlam 2016, Schnoll 2015, Smith 2009, Varghese 2014). The NRT studies included the nicotine patch, the lozenge and the inhaler as well as a combination of these therapies. The nicotine patch as monotherapy was studied in 6 publications (Bolt 2012, Buller 2014, Cook 2016, Gray 2015, Roth 2005, Smith 2009).

In the monotherapy nicotine patch use, two studies assessed the 7-day ppa. The study by Cook et al. (Cook 2016) reported that the 7-day ppa at 2 weeks was 5.7% and it increased as follow-up was prolonged (7-day ppa at 6 months was 9.4%). The study by Schlam et al. (Schlam 2016) reported application of a nicotine patch for 8 weeks and for 6 months. The 7-day ppa with use of the nicotine patch for 8-weeks at 6 months follow-up was 34% and at 12 months follow-up it was 27%, while the 7-day ppa in those using the nicotine patch 6 months at 6-months follow-up was 43% and 34% at 12 months follow-up. The 30-day ppa measured at 12 weeks of follow-up was reported by 1 study (Buller 2014) as

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

19.4%. Finally, 7-day ppa at 12 weeks was assessed by 1 study (Roth 2005) which found it to be 18.6%.

Continuous abstinence in those administered the nicotine patch alone was assessed in 5 studies (Bolt 2012, Buller 2014, Gray 2015, Roth 2005, Smith 2009). The study by Gray et al. (Gray 2015) reported 1 week abstinence rates of 20.6%, 2 weeks abstinence rates of 17.8% and 4-weeks abstinence rates of 9.6%. The study by Roth et al. (Roth 2005) reported the 6-week abstinence rate at 12 months which was 22.9%. The study by Bolt et al. (Bolt 2012) reported an 8-week abstinence rate of 47%. The studies by Buller et al. (Buller 2014) and Smith (Smith 2009) reported 6-months abstinence rates ranging from 8% to 17.7%.

There were 5 studies assessing the impact of the nicotine patch plus psychotherapy in smoking cessation (Bricker 2014, Lukowski 2015, Piper 2009, Schnoll 2015, Varghese 2014). The study by Schnoll et al. (Schnoll 2015) reported a 7-day ppa at week 24 of follow-up of 21.7% in those who received 8 weeks of the nicotine patch plus CBT versus 27.2% in those who received the nicotine patch for 24 weeks plus CBT, while the study by Piper et al. (Piper 2009) reported a 7-day ppa at 6 weeks of follow-up of 42.8% in those receiving the nicotine patch plus counseling while subjects who received either the nicotine patch or counseling reported lower abstinence rates (29.1%-31.1%). The study by Bricker et al. (Bricker 2014) reported a 30-day ppa at 6-months of follow-up in subjects receiving the nicotine patch plus acceptance and commitment therapy (ACT) of 31% versus 22% for those who received the nicotine patch plus CBT. There was 1 study assessing continuous cessation in patients administered the nicotine patch and psychotherapy (Varghese 2014). At 6 weeks (EOT) 31.9% were abstinent, at 3 months 29.3% were abstinent and at 6 months 28.6% were abstinent. Finally, 1 study reported the effect of nicotine patch administration along with coaching on smoking cessation (Lukowski 2015) and reported a 30-day ppa at 3-months of 31% in those with emotional challenges or mental illness versus 34% in those without either condition, while the abstinence at 6-months was 33% in those with emotional challenges or mental illness versus 43% in those without either condition.

There were 2 studies assessing the use of the nicotine lozenge alone or in combination with the nicotine patch in smoking cessation (Bolt 2012, Smith 2009). The study by Bolt et al. (Bolt 2012) reported 8-week abstinence rates of 44% for the nicotine lozenge group, 56% for the nicotine patch plus lozenge group and 33% for the placebo group. The study by Smith et al. (Smith 2009) reported 6-month abstinence rates 26.9% for the nicotine lozenge plus patch group and 19.9% for the nicotine lozenge group.

Lastly, there was 1 study that assessed the nicotine patch plus nicotine inhaler on smoking cessation (Roth 2005) in which the authors reported that continuous 6-week cessation rates were 25% in the nicotine patch plus inhaler group while the 7-day ppa at 12-weeks follow up was 22.2%.

Behavioral therapy and psychotherapies

There were 8 studies that assessed the effect of diverse types of behavioral therapies or psychotherapies on smoking cessation (Catley 2016, Cherrington 2015, Cook 2016, Fu 2014b, Gariti 2009, Kahler 2015, Ramo 2015a, Webb 2010).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

One study assessed the influence of a CBT-based therapy on the trans-theoretical model of behavior change (which assesses an individual's readiness to act on a new healthier behavior, and provides strategies, or processes of change to guide the individual through the stages of change to action and maintenance) delivered through Facebook and were randomized into 1 of 3 monetary incentive groups tied to engagement (commenting in groups) (Ramo 2015a). The authors reported 7-day ppas of 9% (7/79), 18% (14/79), and 13% (10/79) at 3-, 6-, and 12-months follow-up, respectively.

Two studies evaluated motivational interviewing versus either behavioral reduction (Cook 2016), or personalized advice or health education (Catley 2016). Both studies reported 7-day ppas at 12-weeks and 3-months follow-up. The 7-day ppa at 12 weeks ranged from 5% to 8.3% in the motivational interviewing group, 10.8% in the behavioral reduction group and 8% in the health education group. The group receiving personalized advice had a 7-day ppa of 0%. The 7-day ppa at 6 months ranged from 6%-9.1% in the motivational interviewing group, while it was 10.8% in the behavioral reduction group, 15% in the health education group and 4% in the personalized advice group. Other 7-day ppas were reported by two studies assessing either psychotherapy (Kahler 2015) or proactive care versus usual care which involved either telephone or in-person support (Fu 2014b). The 7-day ppa at 8-weeks follow-up was 25.8% for standard psychotherapy versus 40% for positive affect therapy. At 16-weeks of follow-up the rates decreased to 6.5% and 22.9% respectively and at 6 months they were 6.5% and 17.1% respectively (Catley 2016). The 7-day ppa for proactive care at 1 year was 15.1% and for usual care it was 17.1%, while 6-month continuous abstinence at 1 year was 13.5% and 10.9% respectively (Fu 2014b).

Another study compared general health education (GHE) with CBT (Webb 2010). The authors reported a 7-day ppa at EOT of 51% in CBT and 27% in GHE; at 3 months the 7-day ppa went down to 34% for the CBT group and to 20% for the GHE group and at 6 months post treatment it was 31% for CBT and 14% for GHE. A study by Gariti et al. (Gariti 2009) reported the 7-ppa at 12 weeks follow-up for subjects who were randomized to high or low frequency counselling yielding a rate of 32.8% and 21.2%, respectively.

The last study assessed storytelling DVD intervention versus a control group (Cherrington 2015). The authors reported a quit rate at 2 weeks of 43.3% for the storytelling arm versus 36.7% in the control arm. Higher quit rates were also observed at 6 months (continuous abstinence) (33.3% and 26.0%, respectively.

Monetary incentives

There was only 1 study that reported the effect of monetary incentives in a smoking cessation trial (Halpern 2015). The authors reported that sustained abstinence at 6-months follow-up ranged from 9.4-16% of participants, while the usual care arm reported a sustained abstinence rate of 6%.

Non-interventional studies

There were 8 observational studies identified through the literature search (Bush 2014, Frieden 2011, Kendzor 2014, Rafful 2013, Reitzel 2015, Shen 2014, Slopen 2013, Vickerman 2015b).

Six publications reported results from longitudinal studies. A study by Vickerman et al. (Vickerman 2015b) reported 7-day ppa at 7 weeks post quit date of 27.7% and a 30-day

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

ppas of 24.5%, while a study by Kendzar et al. (Kendzor 2014) reported a 7-day ppa of 15.8% post quit and continuous abstinence at 6 months of 7.4%, A study by Bush et al. (Bush 2014) reported 30-day ppas by weight. Those who were overweight had a rate of 40%, while those of normal weight or obese had a rate of 25%. A study by Reitzel et al. (Reitzel 2015) reported biochemically verified quit rates, 27.5% at 1 week, 22.4% at 2 weeks, 20% at 4 weeks and 1.3% at 3 months. Additionally, a study by Shen et al. (Shen 2014) reported cumulative quit rates at 1 month to be 29.3%, 23.3% at 3 months and 18% at 6 months of follow-up. Finally, a study by Slopen et al. (Slopen 2013) reported that in a cohort of almost 5000 participants, the quit rate over 9-10 years of follow-up was 6.8%.

There were also 2 studies reporting results from surveys (Frieden 2011, Rafful 2013). The study by Frieden et al. (Frieden 2011) using NHIS data, showed that 6.2% of smokers reported quitting recently (although the length was not specified), and a study by Rafful et al. (Rafful 2013) reported that from wave 1 to wave 2 of their longitudinal survey, 4.6% of those smokers who had tried to quit had quit successfully (1.8% of all smokers).

6.3.2.2.3.2.2 Smoking cessation rates in youth populations

There were 10 studies assessing the cessation rates in youth populations (Burton 2009, Fritz 2008, Gray 2015, Hanson 2003, Horn 2004, Joffe 2009, Morean 2015, Muramoto 2007, Peterson 2009, Piper 2009, Walker 2014). Study characteristics can be found in Table 21.

Of the 10 studies, 9 studies were interventional (Burton 2009, Fritz 2008, Gray 2011, Hanson 2003, Horn 2004, Joffe 2009, Morean 2015, Muramoto 2007, Peterson 2009) while 1was observational (Walker 2014).

Interventional studies

There were 6 studies assessing the effect of behavioral or psychotherapies on smoking abstinence (Burton 2009, Fritz 2008, Horn 2004, Joffe 2009, Morean 2015, Peterson 2009). One assessed the effect of bupropion plus behavioral therapy versus bupropion plus compensation or placebo (Gray 2011), while another assessed the effect of different doses of bupropion (Muramoto 2007) and 1 assessed the use of NRT (Hanson 2003).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 21. Characteristics of studies assessing cessation rates in youth populations

Study	Period	Study characteristics	Intervention	Definitions	Rates
Morean et al (Morean 2015)	2015	Secondary data analyses on 64 teen smokers (mean age = 16.36 [1.44]; cigarettes/day = 13.97 [6.61]; 53.1% female; 90.6% Caucasian) who completed a four-week smoking cessation trial	Cognitive behavioral therapy (CBT), contingency management (CM), or the combination of the two (CM/CBT).	• Biochemically-confirmed 7-day ppa at EOT	• CM = 77% • CM/CBT = 81% • CBT = 30%
Gray et al (Gray 2011)	2015	Double-blind, placebo-controlled study of 134 adolescent smokers aged 12-21 years who smoked at least 5 cigarettes per day and express interest in quitting	Smokers were randomized to receive a 6-week course of bupropion SR plus contingency management (CM), bupropion SR plus non-CM, placebo plus CM, or placebo plus non-CM, with final follow-up at 12 weeks.	• 7-day cotinine-verified point prevalence abstinence (following a 2 week grace period)	• At 3 weeks: o Bupropion SR plus CM = 27.8% o Bupropion SR plus Non-CM = 19.4% o Placebo plus CM = 10.3% o Placebo plus Non-CM = 9.4% • At week 4 : o Bupropion SR plus CM = 37.8% o Bupropion SR plus Non-CM = 16.7% o Placebo plus CM = 10.3% o Placebo plus Non-CM = 15.6%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
					• At week 5 : o Bupropion SR plus CM = 29.7% o Bupropion SR plus Non-CM = 13.9% o Placebo plus CM = 10.3% o Placebo plus Non-CM = 9.4% • At EOT : o Bupropion SR plus CM = 27.0% o Bupropion SR plus Non-CM = 8.3% o Placebo plus CM = 10.3% o Placebo plus Non-CM = 9.4% • At 12 week follow-up o Bupropion SR plus CM = 10.8% o Bupropion SR plus Non-CM = 5.6% o Placebo plus CM = 0% • Placebo plus Non-CM = 6.3% • Asians = 25% • African Americans = 16% • Native Americans = 11% • Other = 29%
Croghan et al (Croghan 2010)	2010	Multi-center, open-label randomized, clinical trial of 1,684 adult smokers. 60% women, with a mean age of 46.3 years.	Participants were randomized into 1 of 3 medication groups (nicotine inhaler, bupropion or a combination of both).	Abstinence at week 12 by race/ethnicity	

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
Fritz et al (Fritz 2008)	2008	Quasi experimental cohort of 61 high school students	Cognitive behavioral approach techniques vs. control.	Quit rate at 1 month	• Quit rate at 1 month = 20%
Horn et al (Horn 2004)	2004	Interventional study of 113 male and 145 female adolescents aged 14-19 from rural West Virginia and North Carolina	Adolescents were enrolled in the American Lung Association's 10 week Not On Tobacco (NOT) program or a 15-min single-dose brief intervention (BI).	Carbon monoxide validated 3 month post baseline quit rate	• Overall: NOT = 8.3%, BI = 1.7% • Male: NOT = 4.3%, BI = 2.0% • Female: 12.2%, BI = 1.4%
Walker et al (Walker 2014)	2003	Data from the 2003–2005 National Youth Smoking Cessation Survey were used. Of 2,582 smokers aged 16–24 years sampled, 1,354 provided complete baseline telephone interview data on the study variables, and their self-reported smoking status at 2-year follow-up was known (currently smoking vs. not smoking).	None	Quit rate at 2 year follow-up	• 20%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
Hanson et al (Hanson 2003)	2003	Double blind, placebo-controlled randomized trial including 107 participants who were provided cognitive-behavioral therapy and a contingency-management procedure. Participants were aged 13-19 years that smoked at least 10 CPD for the last 6 months.	Randomization arms were nicotine patch or placebo patch.	7-day and 30-day prevalence at 10 weeks	• 7-day prevalence = 28% NRT and 24% in placebo • 30-day prevalence = 20% NRT and 18% in placebo
Joffe et al (Joffe 2009)	2002-2003	Experimental study including 407 students with a mean age of 16 years (52% females)	Behavioral training according to 2 programs, the Not on Tobacco (NOT) or Kickin' Butts (KB) or controls. Which included bi-weekly sessions.	Quit rates (cotinine-confirmed) at end of program (EOP), 1, 6 and 12 months	• End of program: o KB = 14%, KB control = 13% o NOT = 18%, NOT control = 17% • 1 month: o KB = 9.0%, KB control = 6.0% o NOT = 13%, NOT control = 9.0% • 6 months: o KB = 10%, KB control = 15% o NOT = 5.0%, NOT control = 9.0% • 12 months: o KB = 9.0%, KB control = 12% o NOT = 7.0%, NOT control = 6.0%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
Peterson et al (Peterson 2009)	2001-2003	Group randomized trial including 2,151 high school juniors.	Intervention using multiple-component personalized counseling by telephone vs no intervention of more than 2000 high school senior smokers who were proactively identified as high school juniors in 50 schools.	6-months prolonged abstinence from smoking after 1-year follow-up.	• Intervention = 21.8% • Control = 17.7%
Muramoto et al (Muramoto 2007)	1999-2002	Randomized, double blind placebo controlled dose ranging trial of 312 adolescents aged 14-17 years, smoked 6 or more CPD and had at least 2 quit attempts.	Sustained release bupropion hydrochloride 150 mg/d or 300 mg/d or placebo for 6 weeks	Cotinine-confirmed 7-day point prevalence abstinence rates at 6 and 26 weeks	• At 6 weeks: o Placebo = 5.6% o Bupropion SR 150 mg/d = 10.7% o Bupropion SR 300 mg/d = 14.5% • At 26 weeks: o Placebo = 10.3% o Bupropion SR 150 mg/d = 3.1% o Bupropion SR 300 mg/d = 13.9%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
Burton et al (Burton 2009)	1988-1992	Data from a randomized trial including 448 high school students	Students volunteering to participate in a cessation group were randomly assigned to be in 1 of the 2 groups offered at each school (therapy based on addiction or on psychosocial dependence) or to not be in a group (control subjects). All students had been informed ahead of time that they might or might not be randomly assigned into the groups, but that they all would be invited to a follow-up session in 4 months.	Biochemically-confirmed cessation at 4 months	• Cigarette smokers: o Intervention = 6.5% o Control = 3.2% • Smokeless tobacco users: o Intervention = 14.3% o Control = 0%

MS: middle school, HS: high school

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Behavioral therapy or psychotherapies

Of the 6 studies reporting on the influence of behavioral therapy or psychotherapies on smoking cessation, 1 studied contingency management (CM) versus CB and combined therapy. The authors reported that the 7-day ppa at 4 weeks (EOT) was 77% for CM, 30% for CBT and 81% for combined therapy (Morean 2015). Another study which evaluated CBT alone (Fritz 2008) reported that the 1-month quit rate was 20% which was slightly lower than in the study by Morean et al. (Morean 2015), Burton et al. (Burton 2009) studied the effect of focus groups and motivating campaigns versus no intervention in high school students and found that after 4 months of follow-up 6.5% of the intervention group had quit while only 3.2% had quit in the control group. A study by Horn et al. (Horn 2004) assessed the effect of behavioral interventions on smoking cessation involving group sessions and they reported that at 3 months of follow-up those in the intervention group had a quit rate of 4.3% (for men) and 12.2% (for women) versus 2.0% (for men) and 1.4% (for women).

There were two studies that compared different behavioral interventions in youth populations. The study by Joffe et al. (Joffe 2009) assessed two different behavioral therapies and their effect on smoking cessation versus control groups. The authors reported that at EOT the quit rate ranged from 14%-18% in the behavioral intervention groups versus 13%-17% in the control groups, at 1 month post-treatment, the quit rates ranged from 9%-13% in the intervention group versus 6%-9% in the control group. The longer the follow-up post treatment, the less difference there was for quit rates between the treated and untreated groups (at 6 months post-treatment the quit rates ranged from 5%-10% versus 9-15% and at 1-year post-treatment they ranged from 7%-9% and 6%-12% in treated and untreated groups respectively). Finally, the study by Peterson et al. (Peterson 2009) looked into CBT or focus groups interventions and found that those in the intervention arms had a 6-month continuous abstinence rate at 1 year of 21.8% versus 17.7% in the control groups.

Pharmacotherapy

There were 3 articles that reported the effects of pharmacotherapy on smoking cessation. The study by Gray et al. (Gray 2011) assessed the effects of CM, bupropion or combined therapy versus placebo on smoking cessation. The authors reported the 7-day ppa at 3-weeks as follows: 27.8% for those receiving bupropion plus CM, 19.4% for bupropion alone, 10.3% for the placebo plus CM group and 9.4% for those receiving placebo only. Similar results favoring combined therapy were reported at all time-points (Table 22). The second study assessed the use of a nicotine patch on smoking cessation (Hanson 2003). This study reported 7-day ppa at 10 weeks of follow up of 28% for those receiving the nicotine patch and 24% for the placebo group. The 30-day ppa was 20% for the nicotine patch and 18% for the placebo group.

Finally, the study by Muramoto et al. (Muramoto 2007) assessed the effect of bupropion (150 mg and 300 mg) against placebo. The authors reported a 7-day ppa at 6-weeks of follow-up of 10.7% for the 150 mg bupropion group, 14.5% for the 300 mg bupropion group and 5.6% for the placebo group. At 6-months follow up the 7-day ppa was1.5% for the 150 mg bupropion group, 13.9% for the 300 mg bupropion group and 10.3% for the placebo group.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Observational studies

There was only 1 observational study found which reported the abstinence rates in youth populations (Walker 2014). In a cohort study including 2,582 smokers aged 16-24 years they found that the quit rate at 2-years of follow up was 20%.

6.3.2.2.3.2.3 Smoking cessation rates in specific populations

There were 14 studies assessing cessation rates in different specific populations: 9 studies evaluated mental health patients, 2 studied sexual minorities and 3 studied populations of HIV positive individuals. Their details can be found in Table 22.

Mental health patients

There were 9 studies evaluating cessation rates in mental health populations. Out of the 9 studies, 8 were interventional and only 1 was observational (Table 22).

All interventional studies assessed the effect of diverse pharmacotherapies on smoking cessation. There were 4 studies assessing varenicline and 4 assessing bupropion. Among the varenicline studies 1 evaluated varenicline versus placebo in bipolar disorder smokers (Chengappa 2014) and reported that the 7-day ppa was 48.4% in the varenicline group versus 10.3% in the placebo group, while the 4-week continuous abstinence prevalence was 19.3% in the varenicline group versus 6.9% in the placebo group. The second study (Dutra 2012) evaluated the effects of varenicline plus CBT in a group of patients diagnosed with schizophrenia and reported a 14-day ppa at 12 weeks of follow-up of 60.4%. A similar study assessing the role of varenicline and CBT in smokers with schizophrenia or schizoaffective disorder, report a 14-day ppa of 47.3% and a 28-day ppa of 34% (Pachas 2012). Finally, a study by Evins et al. (Evins 2014), which also combined varenicline with CBT versus a placebo group, reported higher abstinence rates for the varenicline group compared to the placebo group (Table 22).

Of the 4 studies assessing bupropion use on smoking cessation, two evaluated the use of bupropion plus NRT (Evins 2007, Evins 2008) and 1 that evaluated bupropion plus NRT and CBT (Culhane 2008). The first study (Evins 2008) reported an overall 7-day ppa at EOT of 72% (13 weeks) in patients with unipolar depression. The second study (Evins 2007) reported the results of a trial comparing bupropion plus NRT versus placebo plus NRT in patients with schizophrenia. Bupropion plus NRT worked better in preventing relapse than placebo plus NRT through 3 months follow-up; however, there was no difference at the 12-month follow-up time point. A study by Culhane et al. (Culhane 2008) evaluated bupropion, NRT and CBT in patients with schizophrenia showed that the 4-week abstinence rate was 12.3% in those who used any treatment.

Finally, a study by Covey et al. (Covey 2008) evaluated the effect of bupropion plus counseling and found that the overall abstinence during the last 4 weeks of the study was 53%.

The only observational study (Vickerman 2015a) reported that the 30-day ppa at 7-months of follow-up was 22% in those with mental health conditions while for those without health conditions it was 31%

Sexual minorities

Among sexual minorities, a study by Covey et al. (Covey 2009) reported abstinence rates for those receiving different types of pharmacotherapies for 8 weeks. At 1 week of

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

treatment 89% of those who belonged to a sexual minority reported having quit while 83% of heterosexuals had quit. The longer the follow-up the lower the quit rates become, and by 8-weeks of treatment the sexual minorities group reported quit rates of 59% versus 57% in the heterosexual group.

A second article reported the effect of behavioral interventions on smoking cessation and reported a 7-day ppa of 32.3% at EOT (Matthews 2013).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 22. Characteristics of studies assessing the quit rates in specific populations

Study	Period	Study characteristics	Intervention	Definitions	Rates
Psychiatric Disorders					
Vickerman et al (Vickerman 2015a)	2012-2013	Longitudinal study including 3,132 callers to quit line programs aged ≥ 18 years.	None	30-day point prevalence quit rates at 7-month follow-up differences between those reporting mental health conditions (MHC) and those not reporting these.	• MHC abstinence = 22.0% • No MHC abstinence = 31.0%
Chengappa et al (Chengappa 2014)	2010-2013	Randomized, double-blind, placebo-controlled trial of 60 smokers diagnosed with bipolar disorder who smoked ≥ 10 CPD and were aged 18-65 years.	Subjects were randomized 1:1 to varenicline or placebo. All patients received smoking cessation counseling.	7-day point prevalence of self-reported no smoking verified by expired CO levels < 10 ppm at 12 weeks and 4-week continuous abstinence at 12 weeks.	• 7-day prevalence abstinence: o Varenicline = 48.4% o Placebo = 10.3% • 4-week prevalence abstinence: o Varenicline = 19.3% o Placebo = 6.9%
Dutra et al (Dutra 2012)	2012	12-week smoking cessation trial including 53 patients with schizophrenia aged 18 – 70.	Varenicline with CBT.	14-day point-prevalence abstinence at week 12.	• 60.4%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
Evins et al (Evins 2014)	2008-2012	Randomized, placebo-controlled, parallel-group including 247 smokers with schizophrenia or bipolar disorder	Participants received 12-weeks open-label for cognitive behavioral therapy and double-blind varenicline (1 mg, 2 times per day) or placebo from weeks 12 to 52. Participants then discontinued treatment and were followed till week 76.	7-day rate of continuous abstinence at study week 52 confirmed buy exhalation of carbon monoxide. Also continuous abstinence rates at week 12 and 64 based on biochemically verified abstinence.	• 7-day abstinence at week 52: o Varenicline =60% o Placebo = 19% • 7-day abstinence at week 64 o Varenicline =45% o Placebo = 13% • Continuous abstinence from week 12-52: o Varenicline =45% o Placebo = 15% • Continuous abstinence from week 12-64 (after discontinuation): o Varenicline =40% o Placebo = 11%
Pachas et al (Pachas 2012)	2008-2010	Open-label smoking cessation trial including 112 participants aged 18-70 years with a DSM-IV-TR diagnosis of schizophrenia or schizoaffective disorder, and who smoked ≥ 10 CPD	Varenicline 0.5 mg/day for 3 days, 0.5 mg bid for 4 days, then 1 mg twice daily for 11 weeks and weekly, 1-hour, manualized, cognitive behavioral therapy smoking cessation groups based on the Freedom From Smoking program	14- and 28-day continuous abstinence rates at 12 weeks of follow-up, carbon monoxide verified.	• 14-day abstinence = 47.3% • 28-day abstinence = 34.0%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
Evins et al (Evins 2008)	2008	Controlled trial of 90 adult smokers aged 18–70 years who smoked ≥10 cigarettes per day for ≥2 years prior to enrollment and met DSM-IV criteria for lifetime diagnosis of a unipolar depressive disorder.	Bupropion added to nicotine replacement therapy and group cognitive behavioral therapy.	7-day point prevalence abstinence at end of treatment, confirmed by expired air carbon monoxide concentration < 9 ppm at study week 13.	• Overall 72%
Covey et al (Covey 2008)	2008	Open-label, randomized trial with 559 smokers with a mean age of 41.8 years.	All participants received treatment for 8 weeks with open-label bupropion, the nicotine patch, and individual counseling. Those who achieved abstinence at 4-weeks were randomized to a 16-week placebo-controlled maintenance treatment trial and followed-through a 24-week non-treatment period.	Sustained abstinence during the last 4 weeks of the eight week treatment period confirmed by expired carbon monoxide level ≤ 8ppm.	• Overall abstinence = 53%
Evins et al (Evins 2007)	2002-2004	Double-blind, placebo-controlled study of 51 adult smokers with schizophrenia (mean age 43.6 to 44.8 years).	A12-week trial of bupropion SR 300 mg/d or placebo added to transdermal nicotine patch, nicotine polacrilex gum, and cognitive behavioral therapy.	Continuous confirmed abstinence from target quit date at 8 weeks, 12 weeks, 3 months and 12 months	• Week 8: • Bupropion plus NRT = 13% • Placebo plus NRT = 5% • Week 12 • Bupropion plus NRT = 9% • Placebo plus NRT = 5% • 3-month: • Bupropion plus NRT = 5% • Placebo plus NRT = 2% • 12-month: • Bupropion plus NRT = 3% • Placebo plus NRT = 2%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
Culhane et al (Culhane 2008)	1999-2004	114 adult participants with stable schizophrenia participating in 1 of 2 smoking cessation trials,	One was a double blind placebo-controlled trial of bupropion or placebo added to cognitive therapy and the second one a double blind placebo-controlled trial of bupropion or placebo added to NRT	4-week continuous abstinence at the end of a 12-week , biochemically confirmed	• 12.3% • Of these 14 subjects 9 (64%) received either bupropion or NRT, 5 (36%) received both bupropion and NRT, and none (0%) received placebo
Sexual Minorities					
Covey et al (Covey 2009)	2009	Experimental study if 54 gay/bisexual (GB) and 243 heterosexual (HT) male smokers	8 week open treatment with nicotine patch, bupropion and counseling	Abstinence at 1,2 and 8 weeks	• At 1 week: GB = 89%, HT = 82% • At 2 weeks: GB = 77%, HT = 68% • At 8 weeks: GB = 59%, HT = 57%
Matthews et al (Matthews 2013)	2002-2008	Community-based smoking cessation treatment program of 198 LGBT smokers with a mean age of 40.5 years	Sessions were based on the American Lung Association's Freedom of Smoking Program' and were tailored to LGBT smoker's needs.	7-day prevalence abstinence (self-reported)	• 32.3% post-treatment assessment

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Intervention	Definitions	Rates
HIV patients					
Vidrine et al (Vidrine 2015)	2007-2008	Data from 350 PLWH enrolled in a randomized smoking cessation treatment trial and were aged ≥ 18 years, willing to set a quit date within 7 days, and English or Spanish speaking.	Usual care or a cell phone intervention (CPI) group.	7-day abstinence at 3-months follow-up	• UC = 4.7% • CPI = 15.7%
Moadel et al (Moadel 2012)	2012	Randomized controlled trial including 145 HIV + individuals living in New York aged 29-70 years	Participants were given a 3-months' supply of NRT and received either a tailored program to address the needs and concerns of HIV infected smokers (PSF) or standard of care.	Biochemically-confirmed 7-day ppa at 3 months	• PSF = 19.2% • Standard of care = 9.7%
Stanton et al (Stanton 2015)	2006-2011	Randomized controlled trial including 302 HIV + participants aged ≥ 18 years.	Participants were randomized to 4 in-person sessions of a tailored intervention (Aurora) or 2 in-person sessions of brief advice (enhanced standard care [ESC]). Both groups received 8 weeks of nicotine patch.	Biochemically validated 6- and 12-month 7-day ppa.	• 6-month: o Aurora = 8.1% o ESC = 11% • 12-month: o Aurora = 6.0% o ESC = 7%

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

HIV positive patients

There were 3 studies that investigated HIV positive populations. The study by Vidrine et al. (Vidrine 2015) reported results from a group of HIV positive individuals that received support via either usual care or cell phone, and the 7-day ppa at 3-months was 4.7% in those receiving usual care compared to 15.7% among those receiving cell phone support.

A study by Moadel et al. (Moadel 2012) reported results from a study administering standard care versus intensive group therapy (called Positive Some Free or PSF). The authors reported that those receiving PSF had a 7-day ppa at 3-months post treatment of 19.2% compared to 9.7% for those receiving standard care support.

The third study was published by Stanton et al. (Stanton 2015), which evaluated a tailored intervention called Aurora compared to receiving 2 in-person interventions of brief advice about quitting. The authors report a 7-day ppa at 6 months of 8.1% in those receiving Aurora and 11% in those receiving the brief advice, while at 12 months the 7-day ppa was 6.0% for those in the Aurora arm versus 7.0% for those who received the brief advice intervention.

6.3.2.2.3.2.4 Determinants of cessation

There were 40 studies assessing the determinants of smoking cessation in adults, youth and specific populations, their characteristics can be found in Table 23.

Determinants in youth populations

There were 5 studies that assessed determinants of smoking cessation in youth populations. The determinants associated with smoking cessation among youth populations were: Self efficacy at both social situations and in stressful situations (Bricker 2010), being Hispanic (Walker 2014), commitment and confidence in quitting (Bricker 2010), ego integration (Brook 2010), reduced dependency (Burton 2009, Walker 2014), later age at initiation (Walker 2014), not having peers that smoke (Walker 2014). On the other hand, high behavioral impulsivity (Morean 2015), high impaired self-regulation (Morean 2015), being a daily smoker (Peterson 2009), parental smoking (Brook 2010), unconventionality (Brook 2010) and internalizing behavior (Brook 2010). All of these were associated with being less likely to stop smoking. On the other hand, social norms (Bricker 2010), being female (Walker 2014), education (Brook 2010, Walker 2014), age (Walker 2014), exercise (Walker 2014), health status (Walker 2014) and concern for weight gain (Walker 2014) did not appear to be associated with smoking cessation.

Determinants in Adult populations

There were 31 studies that assessed determinants of smoking cessation in adult populations. Higher education was positively associated with smoking cessation in 5 studies (Biener 2010, Dale 2001, Frieden 2011, Klein 2013, Shopland 2006), while 5 studies found no relationship (Messer 2008, Nordstrom 2000, Puckett 2015, Sachs-Ericsson 2009, Shen 2014). Other factors positively associated with cessation were a home smoking ban (Biener 2010, Klein 2013, Messer 2008, Shen 2014, Shopland 2006, Zablocki 2014); self-efficacy (Abrams 2000, Baldwin 2006); receiving treatment (either pharmacological or behavioral) (Croghan 2010, Fu 2014b, Harris 2004, Javitz 2011, Kinnunen 2008, Puckett 2015, Shen 2014, Stead 2012), confidence in quitting (Daza 2006, Shen 2014); having private insurance (Frieden 2011); statewide clean indoor policy

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

(Klein 2013); being ready to quit (Dale 2001); duration of cessation period (Abrams 2000) and satisfaction (Baldwin 2006). Conflicting results were found for age (Biener 2010, Croghan 2010, Dale 2001, Frieden 2011, Klein 2013, Merzel 2015, Messer 2008, Nordstrom 2000, Puckett 2015, Reitzel 2015, Shopland 2006, Swan 2003), sex (Collins 2004, Dale 2001, Klein 2013, Messer 2008, Puckett 2015, Reitzel 2015, Shen 2014, Swan 2003), living with a smoker (Dale 2001, Klein 2013, Merzel 2015, Messer 2008, Puckett 2015), peer smoking (Biener 2010, Klein 2013), age of initiation (Croghan 2010, Dale 2001, Klein 2013), cigarettes smoked per day (CPD) (Abrams 2000, Collins 2004, Croghan 2010, Dale 2001, Daza 2006, Harris 2004, Javitz 2011, Klein 2013, Merzel 2015, Nordstrom 2000, Rafful 2013, Reitzel 2015), marital status (Biener 2010, Collins 2004, Croghan 2010, Merzel 2015, Puckett 2015, Reitzel 2015), strength of addiction or higher Fagerström Test for Nicotine Dependence scale score (Biener 2010, Croghan 2010, Dale 2001, Javitz 2011, Stewart 2014), income (Cobb 2014a, Merzel 2015, Messer 2008, Sachs-Ericsson 2009, Stewart 2014, Varghese 2014), race/ethnicity (Biener 2010, Frieden 2011, Klein 2013, Messer 2008, Puckett 2015, Reitzel 2015, Sachs-Ericsson 2009, Shen 2014, Shopland 2006), having or living with young children (Messer 2008, Shopland 2006, Zablocki 2014), suffering from depression (Dale 2001, Harris 2004, Hitsman 2003, Kinnunen 2008, Nakajima 2012, Sachs-Ericsson 2009), having had a quit attempt in the last year (Abrams 2000, Biener 2010) and number of quit attempts (Abrams 2000, Croghan 2010, Harris 2004, Swan 2003). On the other hand, the following variables were associated with reduced quitting: being a single parent (Shopland 2006), increased smoking frequency (Klein 2013), finding cigarettes calming (Klein 2013), alcohol use (Daza 2006), using a waterpipe (Thomas 2015), stress (Slopen 2013), number of years smoked (Harris 2004, Messer 2008), motivation to reduce craving (Nakajima 2012) and having mental disorders (Lukowski 2015).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 23. Determinants of smoking cessation in different populations

Author	Population & study methods	Analyses performed	Determinants
Youth			
Bricker et al 2010 (Bricker 2010)	Randomized clinical trial including 2,151 high school seniors.	Regression analyses.	Increased probability: Self-efficacy to resist smoking in social situations ($p<0.001$) Self-efficacy to resist smoking in stressful situations ($p<0.001$) Commitment to quit ($p<0.001$) Confidence to quit ($p<0.001$) Decreased probability: N.A. No Difference: Social norms for smoking ($p> 0.05$)
Morean et al 2015 (Morean 2015)	Secondary data analyses on 64 teen smokers (mean age = 16.36 [1.44]; cigarettes/day = 13.97 [6.61]; 53.1% female; 90.6% Caucasian) who completed a four-week smoking cessation trial.	Linear regression modeling.	Increase probability: N.A. Decreased probability: High behavioral impulsivity (OR=11.25, $p<0.05$) High impaired self-regulation (OR=8.31, $p<0.05$) No Difference: N.A.
Brook et al 2010 (Brook 2010)	Cross-sectional study of a random sample of 400 adolescent New York inhabitants.	T-test	Increased probability: Ego integration ($p<0.05$) Decreased probability: Parental smoking ($p<0.01$) Unconventionality ($p<0.01$) Internalizing behaviors ($p<0.05$) No difference: Educational aspirations and expectations ($p>0.05$)
Burton et al 2009 (Burton 2009)	Data from a randomized trial including 448 high school students.	Pearson chi-squared tests.	Increased probability: ↓ Dependency ($p<0.01$) Decreased probability: N.A. No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Walker et al 2014 (Walker 2014)	Data from the 2003–2005 National Youth Smoking Cessation Survey were used. Of 2,582 smokers aged 16–24 years sampled, 1,354 provided complete baseline telephone interview data on the study variables, and their self-reported smoking status at 2-year follow-up was known (currently smoking vs. not smoking).	Logistic regression, presented as ORs of cessation.	Increased probability: Initiation later in life (not shown) Being Hispanic (OR= 2.52, 95%CI: 1.56–4.07) Decreased probability: ↑ Nicotine dependence (OR= 0.77, 95%CI: 0.66–0.90) No difference: Education (OR= 0.98, 95%CI:0.55–1.74) Exercise (OR= 1.01, 95%CI: 0.97–1.05) Health status (OR= 0.90, 95%CI:0.61–1.31) Concern for weight gain (OR= 1.02, 95%CI:0.64–1.62) Age (OR= 0.98, 95%CI:0.48–2.02) Sex (OR=1.03, 95%CI:0.71–1.50)
Adult			
NHIS 2011 (Frieden 2011)	National representative cross-sectional survey of the US population. The sample included in this report included 27,157 adults aged 25-64 years.	Logistic regression (values not shown)	Increased probability: ↑ Being Caucasian or African American ↑ Education Private insurance Decreased probability: ↑ Age No difference: N.A.
Klein et al 2013 (Klein 2013)	Longitudinal population-based cohort of mid-western youth, semi-annual surveys were analyzed when study participants were between the ages of 18 and 21.	Logistic regression analyses.	Increased probability: Older age (OR= 1.84, 95%CI:1.70 – 2.00) ↑ Education (OR= 1.29, 95%CI: 1.08 – 1.54) Home smoking ban (OR= 1.65, 95%CI: 1.35 – 2.02) State-wise clean indoor policy (OR= 1.44, 95%CI: 1.06 – 1.94) Decreased probability: Sex (male) (OR= 0.64, 95%CI:0.54 – 0.76) Smoking frequency at baseline (OR= 0.47, 95%CI: 0.42 – 0.52) Finding cigarettes calming (OR= 0.57, 95%CI: 0.47 – 0.68)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
			Living with a smoker (OR= 0.76, 95%CI: 0.64 – 0.92) Peer smoking (OR= 0.32, 95%CI:0.25 – 0.40) No difference: Being Caucasian (OR= 1.00, 95%CI:0.78 – 1.27) Age of initiation (OR= 1.03, 95%CI: 0.99 – 1.07) CPD (OR= 0.70, 95%CI:0.13 – 3.64) Finding cigarettes good for weight control (OR= 0.85, 95%CI: 0.72 – 1.01) Self-efficacy (OR= 2.97, 95%CI:0.62 – 14.30)\
Puckett et al 2015 (Puckett 2015)	CDC conducted a survey of users of telephone and Web-based cessation services in four states to determine the cessation success of users of these interventions which included 5,393 users	Logistic regression analyses.	Increased probability: Dual platform use (telephone and web-based) (OR= 1.54, 95%CI:1.31–1.82) Decreased probability: Being single or having a partner (OR= 0.60, 95%CI:0.50–0.72) No difference: Sex (male) (OR= 0.92, 95%CI:0.82–1.05) Age (OR= 0.98, 95%CI:0.95–1.01) Race (All ORs not significant) Education (OR= 0.81, 95%CI:0.65–1.01) Other smoker in household (OR= 0.90, 95%CI: 0.73–1.11) Employment status (All ORs mot significant)
Reitzel et al 2015 (Reitzel 2015)	Cohort study of 58 smokers aged 18-64 years (65.5% men).	Logistic regression analyses.	Increased probability: Being Caucasian (OR= 3.19, 95%CI:1.15–8.86) Decreased probability: N.A. No difference: Age (OR= 1.00, 95%CI: 0.97–1.03) CPD (OR= 1.02, 95%CI: 0.95–1.09) Sex (female) (OR= 1.31, 95%CI: 0.66–2.59) Marital status: (OR= 2.03, 95%CI: 0.93–4.45)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Fu et al 2014 (Fu 2014b)	A pragmatic randomized clinical trial involving a population-based registry of current smokers aged 18 to 80 years. A total of 6400 current smokers, identified using the Department of Veterans were included.	Logistic regression analyses.	Increased probability: Telephone counseling (OR= 1.90, 95%CI: 1.36-2.67) Counseling plus medication (OR= 1.27,95% CI: 1.03-1.57) Decreased probability: N.A. No difference: Interest in quitting (not shown) In person counseling (not shown)
Dale et al (Dale 2001)	Double-blind, placebo-controlled, dose-response trial including 615 healthy men and women aged ≥ 18 years who were smoking ≥ 15 CPD and were motivated to stop smoking.	Logistic regression analyses (values not shown)	Increased probability: Sex (male) (p<0.001) No history of depression (p<0.001) No smokers in household (p<0.001) ↓ FTND (p<0.001) ↑ Age (p<0.001) ↑ Education (p<0.001) ↑ Age of initiation (p<0.001) Ready to quit (p<0.001) Decreased probability: ↑CPD (p<0.001) No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Shen et al 2014 (Shen 2014)	Data from the New Mexico Pharmaceutical Care Foundation which provided cessation programs. Participants included 1,437 adults aged ≥ 18 years.	Logistic regression analyses.	Increased probability: Use of pharmacotherapy: Varenicline (OR= 2.04, 95%CI:1.21, 3.43) NRT (OR= 2.16, 95%CI: 1.31, 3.56) Limited use of cigarettes at home (OR= 0.65, 95%CI: 0.44, 0.96) ↑ Confidence in quitting (OR= 2.16, 95%CI: 1.27, 3.67) Decreased probability: N.A. No difference: Sex (male) (OR= 0.85, 95%CI: 0.61, 1.18) Race (other than Hispanic) (OR= 1.09, 95%CI: 0.56, 2.11) FTND (OR= 0.80, 95%CI: 0.47, 1.36) ↓Education (OR= 1.98, 95%CI:0.89, 4.40)
Shopland et al 2006 (Shopland 2006)	Longitudinal survey including 128,024 employed women aged ≥ 18 years.	Logistic regression analyses.	Increased probability: Home smoking ban (OR= 6.54, 95%CI: 4.61,9.28) ↑ Education (OR= 2.17, 95%CI: 1.44,3.27) ↑Age (OR= 2.09, 95%CI: 0.75,5.85) Decreased probability: Being a single parent (OR= 0.61, 95%CI: 0.41,0.91) No difference: Race (All ORs not significant) Workplace smoking policy (OR= 1.11, 95%CI: 0.81,1.53) Having young children (OR= 1.10, 95%CI: 0.70,1.74) Occupation (All ORs not significant)
Stewart et al 2014 (Stewart 2014)	Cross-sectional study including 200 low-SES racially diverse smokers.	Logistic regression analyses (reported as OR of not quitting)	Increased probability: N.A. Decreased probability: Lower health literacy (OR= 3.26, 95%CI: 1.15 – 9.26) No difference: SES (OR= 1.16, 95%CI: 0.39-3.45) Nicotine dependence (OR= 1.24, 95%CI: 0.86-1.79)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Nordstrom et al 2000 (Nordstrom 2000)	Longitudinal study including 986 male smokers aged 22-82 years.	Cox regression analyses.	Increased probability: N.A. Decreased probability: ↑CPD (p<0.001) ↑Age (p<0.01) No difference: Psychological addiction (p=0.54) Education (p=0.51)
Daza et al 2006 (Daza 2006)	Study participants (709) were enrolled in the Working Well Trial (WWT), which was developed to evaluate a worksite intervention for cancer prevention and control.	Logistic regression analyses (values not shown)	Increased probability: ↓CPD (p<0.0001) ↓TTFC (p<0.0001) Confidence in quitting (p<0.0001) Decreased probability: Alcohol use (p=0.05) No difference: Health status (not shown)
Zablocki et al 2014 (Zablocki 2014)	Longitudinal survey including 1,718 smokers aged ≥ 18 years.	Logistic regression analyses.	Increased probability: Home smoking ban (OR= 2.3, 95%CI: 1.3–3.9) Decreased probability: N.A. No difference: Partial home smoking ban (OR= 1.0, 95%CI: 0.5–2.1) Living with children (All ORs not significant)
Hitsman et al (Hitsman 2003)	Meta-analysis of 15 studies evaluating the association of depression and smoking cessation.	Meta-analysis.	Increased probability: N.A. Decreased probability: N.A. No difference: Depression (p=0.18)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Abrams et al 2000 (Abrams 2000)	Data from the Working Well Trial including 2,379 participating smokers with a mean age at baseline of 41 years who were followed up for 2 years..	Wald's test	Increased probability: Duration of quit (p<0.0001) Quit attempt last year (p<0.0001) ↑ Number of quit attempts (p<0.0001) Self-efficacy (p<0.0001) Decreased probability: ↑CPD (p<0.0001) No difference: N.A.
Messer et al 2008 (Messer 2008)	Longitudinal survey part of the TUS-CPS including 3,292 adult recent smokers aged ≥ 18 years.	Chi-squared and logistic regression analyses.	Increased probability: Home smoking ban (OR= 4.81, 95% CI:3.06, 7.59), Child in household (p=0.009) Decreased probability: N.A. No difference: Age (p=0.95) Sex (p=0.27) Race (p=0.53) Education (p=0.38) Income (p=0.85) Smoker in household (p= 0.12)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Sachs-Ericsson et al 2009 (Sachs-Ericsson 2009)	Population survey that was part of a multicenter, collaborative epidemiological investigation of physical, psychological, and social functioning of 4,162 persons aged ≥ 65 years.	Logistic regression analyses (values not shown).	Increased probability: ↓ Income (p=0.04) ↓ Age (P=0.02) Decreased probability: N.A. No difference: Being Caucasian Education High blood pressure (p= 0.05) Diabetes (p=0.22) Broken hip (p= 0.42) Stroke (p=0.50) Cancer (p=0.07) Heart Attack (p=0.14)
Biener et al 2010 (Biener 2010)	Longitudinal survey of 6,739 adults with smokers oversampling. The participants were aged 18-30 years.	Logistic regression analyses.	Increased probability: ↓Age (OR= 1.67, 95%CI:1.15, 2.42) Smoking ban (OR= 1.63, 95%CI: 1.18- 2.25) ↑ Education (OR= 1.45, 95%CI: 1.03-2.04) ↑Smoking dependence (OR= 1.47, 95%CI:1.06- 2.03) Decreased probability: N.A. No difference: Race (Caucasian) (OR= 1.36, 95%CI:0.79-2.32) Marital status (OR= 0.87, 95%CI:0.60-1.24) Spouse smoking (OR= 0.92, 95%CI: 0.61-1.41) Workplace smoking policy (OR= 1.66, 95%CI: 0.88-3.16) Income (OR= 1.16, 95%CI: 0.83- 1.61) Quit attempts (OR= 1.01, 95%CI: 0.74-1.34) Peer smoking (OR= 0.86, 95%CI: 0.65-1.15)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Harris et al 2004 (Harris 2004)	A double-blind placebo-controlled, randomized trial including 535 adult participants	Chi-squared and T-tests and logistic regression analyses.	Increased probability: Use of bupropion (OR= 2.62, 95%CI: 1.77-3.88) Decreased probability: ↓ TTFC (OR= 0.39, 95%CI: 0.25-0.62) ↑ CPD (p=0.004) No difference: Number of quit attempts (p=0.98) Depression (p=0.63) Hassle score (p=0.22) Perceived stress scale (p=0.32) ↑ Years smoked (p=0.08)
Thomas et al 2015 (Thomas 2015)	Randomized trial including 1,217 participants with a mean age of 26.3 years.	Logistic regression analyses.	Increased probability: N.A. Decreased probability: Hookah use (OR = 0.37, 95%CI: 0.14-0.99) No difference: N.A.
Merzel et al 2015 (Merzel 2015)	Data are from the Hispanic Community Health Study/Study of Latinos, a population-based study of 16,415 non-institutionalized Hispanics/Latinos ages 18–74 from a stratified random sample of households in Chicago, Miami, the Bronx, and San Diego.	Logistic regression analyses.	Increased probability: Married or living with partner (OR= 1.34, 95%CI: 1.00-1.79) ↑ Income (OR= 1.50, 95%CI: 1.09-2.06) Decreased probability: ↑ CPD (OR= 0.38, 0.22-0.64) ↑ Age (All ORs significant) Living with a smoker (OR= 0.26, 0.18-0.38) Started smoking after age 25 (OR= 0.38, 95%CI: 0.22-0.64) No difference: Education (OR= 1.05, 95%CI: 0.71-1.56)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Slopen et al 2013 (Slopen 2013)	Cohort study including 4,938 adults aged 25-74 years followed-up for 9-10 years.	Logistic regression reported as smoking persistence.	Increased probability: N.A. Decreased probability: ↑ Relationship stress (OR=1.34–95% CI:1.02–1.77) ↑ Financial stress (OR=1.64, 95% CI:1.19–2.25) ↑ Work stress (OR=1.36, 95% CI:1.00–1.84) Perceived inequality (OR=1.44, 95% CI:1.10–1.88) No difference: N.A.
Collins et al 2004 (Collins 2004)	Randomized, placebo-controlled trial including 314 women and 241 men who smoked ≥ 10 CPD and were aged ≥ 18 years.	Logistic regression reported as abstinence failure	Increased probability: Marital status (married) (OR= 0.59, 95%CI: 0.38-0.90) Decreased probability: Sex (male) (OR= 6.38, 95%CI: 1.00-40.71) No difference: Using drugs (OR= 1.54, 95%CI: 0.30-7.75)
Varghese et al (Varghese 2014)	Interventional study including 6,626 smokers with a mean age of 43.07 years.	Chi-squared test.	Increased probability: ↑ SES ($p<0.001$) Decreased probability: N.A. No difference: N.A.
Nakajima & Al-absi 2012 (Nakajima 2012)	Longitudinal studies with 12 month follow-up including 33 women (mean age 24.9 years) and 38 male (mean age 27.1 years).	Cox regression analyses reported as cessation failure.	Increased probability: Decreased probability: Depressive mood in women (HR=1.07, 95%CI: 1.01-1.12) Motivation to reduce craving in men (HR= 1.26, 95%CI: 1.03-1.54) Anxiety in women (HR= 1.05, 95%CI: 1.01-1.10) Anger in women (HR= 1.12, 95%CI: 1.02-1.23) No difference: Perceived stress (Both in men and women not significant)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Stead et al 2012 (Stead 2012)	Meta-analysis including 117 trials with over 50,000 participants.	Meta-analysis.	Increased probability: Nicotine gum (OR= 1.49, CI95%CI 1.61-2.36) Nicotine patch (OR= 1.64, 95%CI: 1.52-1.78) Oral tablets or lozenges (OR= 1.95, 95%CI: 1.49-2.73) Nicotine inhaler (OR= 1.90, 95%CI: 1.36-2.67) Nicotine nasal-spray (OR= 2.48, 95%CI: 1.24-4.94) Decreased probability: N.A. No difference: Use of NRT for a short amount of time (OR= 1.18, 95%CI: 0.98-1.40)
Baldwin et al 2006 (Baldwin 2006)	Longitudinal study of 591 regular smokers who had been recruited into an 8-week cessation program. Participants were aged ≥ 18 years and smoked ≥ 10 CPD for at least 2 years.	Logistic regression analyses.	Increased probability: Self-efficacy at 9 months (OR= 1.61, 95%CI 1.18-2.20) Satisfaction at 2 months (OR= 1.32, 95%CI: 1.08-1.61) Decreased probability: N.A. No difference: N.A.
Javitz et al 2011 (Javitz 2011)	Results from 2 clinical trials including 935 adults who were seeking treatment for smoking cessation and were aged ≥ 18 years.	Logistic regression analyses.	Increased probability: Using Nicotine Spray (OR= 1.69, 95%CI: 1.04-2.73) Using Bupropion (OR= 1.98, 95%CI: 1.22-3.21) Decreased probability: Sex (female) (OR= 0.64, 95%CI: 0.46-0.89) No difference: FTND (OR= 0.98, 95%CI: 0.89-1.08) CPD (OR= 0.99, 95%CI: 0.97-1.02) Using Transdermal Nicotine (OR= 1.41, 95%CI: 0.88-2.27) Being Asian (OR=0.13, 95%CI: 0.02-1.03) Depression (OR= 1.00, 95%CI: 0.98-1.02)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Lukowski et al 2015 (Lukowski 2015)	Interventional study of 4,960 (subset) participants who had called into 6 state quit lines and were aged ≥ 18 years.	Chi-squared test.	Increased probability: N.A. Decreased probability: Mental disorder or recent emotional challenges (p<0.001) No difference: N.A.
Croghan et al 2010 (Croghan 2010)	Multi-center, open-label randomized, clinical trial of 1,684 adult smokers. 60% women, with a mean age of 46.3 years.	Logistic regression reported as failure to quit)	Increased probability: ↑ Age (OR= 0.97, 95%CI: 0.96-0.99) ↑ Age at starting to smoke (OR= 0.97, 95%CI= 0.96-0.99) Being married (OR= 0.62, 95%CI: 0.50-0.78) Using Bupropion SR (OR= 0.49, 95%CI: 0.36-0.66) Using combination therapy (OR= 0.32, 95%CI: 0.24-0.43) Decreased probability: ↑ FTND (Or= 1.20, 95%CI: 1.13-1.26) Prior quit attempts (OR= 1.85, 95%CI: 1.28-2.68) Being a minority (OR= 1.78, 95%CI: 1.17-2.71) ↑ CPD (OR= 1.50, 95%CI: 1.02-1.82) No difference: BMI (OR= 0.99, 95%CI: 0.97-1.01)
Kinnunen et al 2008 (Kinnunen 2008)	Randomized, placebo-controlled trial of 608 participants aged ≥ 20 years regularly smoking ≥ 5 CPD.	Cox regression analyses, reported as failure to quit	Increased probability: Using NRT (OR= 0.69, 95%CI: 0.58-0.82) Decreased probability: Being depressed (OR= 1.23, 95%CI: 1.04-1.46) No difference: N.A.
Cobb et al 2014 (Cobb 2014b)	Cohort including 4,500 spouse pairs aged 45-64 years with a follow-up of 9 years.	Logistic regression analyses.	Increased probability: Spousal former smoking (in women only) (OR = 1.26, 95% CI: 1.04-1.53) Decreased probability: Spousal smoking in men (OR=0.37, 95%CI: 0.29-0.46) Spousal smoking in women (OR= 0.54, 95%CI: 0.43-0.68) No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Special Populations			
Matthews et al 2013 (Matthews 2013)	Community-based smoking cessation treatment program of 198 LGBT smokers with a mean age of 40.5 years		Increased probability: Treatment attendance (OR= 2.45, 95%CI: 1.45-4.15) Use of NRT (OR= 4.24, 95%CI: 1.24-14.50) Decreased probability: ↑ nicotine dependence (OR= 0.73, 95%CI: 0.57-0.94) No difference: N.A.
Evins et al 2014 (Evins 2014)	Controlled trial of 90 adult smokers aged 18–70 years who smoked ≥10 cigarettes per day for ≥2 years prior to enrollment and met DSM-IV criteria for lifetime diagnosis of a unipolar depressive disorder	Logistic regression analyses.	Increased probability: Varenicline (OR= 6.2, 95%CI: 2.2-19.2) Decreased probability: N.A. No difference: N.A.
Culhane et al 2008 (Culhane 2008)	114 adult participants with stable schizophrenia participating in 1 of 2 smoking cessation trials.	Logistic regression analyses (values not shown)	Increased probability: Study Medication (p=0.02) Decreased probability: N.A. No difference: Sex (male) (p=0.38) ↑ Age of initiation (p=0.08) Alcohol use (p=0.59) Level of nicotine dependence Pack-years (p=0.79) Previous quit attempts (p=0.32)
Vidrine et al 2015 (Vidrine 2015)	Data from 350 HIV + subjects enrolled in a randomized smoking cessation treatment trial and were aged ≥ 18 years, willing to set a quit date within 7 days, and English or Spanish speaking.	Mediation analysis for binary outcomes (values not shown)	Increased probability: Self-efficacy Decreased probability: Anxiety No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Moadel et al (Moadel 2012)	Randomized controlled trial including 145 HIV + individuals living in New York aged 29-70 years		Increased probability: Being Hispanic (OR= 4.11, 95%CI: 1.06-16.0) Self-efficacy (p=0.02, data not shown) Decreased probability: Positive affect (OR= 0.91, 95%CI: 0.83-0.99) No difference: Age (OR= 1.09, 95%CI: 0.99-1.21)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Determinants in specific populations

There were 5 studies evaluating determinants of smoking cessation among specific populations. One study included sexual minorities (Matthews 2013), 2 studies included HIV positive individuals (Moadel 2012, Vidrine 2015) and 2 included populations with mental disorders (Culhane 2008, Evins 2014).

For sexual minorities, treatment attendance, use of NRT, and low nicotine dependence were associated with increased cessation (Matthews 2013).

For the HIV positive populations, self-efficacy, and being Hispanic, were associated with cessation, while anxiety and having positive affect (positive moods) were associated with relapse (Moadel 2012, Vidrine 2015).

Finally, for psychiatric populations, 1 study included individuals with depression (Evins 2014), and 1 included populations with schizophrenia (Culhane 2008, Dutra 2012). The determinants positively associated with cessation were: use of varenicline (Evins 2014) and using cessation medication (Culhane 2008).

6.3.2.2.3.3 Discussion

Cessation rates varied widely from study to study. In observational studies, overall cessation frequencies of 6.2%-7.4% were reported, the NHIS survey reports a yearly cessation of 6.2% (Frieden 2011), which was corroborated by the study by Slopen et al. (Slopen 2013) who reported a cumulative cessation of 6.8%. Furthermore, the NHIS reported that the cessation frequency is higher as those with an associated degree (8.1%) and with an undergraduate degree (11.4%) compared to those with a high school diploma or less (3.2%) (Frieden 2011). Furthermore, when studies reported point prevalence values these ranged 37.7% for 3-day ppa (Reitzel 2015) to 25% for 30-day ppa (Bush 2014, Vickerman 2015b) and continuous abstinence for 6 month rates are 7.4% (Kendzor 2014).

As discussed, the variation in cessation rates was affected by the type of measurement of cessation or abstinence used in the studies (quit rates by length of follow-up, point prevalence at different time-points) (Hughes 2010) as well as by cessation aids used. Additionally, different demographic factors also affected the rates of cessation such as ethnicity (Croghan 2010). In general, the longer the follow-up, the more the cessation rates decreased (Abrantes 2014, Fridberg 2014, Reitzel 2015). When analyzing studies assessing different interventions, it became evident that the use of combination therapies were superior, especially when combining pharmacological support with behavioral support (Piper 2016, Schlam 2016).

The determinants of smoking cessation varied greatly by the composition of the population studied. Nevertheless, in both adult and youth populations, personal and family related variables such as a home smoking, readiness to quit (in adults) or parental smoking (in youth) were consistently positively associated with smoking cessation. These variables also played a role in determining the likelihood of cessation in specific populations.

Smoking cessation benefits health and lengthens life expectancy at any age (Services. 2004) and the population of the US has received the personal benefits of stopping smoking (Samet 2014). The decline in smoking over the last four decades reflects the combined effects of multiple factors such as tobacco control laws and regulations as well

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

as the introduction of various therapies, including pharmacotherapy as well as behavioral therapies (Samet 2014). As shown by the articles retrieved by this literature search, the new pharmacologic agents introduced (e.g. varenicline, bupropion) used in conjunction with appropriate counseling and support increase the likelihood of sustained cessation (Samet 2014). These treatments however, are expensive (Cahall 2004), and the use of these aids vary by insurance coverage (Lillard 2007, Murphy 2005). Therefore, there may well be disparities in the use of these therapies among certain specific populations, such as those belonging to LGBT communities (Fallin 2016). Additionally, as with any other medications, pharmacotherapies for cessation have been associated with adverse events which in some cases can be serious (Prochaska 2016).

As successful as therapies have proven to be, smoking cessation remains a difficult task and relapse is common after a quit attempt (Hughes 2014, Yeomans 2011). Cessation has been shown to be a more complex and dynamic process than many theories or treatments assume (Hughes 2010) . For instance, the study by Peters & Hughes showed that the day-to-day process of attempts to change smoking among non-treatment seekers is much more dynamic than previously thought, as there is not a simple pattern of change but rather a pattern of multiple transitions among smoking, abstinence, and reduction over a short period of time.

Moreover, not all smokers are willing to quit (Hughes 2009). For instance the study by Hugues et al.. in a Vermont population reported that 43% of smokers had tried to quit smoking (Hughes 2009). The prevalence of intention to quit ranged from 51.5%-52.8% in a youth population included in a study by Tworek et al. (Tworek 2014). In this particular group of smokers who do not intend to quit, the availability of other options such as modified risk tobacco products could be helpful not only at individual level but also at the population level (Physicians 2014)

6.3.2.2.3.4 Conclusions

Cessation rates varied greatly primarily by methods used to measure the reported rates and type of treatment used. When considering the results from observational studies, cessation rates ranged from 6.2%-6.4% but these values were also affected by demographic characteristics such as education (Frieden 2011). These rates tend to decline as follow-up time increases, and the most common outcome of a quit attempt is relapse. In addition, not all smokers are willing to quit. Hence, the availability of reduced risk products could have a positive impact not only at the individual level but also at the population level.

6.3.2.2.4 Relapse to smoking

6.3.2.2.4.1 Search strategies

The search for articles on relapse to smoking was performed on March 12, 2016 and resulted in 225 articles being identified using the following query: "Smoking relapse"[All Fields] AND ("united states"[MeSH Terms] OR ("united"[All Fields] AND "states"[All Fields]) OR "united states"[All Fields]). The review of the titles and abstracts resulted in 140 articles being extracted and fully reviewed. The relevant articles are discussed in this section.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.4.2 Results

6.3.2.2.4.2.1 Relapse to smoking

Nine publications reporting the rates of relapse after smoking cessation were identified through the literature search (Allen 2008, Baer 1989, Garcia-Rodriguez 2013, Garvey 1992, Gokbayrak 2015, Heffner 2010, Hughes 2008, Krall 2002, Zvolensky 2015). Their characteristics can be found in Table 24. These studies investigated relapse to smoking after different lengths of cessation. There were 2 studies assessing short-term relapse (after up to 1 month of cessation) (Allen 2008, Garvey 1992). The relapse rates in adults ranged from 76.0% in those with no intervention to 81.0% in those receiving behavioral therapy. There were 3 studies assessing relapse rates after 2 months to 1 year after cessation (Baer 1989, Garcia-Rodriguez 2013, Garvey 1992). The relapse rates were higher the longer the subjects were followed up. Baer et al. (Baer 1989) reported results from a trial where cognitive behavioral therapy was administered, and they reported that relapse after 2 months was 25%, after 3 months 35% and at 6 months 48% (Baer 1989). A study by Garcia-Rodriguez et al. in a group with no intervention (Garcia-Rodriguez 2013) reported a relapse rate of 47% after 1 year of follow-up, and Garvey et al. (Garvey 1992) reported a relapse rate of 87.2% also in a group of untreated patients. The study by Garcia-Rodriguez, followed patients for more than 30 years, and they reported that after the first year, rates of relapse decrease from 47% to 36% after 2 years, 25% after 5 years and 10% after 30 years of abstinence (Garcia-Rodriguez 2013). Similar trends are reported by Krall et al. (Krall 2002) who reported a relapse rate of 19% after 2 years of abstinence. They also report that from years 2-6 after cessation the rate of relapse was 2-4% per year, from years 7 to 10 the relapse rate is 2% and after 10 years the relapse rate is 1%. A meta-analysis was also identified (Hughes 2008) through the literature search, which showed an annual incidence of relapse of 10%. Importantly, while some studies showed cumulative rates of relapse (Baer 1989, Garvey 1992, Heffner 2010), other studies (especially those reporting from long-term follow-up studies) reported non-cumulative relapse rates (Garcia-Rodriguez 2013, Hughes 2008, Krall 2002), showing that after 1 year of follow-up or more these rates actually drop instead of increasing.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 24. Characteristics of studies assessing relapse rates in US populations

Author	Population & study methods	Intervention	Relapse rate by cessation length
Short term up to 1 month			
Allen et al 2008 (Allen 2008)	Clinical trial including 137 females aged 18-40 years who were followed for 30 days post treatment. Relapse to smoking was defined as a relapse from continuous abstinence (i.e. a single puff from a cigarette).	Behavioral therapy	**Overall** **At up to 1 month:** 81.0%
Garvey et al 1992 (Garvey 1992)	Longitudinal study of 235 adults aged 20 or older who were followed-up for 1 year after self-initiated attempt to stop smoking. Relapse was defined as 7 or more consecutive days of smoking or 7 or more consecutive episodes of smoking.	None	**Overall** **At 1 month:** 76.0%
Short term from 2 month up to 1 year			
García-Rodriguez et al 2013 (Garcia-Rodriguez 2013)	Longitudinal data drawn from Waves and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. Participants were 5,831 abstinent smokers aged 18 or older who had been abstinent for at least 1 week before baseline.	None	**At 12 months:** 47%
Hughes et al 2008 (Hughes 2008)	Meta-analysis of 7 randomized clinical trials all testing nicotine medications in adult populations.	Nicotine replacement therapies	**Annual incidence:** 10%
Garvey et al 1992 (Garvey 1992)	Longitudinal study of 235 adults aged 20 or older who were followed-up for 1 year after self-initiated attempt to stop smoking. Relapse was defined as 7 or more consecutive days of smoking or 7 or more consecutive episodes of smoking.	None	**Overall** **At 1 year:** 87.2%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Intervention	Relapse rate by cessation length
Baer et al 1989 (Baer 1989)	Longitudinal interventional study of 46 men and 56 women aged 38.2 ± 11.5 years who were clients of the Smoking Control Program. Subjects were abstinent for at least 1 week and were followed-up for 1 year after end of treatment. Relapse was defined as re-starting of smoking.	Cognitive-behavioral	**Overall:** **At 2 months:** 25% **At 3 months:** 35% **At 6 months:** 48%
Long term (longer than 1 year)			
Zvolensky et al 2015 (Zvolensky 2015)	Longitudinal cross sectional study (Midlife Development in the US Survey) including 699 former smokers aged 25-74 years (those reporting having ever been a daily smoker and that the last age at which they were regular smokers was at least 1 year prior to baseline). Relapse was defined as those who reported being daily smoking at follow-up.	None	**Any relapse after 12 months:** **Major depressive disorder:** 27.8% **No depression:** 10.3%
Gokbayrak et al 2015 (Gokbayrak 2015)	Randomized controlled trial of 521 participants aged 18-64 from four population-based smoking cessation interventions and had stopped smoking for at least 12 months. Relapsers were classified as participants who reported they were in any of the pre-action stages (pre-contemplation, contemplation, or preparation).	Treatment group received a trans-theoretical model intervention printed as well as a stage-matched self-help manual, while controls only received assessments.	**At 30 months:** **By Treatment:** Intervention: 19.9% Control: 35.0%
García-Rodriguez et al 2013 (Garcia-Rodriguez 2013)	Longitudinal data drawn from Waves and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. Participants were 5,831 abstinent smokers aged 18 or older who had been abstinent for at least 1 week before baseline.	None	**At 2 years:** 36% **At 5 years:** 25%
Heffner et al 2010 (Heffner 2010)	Post hoc analysis of two randomized controlled trials including 626 smokers who had been classified as treatment respondents. Relapse was defined as any self-report of smoking (even a puff) or use of other tobacco products during the follow-up period (40 weeks). Participants were men and women aged 18 to 75.	Varenicline (titrated to 0.5 mg/d for days 1-3, 0.5 mg/d twice a day for days 4-7, then 1 mg/d twice per day from day 8 through week 12, to both bupropion SR (titrated to 150 mg/d for days 1 to 3, then 150 mg twice per day through week 12) and placebo	**Overall:** **At 52 weeks:** 48.1%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Intervention	Relapse rate by cessation length
Krall et al 2002 (Krall 2002)	Cohort of 483 men former smokers who had participated in a prospective study for up to 35 years. Men were aged 21 years or older. Subjects were evaluated approximately every 3 years and relapse was defined as a report of current cigarette use at 1 or more examinations following a report of having been a former smoker.	None	**Overall:** **At 2 years:** 19% **At 2-6 years:** 2-4% per year **At 7-10 years:** 2% per year **10 years or more:** 1% per year

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.4.2.2 Determinants of relapse

There were 9 studies assessing the association of various factors with relapse to smoking (Table 25) (Allen 2008, Caraballo 2014, Garcia-Rodriguez 2013, Garvey 1992, Gokbayrak 2015, Heffner 2010, Killen 1997, Krall 2002, Zvolensky 2015). All studies were performed in adult US populations. Studied determinants of relapse were either personal determinants or peer/social determinants.

Among personal determinants were major depressive disorder (Zvolensky 2015), receiving no adjuvant therapy (Gokbayrak 2015), the presence of stressors (Garcia-Rodriguez 2013), initiating abstinence late after treatment (Heffner 2010), higher FTND scores (Allen 2008) and drinking coffee (Krall 2002). There was contradictory evidence for race; while some authors found an increased risk of relapse in Caucasians (Caraballo 2014). Other authors showed a similar increase in risk in Hispanics (Garcia-Rodriguez 2013) and Asian-Americans (Garcia-Rodriguez 2013). Associations were also seen for alcohol drinking (Garvey 1992, Krall 2002), the presence of cravings (Garvey 1992, Killen 1997), being a female (Caraballo 2014, Garcia-Rodriguez 2013, Garvey 1992, Gokbayrak 2015), younger age (Garvey 1992, Gokbayrak 2015, Heffner 2010), number of quit attempts (Allen 2008, Gokbayrak 2015), marital status (single) (Garcia-Rodriguez 2013, Gokbayrak 2015, Krall 2002) and education (Allen 2008, Caraballo 2014, Garcia-Rodriguez 2013, Gokbayrak 2015, Krall 2002). Other factors were associated with a decreased risk for relapsing such as motivation to quit and confidence in being able to abstain from smoking (Garvey 1992), trying to control weight (in women only) (Garvey 1992), having an income above $35,000, being unemployed or having poor to fair health (Garcia-Rodriguez 2013). On the other hand, the only peer/social determinant to relapse was peer smoking (Garvey 1992).

6.3.2.2.4.3 Discussion

Relapse to smoking after a quit attempt is greatest in the first few weeks and decreases over time (Hughes 2008, Piasecki 2002), as is shown by the different publications found through our literature search. Although currently available cessation treatments frequently doubled the rates of abstinence relative to not receiving treatment, post-treatment relapse was always more common than continued abstinence (Piasecki 2002). A major factor influencing relapse is time after quitting, since rates of relapse are found to be much lower after 1 year of cessation compared to shorter time periods; however these rates still remain substantial even after prolonged follow-up (Hughes 2008). The major factors influencing the risk of relapse are personal factors. Among these, psychological factors such as stress or major depression are highly associated with smoking relapse and have been identified as being among the most important factors influencing relapse (and initiation) particularly in women (Torres 2016) but in the overall population as well (Piasecki 2002). These stressor can have a marked effect on the degree of withdrawal that is experienced, thus increasing the difficulty of maintaining abstinence. It seems however, that handling these stressors becomes easier with time, which explains the fact that the longer a person remains abstinent, the less likely they will relapse (Piasecki 2002). Other important factors related to relapse are those involving health, such as trying to control weight, or to maintaining health, since those who reported poor to fair health were more likely to report continuous cessation.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 25. Determinants of relapse in the US population

Author	Population & study methods	Analyses performed	Determinants
Zvolensky et al 2015 (Zvolensky 2015)	Longitudinal cross sectional study (Midlife Development in the US Survey) including 699 former smokers aged 25-74 years (those reporting having ever been a daily smoker and that the last age at which they were regular smokers was at least 1 year prior to baseline). Relapse was defined as those who reported being daily smoking at follow-up.	Logistic regression analyses.	Increased probability: Major depressive disorder (OR=2.3, 95%CI: 1.2-4.2) Decreased probability: N.A. No difference: N.A.
Gokbayrak et al 2015 (Gokbayrak 2015)	Cohort study of 521 participants aged 18-64 from four population-based smoking cessation interventions and had stopped smoking for at least 12 months. Relapsers were classified as participants who reported they were in any of the pre-Action stages (pre-contemplation, contemplation, or preparation).	Logistic regression analyses.	Increased probability: No treatment used (OR= 2.17, 95%CI: 1.44-3.25) Having tried to quit 3-10 times (OR= 1.70, 95%CI: 1.05-2.77) Decreased probability: Age 25-44 (OR=0.43, 95%CI:0.23-0.81) Age 45-64 (OR= 0.40, 95%CI: 0.20-0.80) ↑ Quit length (36-71 months) (OR= 0.42, 95%CI: 0.20-0.89) No difference: Sex (female) (OR=1.04, 95%CI: 0.70-1.53) Education (OR= 0.76, 95%CI: 0.52-1.12) Not married (OR= 1.18, 95%CI: 0.68-200.4) Previous daily cigarette use (All ORs not significant) Time to first cigarette (All ORs not significant)
Caraballo et al 2014 (Caraballo 2014)	Retrospective examination of 25 years of data from the Coronary Artery Probability Development in Young Adults (CARDIA) which included 506 former smokers at baseline and were 18 or older.	Logistic regression analyses.	Increased probability: Sex (male) (OR= 1.34, 95%CI: 1.08-1.66) Being African-American (OR= 1.86, 95%CI: 1.49-2.31) Decreased probability: ↑ Education (OR= 0.79, 95%CI: 0.75-0.83) Age at baseline (OR= 0.93, 95%CI: 0.91-0.96) No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
García-Rodriguez et al 2013 (Garcia-Rodriguez 2013)	Longitudinal data drawn from Waves and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. Participants were 5,831 abstinent smokers aged 18 or older who had been abstinent for at least 1 week before baseline.	Logistic regression analyses.	Increased probability: Being Hispanic (OR= 1.57, 955CI: 1.07-2.29) Being Asian (OR= 2.65, 95%CI: 1.34-5.27) ↑ Education (OR= 1.56, 95%CI: 1.06-2.27) Being never married (OR= 3.92, 95%CI: 2.86-5.38) ↑ Life stressors (OR= 1.25, 95%CI 1.18-1.33) Not being overweight (OR = 1.43, 95%CI: 1.12-1.84) Decreased probability: Sex (male) (OR= 0.75, 95%CI: 0.60-0.92) Older than 30 years (OR = 0.24, 95%CI: 0.17-0.33) Income higher than 35,000 USD (OR= 0.68, 95%CI: 0.50-0.91) Unemployed (OR= 0.47, 95%CI: 0.37-0.60) Poor to fair health (OR= 0.69, 95%CI: 0.49-0.96) No difference: Urbanicity (OR= 0.98, 95%CI: 0.76-1.26) US born (OR= 1.25, 95%CI: 0.83-1.86)
Heffner et al 2010 (Heffner 2010)	Post hoc analysis of two randomized controlled trials including 626 smokers who had been classified as treatment respondents. Relapse was defined as any self-report of smoking (even a puff) or use of other tobacco products during the follow-up period (40 weeks). Participants were men and women aged 18 to 75.	Cox regression analyses.	Increased probability: Late initiation of abstinence after treatment period (OR= 1.23, 95% CI: 1.02–1.47) > 30 days of abstinence in the previous year (OR= 2.38, 95%CI: 1.17-5.04) Decreased risk: N.A. No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Allen et al 2008 (Allen 2008)	Clinical trial including 137 females aged 18-40 years who were followed for 30 days post treatment. Relapse to smoking was defined as a relapse from continuous abstinence (i.e. a single puff from a cigarette).	Univariate F-tests.	Increased probability: ↑ CES-D Depression (p=0.041) Withdrawal symptoms (p=0.001) ↑Craving (p=0.016) ↑Smoking urges (p=0.001) Decreased probability: N.A. No difference: N.A.
Krall et al 2002 (Krall 2002)	Cohort of 483 men former smokers who had participated in a prospective study for up to 35 years. Men were aged 21 years or older. Subjects were evaluated approximately every 3 years and relapse was defined as a report of current cigarette use at 1 or more examinations following a report of having been a former smoker.	T-test (continuous variables) or chi-squared test (categorical variables).	Increased probability: ↑ Coffee consumption (p=0.002) Decreased probability: N.A. No difference: Age at initiation (p>0.05) Years prior to quitting (p>0.05) Maximum cigarettes per day (p>0.05) BMI (p>0.05) Gained weight since quitting (p>0.05) Drinking alcohol (p>0.05) Education (p>0.05) Marital status (p>0.05) Living with a smoker (p>0.05)
Killen & Fortmann 1997 (Killen 1997)	Study re-analyzing 3 prospective studies. Participants were aged 18 or above. Relapse was measured as a participant's date on which they resumed smoking for 7 consecutive days.	Chi-squared test.	Increased probability: ↑ Craving (p< 0.001) Decreased probability: N.A. No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Garvey et al 1992 (Garvey 1992)	Longitudinal study of 235 adults aged 20 or older who were followed-up for 1 year after self-initiated attempt to stop smoking. Relapse was defined as 7 or more consecutive days of smoking or 7 or more consecutive episodes of smoking.	T-test (continuous variables) or chi-squared test (categorical variables).	Increased probability: ↓ Motivation for quitting (p=0.006) ↓ Confidence in being able to abstain (p=0.009) Smoking spouse (0.02) ↑ Drinking alcohol (p=0.20) Half or more friends smoking Decreased probability: ↑ Length of abstinence (p=0.001) ↑ Weight control (women) (p=0.02) No difference: Difficulty remaining abstinent (p=0.12 ↑ Stress (p=0.13)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.2.4.4 Conclusions

Relapse to smoking is always more common than abstinence after quitting, but the relapse rates decrease over time presumably as former smokers learn to deal with cravings and temptations. Most determinants of relapse are related to personal factors such as stressors and personal attitude towards quitting.

6.3.2.3 Alternative tobacco and nicotine containing products

6.3.2.3.1 Electronic cigarettes (e-cigarettes)

6.3.2.3.1.1 Search strategies

For e-cigarettes, two searches were performed. The first literature search was for articles on e-cigarette prevalence of use and was performed on March 11, 2016. It resulted in 288 articles identified using the following query: ("electronic cigarettes"[MeSH Terms] OR ("electronic"[All Fields] AND "cigarettes"[All Fields]) OR "electronic cigarettes"[All Fields] OR "e cigarette"[All Fields]) AND ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms]) AND ("united states"[MeSH Terms] OR ("united"[All Fields] AND "states"[All Fields]) OR "united states"[All Fields]) AND English[lang]. The review of the titles and abstracts resulted in 173 articles being extracted and fully reviewed, and the relevant articles are discussed in this section.

The second more general search was performed on March 12, 2016, and resulted in 732 articles being identified using the following query: ("electronic cigarettes"[MeSH Terms] OR ("electronic"[All Fields] AND "cigarettes"[All Fields]) OR "electronic cigarettes"[All Fields] OR "e cigarette"[All Fields]) AND (determinants[All Fields] OR drivers[All Fields]) AND ("united states"[MeSH Terms] OR ("united"[All Fields] AND "states"[All Fields]) OR "united states"[All Fields]). The review of the titles and abstracts resulted in 321 articles being extracted.

6.3.2.3.1.2 Results

6.3.2.3.1.2.1 Prevalence of e-cigarette use

6.3.2.3.1.2.1.1 Prevalence in adult populations

There were 22 studies assessing the prevalence of e-cigarette use in adult populations, but only 3 of these studies used a national sampling frame (King 2015, Primack 2015, Schoenborn 2015). Data from the NHIS 2014 showed that 12.6% of adults had ever tried an e-cigarette (even once) with prevalence of use differing by sex, age, and race (Figure 1). About 3.7% of adults currently used e-cigarettes (defined as using every day or some days), with use differing by age and race. The authors also reported that current cigarette smokers and former smokers who quit smoking within the past year were more likely to use e-cigarettes than former smokers who quit smoking more than 1 year ago and those who had never smoked. Among current cigarette smokers who had tried to quit smoking in the past year, more than one-half had ever tried an e-cigarette and 20.3% were current e-cigarette users. Finally, among adults who had never smoked cigarettes, 3.2% had ever tried an e-cigarette, which was higher among adults aged 18-24 (9.7%). This prevalence of use declined with age.

When considering all studies found, 10 studies evaluated mostly young adults (up to the age of 40, even though age varied greatly from study to study and the majority of these

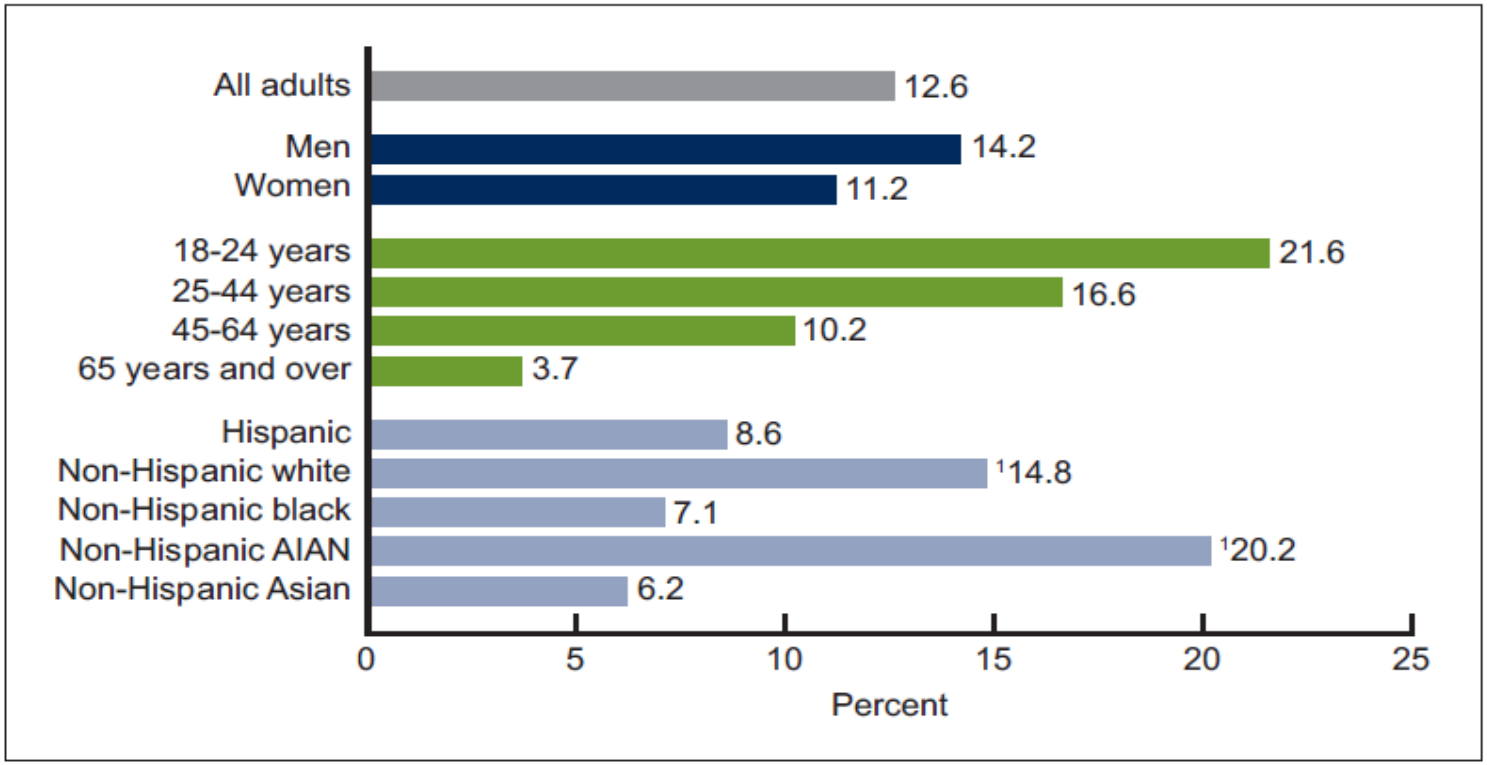
Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

studies included subjects up to the age of 30) and 12 studies had a population defined as ≥ 18 years of age. The detailed characteristics of these studies can be found in Table 26.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.



[1]Significantly different from Hispanic, non-Hispanic African-American, and non-Hispanic Asian subgroups.
NOTES: AIAN is American Indian or Alaska Native. Within sex and age groups, all subgroups are significantly different from each other. There is a significant linear trend by age group.
SOURCE: CDC/NCHS, National Health Interview Survey, 2014.

Figure 1. Prevalence of e-cigarette ever use in adults in the US (Schoenborn 2015)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

The prevalence of e-cigarette use varied by age groups and by the definition of e-cigarette use. Considering only the 10 studies using young adult populations, the prevalence of ever use ranged from 2.3% (data from 2012-2013) using a national US sample (Primack 2015) to 45% (data from 2013) in college adults aged 18-25 (Allem 2015), while the prevalence of past 30 day use in the same group of studies ranged from 1.2% (data from 2010-2011) in adults aged 20-28 in the US Midwest (Choi 2013b) to 12% in adults aged 18-25 (data from 2013) (Allem 2015). When taking into account studies with populations including only adults, the prevalence of e-cigarette ever-use ranged from 1.8% (data from 2010) (McMillen 2014) to 17.7% among adults in Minnesota (data from 2014) (Amato 2016). Past 30 day use ranged from 0.3% (data from 2010) (McMillen 2014) to 8.5% (data from 2013) (King 2015).

The prevalence of e-cigarette use (ever or past 30 days) was shown to be considerably higher among current cigarette smokers than in never-smokers (Amato 2016, Choi 2014, Christensen 2014, King 2015, Loukas 2015, McMillen 2014, Pearson 2012, Regan 2012, Schoenborn 2015, Sutfin 2015, Weaver 2016, Zhu 2013) as evidenced by the study by McMillen et al. (McMillen 2014), which reported that the prevalence of e-cigarette use was higher in current daily smokers (30.3%) and current non-daily smokers (34.1%) than in former smokers (5.4%) and never-smokers (1.4%), as well as by the study by King et al. (King 2015), which reported a prevalence of e-cigarette use in current smokers of 36.5% compared to 9.6% in former smokers and 1.2% in never-smokers.

6.3.2.3.1.2.1.2 Prevalence in youth populations

There were 16 studies assessing the prevalence of e-cigarette use in youth populations, although only two studies used a national sampling frame (Arrazola 2015, Johnston 2016). The MTF survey reported the most recent results (from 2015) (Johnston 2016). The authors reported that e-cigarettes continue to have higher use among teens than do traditional tobacco cigarettes or any other tobacco product. Their 30-day prevalence was 9.5%, 14.0%, and 16.2% in 8th, 10th, and 12th grade, while the corresponding prevalence for tobacco cigarettes was 3.6%, 6.3%, and 11.4%. Prevalence levels did not significantly change from 2014 to 2015 in any grade; they decreased slightly in 12th and 10th grade (by 0.9 and 2.2 percentage points, respectively), and increased in 8th grade (by 0.8 points).

When analyzing all studies retrieved, the prevalence of use varied among youth populations depending on the definition of use (ever vs. past 30 day vs. daily use). Ever use ranged from 4.3% in middle school students in Florida (data from 2013) (Barnett 2015) to 25.2% in high school students in Connecticut (data from 2013)(Krishnan-Sarin 2015), while past 30 day use ranged from 1.9% in high school students in Connecticut and New York (data from 2014) (Camenga 2014a) to 20.5% in high school students in Texas (data from 2014) (Porter 2015). When daily use was considered, the values ranged from 1.0% in adolescents in 9th and 10th grades in Hawaii (data from 2013-2014) (Wills 2016) to 2.0% in high school students in Hawaii (data from 2014) (Wills 2015). The prevalence also varied by the age of the population included in the study. Higher prevalence rates were seen in those surveys where the populations were high school students (grades 9 to 12) (Alcala 2016, Arrazola 2015, Barnett 2015, Barrington-Trimis 2015, Bostean 2015, Camenga 2014a, Camenga 2014b, Johnston 2016, Porter 2015, Wills 2016, Wills 2015), where the past 30 day prevalence ranged from 4.5% (data from 2013) (Arrazola 2015) to 20.5% in overall high school students (data

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

from 2014) (Porter 2015). The prevalence of past 30 day use among middle school students ranged from 1.1% (data from 2013) (Arrazola 2015) to 8.5% (data from 2014) (Porter 2015).

Additional findings were that e-cigarette use was more common among those smoking cigarettes than among those who had never smoked cigarettes (Cooper 2015, Johnston 2016, Krishnan-Sarin 2015). Detailed findings of individual studies can be found in Table 27.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 26. Characteristics of studies assessing the prevalence of e-cigarette use in adult populations

Survey	Period	Study characteristics	Definitions	Prevalence
Weaver et al (Weaver 2016)	2014	Data obtained from the Tobacco Products and Probability Perceptions Survey of a probability sample of 5,717 US adults aged ≥ 18 years.	• E-cigarette use was measured as ever use and currently using (every day or some days).	• Overall ever use = 14.9% • Past 30 day use = 4.9 % • By smoking status: • Current smokers past 30 day use= 20.7% • Former smokers past 30 day use = 3.8 % • Never-smokers past 30 day use = 0.9%
Amato et al (Amato 2016)	2014	Data from the Minnesota Adult Tobacco Survey which included 9,304 participants aged ≥ 18 years.	• E-cigarette use was measured as ever use and currently use (last 30 days, more than 5 days in the past 30 days and every day).	• Overall ever use = 17.7% • Past 30 day use = 6.0% • At least 5 days in the last 30 = 2.4% • Everyday use = 1.1% • Most current smokers (70%) had tried e-cigarettes at least once in their life, compared to smaller percentages of former smokers (15.9%) and never smokers (5.6%). Across all cigarette smoking statuses, fewer than half of those who had ever tried e-cigarettes in their lifetime reported having used them in the past 30 days: current smokers 38.9%; former smokers 30.3% and never-smokers 21.5%.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
National Health and Nutrition Survey (NHIS) (Schoenborn 2015)	2014	NHIS is a large-scale household interview survey of a statistically representative sample of the US civilian noninstitutionalized population. Interviewers visit 35,000–40,000 households across the country and collect data about 75,000–100,000 individuals. Data are adjusted for selection and nonresponse, and weighted to provide nationally representative estimates. The 2014 NHIS included 36, 697 respondents aged ≥ 18 years; the response rate was 58.9%.	• E-cigarette use was measured as ever tried and currently using (every day or some days).	• Overall ever use = 12.6% • Overall current use = 3.7% • Ever use in current smokers = 20.3% • Ever use in never-smokers = 3.2% • Ever having used an e-cigarette was highest among never smokers aged 18–24 (9.7%) and declined with age.
Schmidt et al (Schmidt 2014)	2013	Participants were part of the Montana Adult Tobacco Survey that included 3,311 subjects aged ≥ 18 years.	• E-cigarette use was measured as ever use.	• Overall ever use = 11.2% • Last 30 day use = 1.3%.
Huang et al (Huang 2016)	2013	Cross-sectional online survey of 17,522 adults aged ≥ 18 years.	• Use of e-cigarettes was measured as ever use and as current use (every day or some days use).	• Overall ever use = 15.0% • Last 30 day use = 5.1%.
Allem et al (Allem 2015)	2013	Cross-sectional survey of 555 young adults aged 18-25years.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use = 45% • Overall past 30 day use = 12%
Hampson et al (Hampson 2015)	2013	Longitudinal study including 862 students from high school that were followed-up until emerging adulthood (mean age = 22.4 years).	• E-cigarette was measured as ever use	• Overall ever use in men = 6.6% • Overall ever use in women = 3.6%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
King et al (King 2015)	2010-2013	Cross-sectional web-based study carried out annually of US adults aged ≥ 18 years.	• Ever use of e-cigarettes was assessed using the question, "Have you ever tried any of the following products, even just once"? Respondents who selected "electronic cigarettes or e-cigarettes" were considered to be ever e-cigarette users. • Current Use of e-cigarettes was assessed by the question, "In the past 30 days, which of the following products have you used at least once"? Respondents who selected "electronic cigarettes or e-cigarettes" were considered to be current e-cigarette users.	• Overall ever use = 3.3%–8.5% in 2010 to 2013 • Overall past 30 day use = 1.0%–2.6% in 2010 to 2013 • Ever use in current smokers = 9.8%–36.5% in 2010 to 2013 • Ever use in former smokers = 2.5%-9.6% in 2010 to 2013 • Ever use in never-smokers = 1.3%-1.2% in 2010 to 2013 • An increase in ever use of e-cigarettes occurred among all sociodemographic groups except those aged 18–24 years, Hispanics, and those living in the Midwest.
McMillen et al (McMillen 2014)	2010-2013	Mixed-mode cross-sectional surveys including more than 2,000 adult aged ≥ 18 years respondents (numbers varied by year from 1,689 in 2013 and 2,282 in 2011).	• Use of e-cigarettes was measured as ever use and as current use (every day or some days use).	• Overall Ever use = increased from 1.8% in 2010 to 13.00% in 2013. • Current use = increased from 0.3% in 2010 to 6.8% in 2013. • Current use in young adults 18-24 (14.2%) was higher than adults 25-44 (8.6%), 45-64 (5.5%) and 65+ (1.2%). • E-cigarette use was higher among current daily current smokers (30.3%) and non-daily smokers (34.1%) than former smokers (5.4%) and never-smokers (1.4%).

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
Christensen et al (Christensen 2014)	2012-2013	Cross-sectional study of 9,656 adults aged ≥ 18 years participating in the Kansas Adult Tobacco Survey.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use = 11.8% • Overall past 30 day use = 3.4% • Current smokers ever use = 45% • Current smoker past 30 day use = 14% • Adults who only use e-cigarettes are younger and more affluent than adults who only smoke cigarettes.
Loukas et al (Loukas 2015)	2012-2013	Cross-sectional study including 765 students from 7 Texas universities, the students were aged 18-35 years.	• Use of e-cigarettes was defined as current use (past 30 day use)	• Overall past 30 day use = 3.7% in wave 1 and it increased to 7.7% in wave 2. • Current smoker past 30 day use = 14.5% in wave 1 25.4% in wave 2 • Non-current smokers+ 0.8% in wave 1 and 2.8% in wave 2
Primack et al (Primack 2015)	2012-2013	Cohort study of a national US sample of 694 participants aged 16-26 who were never current smokers.	• Use of e-cigarettes was measured as ever use	• Ever use in never-smokers = 2.3%
Pulvers et al (Pulvers 2015)	2012	Cross-sectional study of 2,376 participants aged 25 or older	• E-cigarette use was defined as current use (past 30 day use).	• Overall past 30 day use = 9.2% • As quit method =4.4%
Zhu et al (Zhu 2013)	2012	Cross-sectional study with a national probability sample of 10,041 participants aged ≥18 years.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use = 8.1% • Overall past 30 day use = 1.4% • Current smokers ever use = 32.2% • Current smokers past 30 day use = 6.3% • Over 80% of e-cigarette users were non-daily users.
Latimer et al (Latimer 2014)	2011	Online cross-sectional study including 5,028 students attending 7 public universities. Students were aged 18-24.	• E-cigarette use was defined as current use (past 30 day use).	• Past 30 day prevalence of use was 3.1%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
Trumbo & Haper (Trumbo 2013)	2011	Cross-sectional study of freshmen and sophomore college students aged 19-22 years	• Use of e-cigarettes was defined as having ever trying e-cigarettes	• Ever trying = 13.0%
Choi et al (Choi 2014)	2010-2011	Cohort study including 1,379 young adults aged 18-24 years from the Minnesota Adolescent Community Cohort.	• Use of e-cigarettes was defined as having ever used e-cigarettes	• At 1-year follow-up, 7.4% of the sample reported ever using e-cigarettes (21.6% among baseline current smokers, 11.9% among baseline former smokers, and 2.9% among baseline non-smokers).
Choi et al (Choi 2013b)	2010-2011	Cohort study of 2624 US Midwestern adults aged 20 to 28 years.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use = 7.0% • Overall past 30 day use = 1.2%
Pearson et al (Pearson 2012)	2010	Study gathering data from 2 cross-sectional surveys conducted in 2010. A national online study (n=2.649) and the Legacy Longitudinal Smoker Cohort (n=3.658). The participants were adults aged ≥18 years.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use = 3.4% • Past 30 days use = 1.2% • Current smoker past 30 day use = 4.1% • Former smokers past 30 day use = 0.5% • Never-smokers past 30 day use = 0.3%
Regan et al (Regan 2013)	2009-2010	Consumer-based mail survey that was completed by 10,587 adults ≥18 years in 2009 and 10,398 adults in 2010	• Use of e-cigarettes was defined as having ever trying e-cigarettes.	• Overall ever trying = in 2009 (0.6%) to 2010 (2.7%). • Current smokers and tobacco users were most likely to try e-cigarettes.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
Sutfin et al (Sutfin 2013)	2009	Cross-sectional study including 4,444 students from 8 colleges in North Carolina. The survey was administered through the web.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use of e-cigarettes = 4.9% • Overall past 30 day use = 1.5% • Almost three quarters (72%) of ever e-cigarette users were former/experimenters (30%), current non-daily current smokers (33%) or current daily current smokers (9%). Although e-cigarette use was more common among conventional current smokers, 12.0% of ever e-cigarette users had never smoked cigarettes.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 27. Characteristics of studies assessing the prevalence of e-cigarette use in youth populations

Study	Period	Study characteristics	Definitions	Prevalence
Monitoring the Future (MTF) (Centers for Disease 2016b)	2014-2015	The MTF s an ongoing study of the behaviors, attitudes, and values of American secondary school students, college students, and young adults. Each year, a total of approximately 50,000 8th, 10th and 12th grade students are surveyed (12th graders since 1975, and 8th and 10th graders since 1991) (7). MTF first asked about them in 2014, and in 2015 the survey included new questions about adolescents' reasons for using vaporizers such as e-cigarettes, as well as the type of substances that adolescents "vape."	• Current use was defined as 30-day prevalence of e-cigarette.	• 8th Grade past 30 day use = 9.5% • 10th Grade past 30 day use = 14.0% • 12th Grade past 30 day use = 16.2% • In 2015 e-cigarettes continued to have higher use among teens than traditional tobacco cigarettes or any other tobacco product. Prevalence levels did not significantly change from 2014 to 2015 in any grade; they decreased slightly in 12th and 10th grade (by 0.9 and 2.2 percentage points, respectively), and increased in 8th grade (by 0.8 points). • One important new finding in 2015 is that very few of the students using electronic vaporizers are using to help them quit smoking regular cigarettes; only 5%, 7%, and 10% of the users in the three grades indicate this as one of the reasons for their use. More than half say they wanted "to experiment—see what it's like" and around one-third gave the reason "because it tastes good." (Johnston 2014).
Alcala et al (Alcala 2016)	2014	Data are from the 2014 Adolescent California Health Interview Survey, which interviewed 1052 adolescents ages 12–17.	• Use of e-cigarettes was defined as having ever trying e-cigarettes.	• Overall ever use = 10.3% • E-cigarette use was higher among ever-smokers of cigarettes

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Definitions	Prevalence
Barrington-Trimis et al (Barrington-Trimis 2015)	2014	Cross-sectional survey including 2,084 11th and 12th grade students participating in the Southern California Children's Health Study during the spring of 20144.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use = 24.0% • Overall past 30 day use = 9.6% • Cigarette and e-cigarette use were correlated. • 40.5% (n = 81) of current e-cigarette users had never smoked a cigarette.
Cooper et al (Cooper 2015)	2014	Participants were 13,602 6th through 12th grade students in Texas who were part of the Texas Youth Tobacco Survey.	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Overall ever use = 25% • Past 30 day use = 14.0% • Both current and lifetime e-cigarette users were more likely than their peers to use other tobacco products, although 24.2% of current e-cigarette users had never smoked conventional cigarettes, and 7.3% had never used any other type of tobacco product besides an e-cigarette.
Leventhal et al (Leventhal 2015)	2013-2014	Longitudinal survey of a school-based cohort at baseline, at 6-month follow-up and a 12-month follow-up high school students in grades 9th and 10th. Subjects included 2,530 adolescents from the Los Angeles area.	• Lifetime and past 6-month use (yes or no) of e-cigarettes was assessed.	• Overall ever use =18.6%
Wills et al (Wills TA 2016)	2013-2014	Longitudinal school-based survey with a baseline sample of 2,338 students (9th and 10th graders, mean age 14.7 years) in Hawaii surveyed in 2013 (time 1, T1) and followed up 1 year later (time 2, T2).	• E-cigarette use was defined as past 30 day use, additionally every day prevalence was also measured.	• Overall 30 day use = 2% • Overall every day = 1%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Definitions	Prevalence
Bostean et al (Bostean 2015)	2013-2014	Cross-sectional survey of 482,179 middle and high school students.	• Use of e-cigarettes was measured by ever use and current use (past 30 days).	• Overall ever use = 24.4% • Never-smokers ever use = 13.4% • Past 30 day use = 12.9%
Porter et al (Porter 2015)	2011-2014	Data are from the annual 2011–2014 Florida Youth Tobacco Survey (FYTS), a school-based, pencil-and-paper questionnaire given to Florida middle (grades 6–8) and high school (grades 9–12) students. The FYTS is a cross-sectional, representative state sample based on a two-stage cluster probability sample design.	• Use of e-cigarettes was measured by ever use (Have you ever tried e-cigarettes?) and current use (past 30 days).	• Overall past 30-day use = 20.5% of high school and 8.5% of middle school students reported ever use of e-cigarettes.
Barnett et al (Barnett 2015)	2013	Data from the Florida Youth Tobacco Survey including students from middle and high school (grade 6-12).	• Use of e-cigarettes was measured as ever use and as current use (past 30 day use).	• Middle school students : o Overall ever use = 4.3% o Overall past 30 day use = 1.8% • Among high school students: o Overall ever use = 12.1% o Overall past 30 day use = 5.4%
Wills et al (Wills 2015)	2013	School-based survey of 1,941 high school students (mean age 14.6 years) in Hawaii.	• E-cigarette use was defined as past 30 day use (once, twice, more than three times) additionally every day prevalence was also measured.	• Overall 30 day use (once) = 7.0% • Overall 30 day (twice) = 3.0% • Overall 30 day (≥ 3 times) = 8.0% • Overall every day = 2.0%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Definitions	Prevalence
National Youth Tobacco Survey (NYTS) (Arrazola 2015, Centers for Disease 2016f)	2013	The NYTS provides nationally representative data about middle and high school youth's tobacco-related beliefs, attitudes, behaviors, exposure to pro- and anti-tobacco influences (5). The latest dataset available is the one for 2014. Data from this survey will be presented in this report.	• In 2014, current use of e-cigarettes was assessed by the question, "During the past 30 days, on how many days did you use e-cigarettes such as Blu, 21st Century Smoke, or NJOY?", and in 2011 to 2013, such use was assessed by the question, "In the past 30 days, which [tobacco products] have you used on at least 1 day?".	• Overall ever use = 13.4% • Middle school past 30 day use = 1.1% • High school past 30 day use = 4.5% (Johnston 2016)
Pentz et al (Pentz 2015)	2013	Cross-sectional study performed among 410 7th grade students from South California (median age=132.4 years).	E-cigarette use was defined as lifetime ever use.	• Overall ever use = 11.0%
Krishnan-Sarin et al (Krishnan-Sarin 2015)	2013	Cross-sectional study of male and female middle and high school students.	• "Lifetime e-cigarette users" were defined as adolescents who had tried an e-cigarette. "Never e-cigarette users" were defined as adolescents who reported that they had never tried an e-cigarette. "Current e-cigarette users" were defined as adolescents who indicated use in the past 30 days.	• Middle school students : o Overall ever use = 3.5% o Overall past 30 day use = 1.5% o Current smokers ever use= 53.8% o Ever-smokers ever use= 52.6% o Never-smokers ever use = 2.1% o Current smoker past 30 day = 38.5% o Ever-smoker past 30 day = 10.5% o Never-smoker past 30 day = 0.9% • Among high school students: o Overall ever use = 25.2% o Overall past 30 day use = 12% o Current smokers ever use = 90.0% o Ever smokers ever use = 60.1%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Definitions	Prevalence
				o Never-smokers ever use = 13.2% o Current smoker past 30 day = 64.1% o Ever-smoker past 30 day = 23.5% o Never-smoker past 30 day = 4.6%
Wills et al (Wills 2015)	2013	Cross-sectional survey of 1,941 high school students (mean age 14.6 years) from Hawaii.	• Use of e-cigarettes was measured by current use (past 30 days) and daily use.	• Overall past 30 day use = 17% • Overall daily use = 2%
Amrock et al (Amrock 2015)	2012	Cross-sectional nationally representative data from 2012 National Youth Tobacco Survey including 24,658 US adolescents in grade 6th to 12th.	• Use of e-cigarettes was measured by ever use and current use (past 30 days).	• Overall ever use = 13.2 • Past 30 day use = 4.0%.
Camenga et al (Camenga 2014b)	2010-2011	Cross-sectional study including 1,556 students from 4 high schools.	• E-cigarette use was defined as current use (past 30 day use).	• Overall past 30 day use = 2.5%. • Occasional (44.7%) or daily smoking (30.3%), 15.7% had ever tried a cigarette but were not current smokers and 9.2% were never smokers.
Camenga et al (Camenga 2014a)	2010-2011	Repeated cross-sectional survey conducted in 2 suburban high schools in Connecticut and New York. Participants were 1,345 students from grades 9-12.	• E-cigarette use was defined as current use (past 30 day use).	• Overall past 30 day use = 1.9%

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.3.1.2.2 Determinants of e-cigarette use

The literature search yielded 27 studies which assessed determinants of e-cigarette use, of which 10 included youth populations and 17 included adult populations. Details on these studies can be seen in Table 28. One interesting finding was that in studies reporting results from youth populations, increased age (close to age 18) was a determinant for e-cigarette use (Bostean 2015, Cardenas 2015, Cooper 2015, Porter 2015), while the opposite was seen in adult populations (King 2015, Pearson 2012, Pokhrel 2014, Ramo 2015b, Weaver 2016).

Determinants of e-cigarette use in adult populations

Among adults, the determinants most commonly found associated with e-cigarette use were being male (Berg 2016, Huang 2016, Ramo 2015b, Sutfin 2013) which was found to increase the probability of using e-cigarettes, in comparison to being female, which was found to be associated with use of e-cigarettes in two studies (King 2015, Zhu 2013) and five found no difference in risk by sex (Giovenco 2014, Huang 2016, Loukas 2015, Ramo 2015b, Weaver 2016). Race and ethnicity were also associated with e-cigarette use. While 4 studies showed Caucasians to be more likely to use e-cigarettes (Berg 2016, Giovenco 2014, Huang 2016, Pearson 2012), 1 study found a decreased probability of use by African-Americans (Huang 2016) and other studies found no relationship(Loukas 2015, Pulvers 2015, Ramo 2015b, Schmidt 2014, Zhu 2013). Tobacco related variables were also associated with e-cigarette use. Current cigarette smoking (Amato 2016, Berg 2016, Choi 2003, Christensen 2014, Huang 2016, King 2015, Loukas 2015, Pokhrel 2014, Ramo 2015b, Sutfin 2015, Weaver 2016) and trying to quit (Amato 2016, Choi 2014, Christensen 2014) were associated with e-cigarette use, while being a never-smoker or never having been an established smoker was associated with a decreased probability of using e-cigarettes (Choi 2003, Huang 2016). Former smokers were associated with e-cigarette use in three studies (Choi 2003, King 2015, Sutfin 2015) and was associated with a decreased probability of use in one (Huang 2016). Use of other tobacco products such as hookah or waterpipe (Berg 2016) was also associated with an increased probability of using e-cigarettes. Detailed findings on a per study basis can be found on Table 28.

Determinants of e-cigarette use in youth populations

Among youth populations, the determinants most commonly associated with e-cigarette use were related to demographic characteristics such as sex, where being male was associated with an increased probability of e-cigarette use (Barnett 2015, Barrington-Trimis 2015, Bostean 2015, Cooper 2015, Leventhal 2015, Porter 2015), although two studies found no difference in risk (Amrock 2015, Wills 2015) and age (Alcala 2016, Bostean 2015, Porter 2015). Increased probability was also seen in those who were current smokers (Alcala 2016, Barnett 2015, Barrington-Trimis 2015, Cardenas 2015, Cooper 2015), ever smokers (Amrock 2015), those who had higher socio-economic status (Alcala 2016), those from the LGBT community (Weaver 2016) and who lived in a household with tobacco use (Cardenas 2015, Porter 2015). Use of other tobacco products was associated with an increased probability of use in 3 studies (Barnett 2015, Barrington-Trimis 2015, Cooper 2015), while 1 found an opposite association (Bostean 2015). On the other hand, higher education or higher parental education were associated with a decreased probability of using e-cigarettes (Bostean 2015, Wills 2015).Finally, different studies identified different race/ethnicity

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

groups to be at a higher probability for e-cigarette use (Porter 2015) while some others found no difference in the probability of using e-cigarettes by race (Alcala 2016, Cardenas 2016). Detailed findings on a per study basis can be found in Table 28.

6.3.2.3.1.2.3 Influence on smoking initiation (gateway effect)

There were 4 studies assessing the risk of cigarette smoking initiation associated with e-cigarette use (Cardenas 2016, Leventhal 2015, Primack 2015, Wills 2016). The details of these studies can be seen in Table 29. All these studies reported an increased risk of cigarette smoking initiation in e-cigarette users. Most studies were performed using youth populations except for the study by Primack et al. (Primack 2015), which included subjects aged 16-26 years. Additionally, while three studies presented data from longitudinal studies, the study by Cardenas et al. (Cardenas 2016) was the only publication reporting data from a cross-sectional study (data from the NYTS survey from 2011-2013). All studies defined e-cigarette use as 'ever use', as well as defining smoking initiation as 'ever cigarette smoking even a few puffs'.

6.3.2.3.1.2.4 Influence on cessation

There was 1 meta-analysis retrieved that included 20 publications assessing the probability of smoking cessation in e-cigarette users (Kalkhoran 2016). In addition 2 other studies were found that had not been included in the meta-analysis (Christensen 2014, Popova 2013). Lastly 4 studies were found that evaluated the effect of e-cigarette use on smoking reduction (Berg 2014, Lechner 2015, Rass 2015, Tseng 2016). Details of these articles can be found in Table 30. The meta-analysis reported results from 15 cohort studies, 3 cross-sectional studies, and 2 clinical trials, all of which had appropriate control groups. The odds of quitting cigarettes were 28% lower in those who used e-cigarettes compared with those who did not use e-cigarettes (odds ratio [OR] 0.72, 95% CI 0·57–0·91). Association of e-cigarette use with quitting did not significantly differ among studies of all smokers using e-cigarettes (irrespective of interest in quitting cigarettes) compared with studies of only smokers interested in cigarette cessation (OR 0·63, 95% CI 0·45–0·86 vs 0·86, 0·60–1·23; p=0·94). Therefore, from this meta-analysis, although e-cigarette users were less likely to quit cigarette smoking, the likelihood of quitting was similar between populations who desired to quit or not. Other study characteristics (design, population, comparison group, control variables, time of exposure assessment, biochemical verification of abstinence, and definition of e-cigarette use) were also not associated with the overall effect size (p≥0·77 in all cases). The results were replicated in additional studies which also showed that e-cigarette use is inversely associated with smoking cessation in current smokers (or past smokers). Interestingly, dual users (cigarette smokers who used e-cigarettes) decreased their daily consumption of cigarettes in three of the studies (Berg 2014, Lechner 2015, Rass 2015, Tseng 2016), although in the fourth study "ever users" of e-cigarette were less likely to decrease cigarette consumption (OR=0.51, 95%CI: 0.30-0.87) (Al-Delaimy 2015).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 28. Determinants of e-cigarette use in adult and youth populations in the US

Author	Population & study methods	Analyses performed	Determinants	No difference
Youth populations				
Amrock et al (Amrock 2015)	Cross-sectional nationally representative data from 2012 National Youth Tobacco Survey including 24,658 US adolescents in grade 6th to 12th.	Logistic regression assessing probability of ever use.	Increase probability Ever use of other tobacco products (OR= 11.45, 95%CI:6.96, 18.8) Decreased Probability N.A. No Difference: Sex (female) (OR=1.12, 95%CI:0.74, 1.69) Perceiving e-cigarettes as less harmful (OR= 3.60, 95%CI: 0.83, 15.7) Age (All ORs not significant) Race (All ORs not significant) Family member uses tobacco (OR= 1.19, 95%CI: 0.69, 2.04)	
Alcala et al (Alcala 2016)	Data are from the 2014 Adolescent California Health Interview Survey, which interviewed 1052 adolescents ages 12–17.	Chi squared and t-tests and binary logistic regression assessing probability of ever use.	Increased probability: Ever smoking ($p<0.001$) ↑ Socio economic status ($p<0.01$) ↑Age ($p< 0.05$) Decreased probability: No US citizenship (OR= 0.21, 95%CI:0.06–0.72) No difference: Race (All ORs not significant)	
Cardenas et al (Cardenas 2015)	Data from the NYTS 2012 survey which included middle and high school students (grades 6 to 12).	Logistic regression analyses.	Increased probability: ↑ Age (adjusted prevalence ratio = 1.6, 95%CI: 1.1-2.6) Ever smoker (adjusted prevalence ratio= 2.2, 95%CI: 2.0-2.3) Living with a smoker (adjusted prevalence ratio = 3.0, 95%CI: 2.6-3.6) Decreased probability: N.A. No difference: Sex (male) (adjusted prevalence ratio= 1.1, 95%CI: 1.0-1.2) Race (All ORs not significant)	

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants	No difference
Porter et al (Porter 2015)	Cross-sectional survey (Florida Youth Tobacco Survey) including 38,972 middle and high school students.	Logistic regression analyses (values not shown)	Increased probability: ↑ Age (p<0.001) Household tobacco use (p<0.001) Household e-cigarette use (p<0.001) Caucasians (p<0.001) Sex (male) (p<0.001) Decreased probability: Being African American (p<0.001) No difference: N.A.	
Barrington-Trimis (Barrington-Trimis 2015)	Cross-sectional survey including 2,084 11th and 12th grade students participating in the Southern California Children's Health Study during the spring of 2014.	Logistic regression analyses.	Increased probability: Having ever smoked (OR= 12.4, 95%CI: 8.06–19.0) Peer use of e-cigarettes (OR= 104, 95%CI: 60.5–179) Current smoking (OR= 62.9, 95%CI: 35.6–111) Sex (male) (OR= 1.76, 95%CI: 1.29–2.39) Decreased probability: ↑ perception of harm (OR for disagreeing with e-cigarettes bad for health = 23.5, 95%CI: 15.3–36.1) No difference: Race (All ORs not significant) Family income (OR= 0.72, 95%CI: 0.41–1.25) Parental education (OR= 1.62, 95%CI: 0.77–3.42)	
Cooper et al (Cooper 2015)	Participants were 13,602 students who were in 6th to 12th grade in Texas and were part of the Texas Youth Tobacco Survey.	Logistic regression analyses (values not shown)	Increased probability: Other tobacco use (p<0.001) Current cigarette smoking (p<0.001) Sex (male) (p<0.001) Being Caucasian (p<0.001) ↑ age (p<0.001) Decreased probability: N.A. No difference: N.A.	

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants No difference
Barnett et al (Barnett 2015)	Data from the Florida Youth Tobacco Survey including students from middle (6,640) and high school (6,175) (grade 6-12)	Logistic regression analyses	Increased probability: Sex (male) (in high school) (OR= 1.5, 95%CI: 1.3, 1.8) Current smoking (middle school OR= 35.6, 95%CI: 22.3, 56.9 and high school= 23.4, 95%CI: 17.6, 31.0) Hookah use (in high school) (OR= 21.7, 95%CI: 16.2, 29.2) Decreased probability: N.A. No difference: Sex (among middle school students) (OR= 1.1, 95%CI: 0.9, 1.5)
Leventhal et al (Leventhal 2015)	Longitudinal survey of a school-based cohort at baseline, at 6-month follow-up and at 12-month follow-up high school students in grades 9^{th} and 10^{th}.	Chi squared and t-tests.	Increased probability: Being Native Hawaiian/Pacific Islander (P=0.02) ↑ Parental education (p=0.03) Sex (male) (p<0.001) Not living with both parents (p<0.001) Delinquent behavior (p<0.001) Substance abuse (p<0.001) ↑ Impulsivity (p<0.001) Decreased probability: N.A. No difference: Depression (p=0.07)
Wills et al (Wills 2015)	School-based survey of 1,941 high school students (mean age 14.6 years) in Hawaii.	Chi squared and ANOVA tests.	Increased probability: Being Native Hawaiians or Asian (p<0.05) Decreased probability: ↑ Parental Education (P<0.01) No difference: Sex (p=0.05) Age (p=0.05)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants	No difference
Bostean et al (Bostean 2015)	Cross-sectional survey of 482,179 middle and high school students.	Logistic regression analyses (not all values shown)	Increased probability: Never having used tobacco (not sbown) ↑ Age (not shown) Being Hispanic (OR= 1.60, 95%CI: 1.53-1.67) Decreased probability: Sex (female) (OR= 0.97, 95%CI: 0.95-0.99) ↑ Parental education (not shown)	No difference: N.A.
Adults				
Weaver et al (Weaver 2016)	Data obtained from the Tobacco Products and Probability Perceptions Survey of a probability sample of 5,717 US adults aged ≥ 18 years.	Associations among variables were tested using weighted logistic regression models and Rao–Scott v2 tests (values not shown).	Increased probability: ↑ Age (p<0.001) ↑ Education (p<0.001) Being LGBT (p<0.001) Current smoker (p<0.001) Decreased probability: ↑ Household income (p<0.001) ↓Perceived health status (p<0.001)	No difference: Children at home (p=0.08) Race (p=0.62) Sex (male) (p=0.20)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants	No difference
Huang et al (Huang 2016)	Nationally representative online survey of 17,522 US adults in 2013	Logistic regression analyses for current and ever use.	Increased probability: Current smoker (reference category) Decreased probability: Never-smoker (OR= 0.02, 95%CI: 0.01-0.03) Being former smoker (OR= 0.09, 95%CI: 0.06-0.13) Age 45-64 (OR= 0.41, 95%CI: 0.30-0.55) Age above 65 years (OR= 0.26, 95%CI: 0.18-0.39) African American (OR=0.62, 95%CI: 0.48-0.81) for ever use ↑ Education (OR= 0.55, 95%CI 0.34-0.90) ↑ Income (OR= 1.67, 95%CI: 1.06-2.63)	No difference: Sexual orientation (OR= 1.27, 95%CI: 0.94-1.70) Sex (male) (OR= 1.16, 95%CI: 0.96-1.39)
Piñeiro et al (Pineiro 2016)	Online cross-sectional survey including 1,815 participants aged ≥ 18 years	Chi squared and t-tests.	Increased probability: N.A. Decreased probability: N.A.	No difference: Sex (male) (p=0.87)
Ramo et al (Ramo 2015b)	Cross-sectional survey of young adults aged 18-25 who had smoked at least 1 cigarette in the last 30 days.	Logistic regression analyses	Increased probability: Cigarette smoking (Study 1 and 2) (OR= 1.85, 95%CI: 1.19, 2.88) Sex (male) (Study 1 and 2) (OR= 2.07, 95%CI: 1.34, 3.18) Past quit attempt (Study 1 for current use and 2, 3 for ever use) (OR= 1.54, 95%CI: 1.03-2.30) Decreased probability: ↑ Age (Study 2) (OR= 0.88,95%CI: 0.78, 0.99)	No difference: Education (All Studies) (OR= 1.06, 95%CI: 0.98, 1.14) Race (All studies) (OR= 1.17, 95%CI: 0.78, 1.78)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants	No difference
Berg (Berg 2016)	Online cross-sectional survey including 1,567 participants aged 18-34. Subjects were recruited through subject in 2014.	Chi squared and ANOVA tests.	Increased probability: ↑ Age (p<0.001) Caucasian (p=0.014) Substance abuse (p<0.001) Current smoker (p<0.001) Current Hookah use (p<0.001) Sex (male) (p=0.013) Education (p<0.001) Decreased probability: N.A. No difference: N.A.	
King et al (King 2015)	Cross-sectional web-based study carried out annually of US adults aged ≥ 18 years.	Logistic regression analyses.	Increased probability: Current smoker (OR= 54.7, 95%CI: 23.5–127.5) Former smoker (OR= 6.4, 95%CI: 2.5–16.4) Sex (female) (OR= 1.8, 95%CI: 1.1–2.8) Decreased probability: N.A. No difference: Age (All ORs not significant) Education (OR= 0.8, 95%CI: 0.4-1.7) Income (OR= 1.6, 95%CI: 0.7-3.4)	
Amato et al (Amato 2016)	Data from the Minnesota Adult Tobacco Survey which included 9,304 participants aged ≥ 18 years.	Unknown	Increased probability: Current smoker (not shown) Trying to quit (not shown) Belief they are less harmful than cigarettes (not shown) Decreased probability: N.A. No difference: N.A.	

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants No difference
Loukas et al (Loukas 2015)	Cross-sectional survey including 765 students from 7 Texas universities, the students were aged 18-35 years.	Logistic regression analyses	Increased probability: Current smoker (OR= 8.45, 95%CI: 4.28-16.70) Decreased probability: N.A. No difference: Sex (male) (OR= 1.27, 95%CI: 0.66-2.44) Age (OR= 0.74, 95%CI: 0.34-1.58) Race (other) (OR= 0.47, 95%CI: 0.16-1.41)
Zhu et al (Zhu 2013)	Cross-sectional survey with a national probability sample of 10,041 participants aged ≥ 18 years	Unknown	Increased probability: Sex (female) (not shown) Current smoker (not shown) Decreased probability: ↑ Education (not shown) No difference: Age (not shown) Race (not shown)
Pulvers et al (Pulvers 2015)	Cross-sectional survey of 2,376 participants aged 25 or older	Bivariate logistic regression analyses.	Increased probability: ↑ Education (OR= 3.43, 95%CI: 1.16-10.09) Nicotine dependence (OR= 1.45, 95%CI: 1.09-1.94) Using other types of tobacco (OR= 2.06, 95%CI: 1.54-2.77) Decreased probability: N.A. No difference: Sex (female) (OR= 1.09, 95%CI: 0.83-1.45) Race (African-American) (OR= 0.76, 95%CI: 0.53-1.10) Income (OR= 1.18, 95%CI: 0.88-1.60)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants	No difference
Christensen et al (Christensen 2014)	Cross-sectional survey of 9,656 adults aged ≥ 18 years participating in the Kansas Adult Tobacco Survey.	Logistic regression analyses.	Increase probability: Current smoker (not shown) Making quit attempt last month (not shown) Decreased probability: Recent cigarette abstinence (OR= 0.21, 95%CI: 0.11–0.38) No difference: N.A.	
Choi et al (Choi 2014)	Cohort study including 1,379 young adults aged 18-24 years from the Minnesota Adolescent Community Cohort.	Logistic regression analyses	Increased probability: Belief in help to quit (OR= 1.98, 95%CI: 1.29-3.04 ↓ Perception of harm (OR= 2.34, 95%CI: 1.49-3.69) Decreased probability: N.A. No difference: Belief e-cigarettes are less addictive (OR= 1.16, 95%CI: 0.73-1.85)	
Schmidt et al (Schmidt 2014)	Participants were part of the Montana Adult Tobacco Survey that included 3,311 subjects aged ≥ 18 years.		Increased probability: Age 18-35 (not shown) Current smoker (not shown) Trying something new (not shown) Belief in help to quit (not shown) Decreased probability: N.A. No difference: Sex (not shown) Race (not shown)	

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants No difference
Giovenco et al (Giovenco 2014)	A web-based survey including a random sample of current and former cigarette smokers who completed the survey in June 2013 (n=2,136). Participant were adults aged ≥ 18 years.	Logistic regression analyses for "ever" and current e-cigarette use	Increased probability: Caucasian (ever use) (OR= 1.42, 95%CI 1.04-1.93) Ages 18-29 years (ever use) (OR= 2.32, 95%CI: 1.49-3.63) Ages 30-44 years (ever use)(OR= 1.42, 95%CI: 1.01-2.01) Decreased probability: Former smoker (ever use) (OR= 0.55, 95%CI: 0.32-0.94) Some-day smoking (ever use) (OR= 0.70, 95%CI: 0.51-0.94) No difference: Sex (OR= 1.15, 95%CI 0.89-1.49)
Pokhrel et al (Pokhrel 2014)	Cross-sectional survey collected from 307 multiethnic 4- and 2-year college students (mean age=23.5)	Logistic regression analyses	Increased probability: ↓ Age (OR= 0.91, 95%CI: 0.86-0.96) Current smokers (OR= 14.2, 95%CI: 6.98-28.7) Decreased probability: N.A. No difference: N.A.
Sutfin et al (Sutfin 2013)	Cross-sectional survey including 4,444 students from 8 colleges in North Carolina. The survey was administered through the web.	Logistic regression analyses	Increased probability: Sex (male) (OR= 1.54, 95%CI: 1.14-2.08) Greek affiliation (OR:1.64 95%CI: 1.12-2.39) Hispanic (OR= 2.02, 95%CI: 1.03-3.98) Other race (OR= 2.06, 95%CI: 1.12-3.77) Current daily smoker (OR=5.61, 95%CI: 2.70-11.6) Former smoker (OR= 5.66, 95%CI: 3.37-9.51) Decreased probability: N.A. No difference: Age (OR= 0.98, 95%CI: 0.92-1.04)) Sensation seeking (OR= 1.19, 95%CI: 0.93-1.51) Ever hookah use (OR= 1.13, 95%CI: 0.79-1.61)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 29. Studies evaluating the probability of initiation of cigarette smoking in e-cigarette users

Study	Period	Study characteristics	Probability of cigarette smoking	Comments
Cardenas et al (Cardenas 2016)		Data from the NYTS survey 2011-2013 including youth aged 11-18 years.	Probability of trying cigarette smoking in ever users of e-cigarettes OR = 2.3 (95%CI: 1.9-2.7), the effect was particularly stronger in those aged 11-13 years (OR = 4.1, 95%CI: 2.6-6.4) compared to those aged 16-18 years (OR = 1.4, 95%CI: 1.1-1.8).	Definition of e-cigarette exposure was ever use, definition of outcome cigarette smoking was defined as ever use.
Primack et al (Primack 2015)	2012-2014	Cohort study of 694 subjects aged 16-26 who were never-smokers who were followed-up for a year	Probability of progression to smoking in e-cigarette users OR = 8.3 (95%CI: 1.2-58.6)	Definition of e-cigarette exposure was ever use, definition of outcome cigarette smoking was defined as ever use
Leventhal et al (Leventhal 2015)	2013-2014	Cohort of 2,530 14 year old students never-smokers who were followed-up for 6 and 12 months.	Probability of smoking after 6-12 months in e-cigarette users OR = 2.73 (95%CI: 2.00-3.73)	Definition of e-cigarette exposure was ever use, definition of outcome cigarette smoking was defined as ever use
Wills et al (Wills 2016)	2013-2014	Cohort study of 2,338 students from 9th to 10th grade (mean age = 14.7 years). Subjects were never smokers who had used e-cigarettes at baseline.	Probability of ever smoking in ever e-cigarette users compared to non-e-cigarette users OR = 2.87 (95%CI: 2.03-4.05)	Definition of e-cigarette exposure was ever use, definition of outcome cigarette smoking was defined as ever use

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.3.1.3 Discussion

The studies retrieved show that the prevalence of e-cigarette use varies widely depending on the age of the populations analyzed as well as the definition of e-cigarette use. The prevalence of e-cigarette use (regardless of the definition used) has increased in the past 4 years, although this increase might be slowing in certain youth age groups (Johnston 2016). This increase in use has been accompanied by a continuous decrease in the prevalence of cigarette smoking. The decrease in cigarette smoking prevalence started well before the introduction of e-cigarettes in the market (Jamal 2015), it would appear that this decrease has not been affected by the introduction of e-cigarettes in the US market among any age group, as shown by the NSDUH results (Table 4) (Hedden S 2015). Nevertheless, the MTF study presents evidence suggesting that e-cigarette use may be overtaking conventional cigarettes in popularity, a trend seen since 2014. The determinants for e-cigarette use were shown to vary by age groups, and the majority of determinants are related to demographic characteristics.

Electronic cigarettes (e-cigarettes) use a battery to power a heating element that aerosolizes a liquid containing solvents, flavorings and can also contain nicotine (Breland 2016). As e-cigarettes are becoming increasingly popular, questions have been raised as to whether they are safer than traditional tobacco products (Paek 2014). While promoters of their use see e-cigarettes as an opportunity for harm reduction, as they have been shown to contain lower amounts of toxicants compared to cigarette smoke, their opponents are concerned that their use may lead to increased cigarette smoking (Friedman 2015). The 'gateway hypothesis', frequently discussed with respect to drug use, suggests that the use of less deleterious drugs can lead to a future risk of using more dangerous hard drugs or crime (Lee 2015). The term 'gateway hypothesis' was first used in an article published by Kandel in 1975 (Kandel 1975) which qualitatively assessed whether the consumption of illegal drugs had been preceded by tobacco smoking (Schneider 2015). As a consequence, an assessment of whether or not e-cigarette use can lead to initiation of cigarette smoking is extremely important in assessing potential harm reduction of e-cigarettes (Lee 2015).

In order to appropriately ascertain an effect of e-cigarette use on initiation of cigarette smoking, consideration of an appropriate study design has to be taken into account. Either a cross-sectional study, in which data on time of starting use of both e-cigarettes and cigarettes (at some defined level) are obtained, or a prospective cohort study design, in which information is obtained at multiple time points on the use of e-cigarettes and cigarettes, could be used (Lee 2015).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 30. Studies evaluating the probability of cigarette smoking cessation in e-cigarette users

Study	Period	Study characteristics	Probability of quitting in e-cigarette users	Comments
Christensen et al (Christensen 2014)	2012-2013	Phone-based cross-sectional study of non-institutionalized Kansas adults.	**Past year abstinence**: OR = 0.10 (95%CI 0.10-0.22)	Similar results were found for past month abstinence.
Al-Delaimy et al (Al-Delaimy 2015)	2011-2012	Longitudinal survey of 1,000 smokers living in California aged 18-59 years.	OR = 0.41 (95%CI: 0.18-0.93)	
Popova et al (Popova 2013)	2009-2011	Nationally representative probability-based survey of 1,836 adult smokers.	OR= 1.09 (95%CI: 0.72-1.65)	
Kalkhoran et al (Kalkhoran 2016)	2015	Meta-analysis of 20 studies assessing the probability of quitting in e-cigarette users versus a control group	OR = 0.72 (95%CI: 0.57-0.91)	Results did not vary by inclusion of studies which included interested in quitting smokers.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Additionally, the terminology of exposure (e-cigarette use) and outcome (cigarette smoking initiation) have to be well defined. Of the studies found assessing the risk of smoking initiation in e-cigarette users, three were longitudinal with a follow-up time of 6-12 months (Leventhal 2015, Primack 2015, Wills 2016) while 1 was a cross-sectional study with a very large sample size (Cardenas 2016). This cross-sectional study was missing important information on confounders, a point acknowledged by the authors, and it used a questionnaire which had not been designed to identify the sequence of use of different tobacco products, limiting causal inference (Cardenas 2016). What is more, all studies found in this literature search assessing the probability of smoking initiation in e-cigarette users, defined e-cigarette use as ever use (or any use) and smoking initiation as ever smoking or any smoking (even a few puffs). Given the fact that not all ever users or ever smokers continue to either use e-cigarettes or smoke cigarettes (Cardenas 2016, Kessler 1995, Reidpath 2014), this does not give a clear picture of the role of e-cigarettes as precursors of cigarette smoking. Also, these studies did not take into account the possibility that e-cigarette users could be a separate population more likely to initiate cigarette smoking (Cardenas 2016), which needs to be considered, as well as a number of other variables, especially those evaluating attitudes to experimentation in general, as well as those associated with certain behaviors like alcohol use, drug use etc. (Friedman 2015, Lee 2015). Supporting this theory, the study by Friedman et al. (Friedman 2015) found that banning e-cigarettes sales to minors (as is currently done in certain states in the US) yielded a statistically significant 0.9 percentage point increase in the recent smoking rate among 12-17 year olds, relative to states without such bans, which was consistent with e-cigarettes reducing smoking among minors as well as with the hypothesis that those who experiment with e-cigarettes might be at a higher risk for cigarette smoking before they start e-cigarette use. Finally, there seems to be a clear reverse-association between e-cigarette use and cigarette smoking as most surveys show that the prevalence of use of e-cigarettes is much more common in current smokers than in never-smokers. Considering the information presented above, there is little evidence of a gateway effect for e-cigarettes with respect to cigarette smoking.

If one is to consider the harm reduction potential of e-cigarettes, one must consider their pros and cons. Among the pros, the importance of e-cigarettes as harm reduction agent lies in the fact that they seem to have a safer profile than cigarettes (Breland 2014, Farsalinos 2014a), the environmental exposure to volatile organic compounds is significantly lower than levels after cigarette smoking (Breland 2014) and that they have been shown to at least reduce the number of cigarettes smoked per day (Berg 2014, Lechner 2015, Rass 2015, Tseng 2016). This last point is an important factor to take into account, given that smoking cessation protocols fail in about 90% of smokers who use them as directed and the majority of e-cigarette users are current smokers who use them to cut down or quit cigarette smoking (Nitzkin 2014), although the latter goal does not appear to be particularly successful.

An important factor to take into account when analysing the overall effect of a potential modified risk tobacco product is its potential acceptability in current smokers. E-cigarettes are used by youth because of their novelty (Schmidt 2014) as well as because of the perception of reduced harm in comparison to cigarettes (Amato 2016, Barrington-Trimis 2015, Choi 2014). However, a number of cigarette smokers continue to smoke after starting to use e-cigarettes, and a major reason is that they find them less satisfying (Harrell 2015) and in general do not taste as good as their usual product (Harrell 2015).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

The fact that the yield of nicotine, particularly in earlier models, is not comparable to the yield from cigarette smoking (Bhatnagar 2014, Breland 2014) resulting in a lower blood level of nicotine could be also a deterrent for adoption by current smokers looking for a less harmful alternative. One of the few studies assessing the absorption of nicotine from e-cigarettes, by Williams et al. (Williams 2013), reported that absorption of nicotine from e-cigarettes was lower than from tobacco cigarettes. This is true for even the new generation cartomizers, suggesting that most absorption from the devices occurs in the buccal mucosa or upper airways (Bhatnagar 2014). Compared to smoking 1 cigarette, the e-cigarettes and liquids used delivered one-third to one-fourth the amount of nicotine after 5 minutes of use (as measured in blood samples after 5 minutes of use [taking 10 puffs]) (Farsalinos 2014b). Newer or third generation models seems to improve the nicotine yield, although the downside of these is their substantial size and weight (Bhatnagar 2014, Rass 2015). It is interesting to note, that e-cigarettes are more accepted than smokeless tobacco as harm reduction products (Berg 2015), probably due to e-cigarettes having a ritual and experience more similar to cigarette smoking than smokeless tobacco products do.

In order to appropriately evaluate the harm reduction of e-cigarettes, information is still needed (Walton 2015). For instance, it is most difficult to elucidate the true toxicological profiles of e-cigarettes, since there are more than 400 brands and 7000 unique flavors (Bhatnagar 2014). It would be impossible to come up with one safety/risk profile to characterize all of these. The use of specific flavorings could affect the toxic potential of e-cigarettes (Barrington-Trimis 2014). For example, one potentially dangerous flavoring is diacetyl, which has been shown to cause acute-onset bronchiolitis obliterans, a severe and irreversible obstructive lung disease, when inhaled by workers exposed to particulate aerosolized flavorings containing this substance. Furthermore, publications have shown that as the use of e-cigarettes becomes more common, there has been an increase of poison center calls related to e-cigarette use, mainly for young children where ingestion (misuse) of the e-cigarette liquid is reported (Ordonez 2015, Vakkalanka 2014). Besides the toxicological profiles, more research needs to be done on biomarkers of exposure and physiological effects on tissues and organ systems, particularly the pulmonary and cardiovascular systems, following the use of e-cigarettes, (Walton 2015) as well as information on users' profiles and how devices are used (Walton 2015) in order to give a complete picture of the harm reduction potential of these devices.

6.3.2.3.1.4 Conclusions

The prevalence of e-cigarette use has increased substantially since they were first introduced into the US market. However this growth appears to be stabilizing in certain age groups, particularly older adolescents. To date, there is little evidence of a gateway effect of e-cigarettes with respect to smoking initiation. On the other hand e-cigarettes have not been proven to promote smoking cessation, although most studies reported a reduction in cigarettes smoked per day.

The data retrieved through this review are in line with the latest recommendations of the Royal College of Physicians and Public Health England (Physicians 2014), which suggested that electronic cigarettes are devices that can provide an effective, affordable and readily available retail alternative to conventional cigarettes. Moreover, on the basis of available evidence, it seems that e-cigarette use could lead to a significant decrease in

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

cigarette-associated mortality and morbidity and help to reduce the social inequalities in health that tobacco smoking currently exacerbates.

6.3.2.3.2 Smokeless tobacco

6.3.2.3.2.1 Definitions

According to the CDC (Prevention 2016) there are four different types of smokeless tobacco: 1) chew or chewing tobacco, which comes in the form of loose leaf, plug or twist/roll; 2) snuff, which is finely ground tobacco than can be dry or moist; 3) (US) snus, which is moist snuff packaged in ready-to-use pouches that resemble small tea bags; and 4) dissolvables, which are finely ground tobacco pressed into shapes such as tablets, sticks or strips.

6.3.2.3.2.2 Search strategies

The search for articles on smokeless tobacco was performed on March 12, 2016, and resulted in 1496 articles identified using the following query: (snus[All Fields] OR ("tobacco, smokeless"[MeSH Terms] OR ("tobacco"[All Fields] AND "smokeless"[All Fields]) OR "smokeless tobacco"[All Fields] OR "snuff"[All Fields]) OR ("tobacco, smokeless"[MeSH Terms] OR ("tobacco"[All Fields] AND "smokeless"[All Fields]) OR "smokeless tobacco"[All Fields] OR ("smokeless"[All Fields] AND "tobacco"[All Fields]))) AND ("united states"[MeSH Terms] OR ("united"[All Fields] AND "states"[All Fields]) OR "united states"[All Fields]). The review of the titles and abstracts resulted in 285 articles being extracted and fully reviewed. The relevant articles are discussed in this section.

6.3.2.3.2.3 Results

6.3.2.3.2.3.1 Prevalence of use in adult populations

There were 15 studies assessing the prevalence of smokeless tobacco (any smokeless tobacco, snus, snuff, chew, dip or dissolvable tobacco) (Agaku 2014b, Biener 2011, Cabrera-Nguyen 2016, Choi 2013a, Fu 2014a, Hedden S 2015, Kaufman 2014, Latimer 2014, Mazurek 2014, Mumford 2006, Nguyen 2015, Regan 2012, Spangler 2014, Weaver 2016, Zhu 2013) (Table 31).

There were 3 studies that assessed the prevalence of use of chew (Fu 2014a, Latimer 2014, Weaver 2016). The prevalence of chew ever use ranged from 2.5% (Fu 2014a) to 17.9% (Weaver 2016), while past 30-day use ranged from 2.1% (Weaver 2016) to 2.8% (Latimer 2014).

The prevalence of use of snus was evaluated in 6 studies. The prevalence of snus ever use ranged from 3.1% (Zhu 2013) to 14.5% (Choi 2013a), while past 30-day snus use ranged from 0.3% (Weaver 2016) to 4.1% (Regan 2012). Furthermore, the prevalence of current (every day or some days use) snus use was 0.6% (Zhu 2013). The prevalence of ever use of snus among current smokers was 17.3% (Zhu 2013) and the prevalence of current use in the same group was 3.2% (Zhu 2013). Additionally, there was only 1 study assessing snuff ever use which was 2.2% (Fu 2014a).

There were 3 publications assessing the prevalence of dissolvable tobacco use in adult populations (Fu 2014a, Regan 2012, Weaver 2016). The prevalence of ever use ranged from 1.1% (Weaver 2016) to 3.5% (Regan 2012), while the past 30-day use ranged from 0% (Weaver 2016) to 0.4% (Regan 2012).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Finally there were 7 studies reporting the prevalence of smokeless tobacco use in general. The prevalence of smokeless tobacco ever use ranged from 1.5% (Mumford 2006) to 3.0% (Mazurek 2014) . Both cited studies reported that the prevalence of ever used had decreased in recent years. The past 30-day use was reported by 2 studies (Hedden S 2015, Spangler 2014), and it ranged from 3.0% (Hedden S 2015, Spangler 2014) and 5.6% in those aged 18-25 years (Hedden S 2015). Additionally, the prevalence of current use (every day or some days) ranged from 0.3% in women to 4.8% in men (Agaku 2014b). These authors reported that current use was more common in the 18-24 year old group (4.4%) and decreased as age increased. Finally, the study by Nguyen et al. (Nguyen 2015) reported the prevalence of current use of smokeless tobacco by state, and they reported current use prevalence from 1.4% to 9.8% in 2011 and between 1.5% to 9.4% in 2003.

6.3.2.3.2.3.2 Prevalence of use in youth populations

There were 7 studies assessing the prevalence of smokeless tobacco (any smokeless tobacco, snus, snuff, chew, dip or dissolvable tobacco) in youth populations (Arrazola 2015, Camenga 2014b, Cooper 2015, Elfassy 2015, Hedden S 2015, Johnston 2016, Loukas 2012). The use of smokeless tobacco was shown to be more common among e-cigarette users than non-users (15.7%-25% vs. 0.9%-1.6%), it was mainly a male habit (Johnston 2016) and while its use has decreased across the US (Hedden S 2015) it has increased in the New York City area (Elfassy 2015).

There were 3 studies reporting the prevalence of use of snus. The prevalence of ever use was 1.3% in middle school students (Arrazola 2015) to 6.2% in high school students. Additionally 2 studies reported results from populations from the 6th to the 12th grade. The prevalence of ever use ranged from 7.1% to 8.9%.In middle school students the prevalence of past 30-day use ranged from 0.4% (overall) (Arrazola 2015) to 1.9% (among those in 8th grade) (Johnston 2016), while in high school students it ranged from 1.8% (overall) (Arrazola 2015) to 5.8% in those in 12th grade (Johnston 2016).

The prevalence of use of dissolvable tobacco was reported by 2 studies. The prevalence of ever use in middle school was 0.5% (Arrazola 2015) , there were no data from high school students. The prevalence of past 30-day use ranged from 0% (Arrazola 2015) in middle school to 0.9% among those in 8th grade (Johnston 2016), while in high school students the past 30-day use prevalence ranged from 1.1% in those in 10th grade to 1.4% in those in 12th grade (Johnston 2016).

The prevalence of use of chew was assessed in 3 studies (Arrazola 2015, Camenga 2014b, Cooper 2015). The prevalence of ever use was 3.6% in middle school students (Arrazola 2015), 13.4% in high school students according to the NYTS (Arrazola 2015) and 14.4% in students from 6th to 12th grade in Texas . The past 30-day use of chew was 1.4% in middle school (Arrazola 2015) it ranged from 3.0% to 5.7% in high school students (Arrazola 2015, Camenga 2014b) while the study by Cooper et al (Cooper 2015) in Texas students reported a prevalence of past 30-day use of 8.6%.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 31. Characteristics of studies assessing the prevalence of smokeless tobacco use in adult populations

Survey	Period	Study characteristics	Definitions	Prevalence
Weaver et al (Weaver 2016)	2014	Data obtained from the Tobacco Products and Probability Perceptions Survey of a probability sample of 5,717 US adults aged ≥ 18 years.	• Chew, snus and dissolvables use was measured as ever use and currently using (every day or some days).	• Overall chew ever use = 17.9% • Chew past 30 day use = 2.1 % • Overall snus ever use = 4.0% • Snus past 30 day use = 0.3 % • Overall dissolvables ever use = 1.1% • Dissolvables past 30 day use = N.A.
NSDUH (Hedden S 2015)	2014	NSDUH is a face-to-face household interview survey of those aged ≥ 12 years. In 2014, screening was completed at 127,605 addresses, and 67,901 completed interviews were obtained, including 17,046 interviews from adolescents aged 12 to 17 and 50,855 interviews from adults aged 18 or older. In this section we will cover the results for adults.	• Smokeless tobacco use prevalence was measured as past 30 day use.	• Past 30 day prevalence 18-25 year olds = 5.6% • Past 30 day prevalence 26 and older = 3.0%
Kaufman et al (Kaufman 2014)	2013	Cross-sectional study using a web panel representative of the US population including 2,067 adults aged ≥ 18 years.	• Snus prevalence was measured as ever use	• Snus ever use = 5.2%
Cabrera-Nguyen et al (Cabrera-Nguyen 2016)	2013	Cross-sectional study using a nationally representative sample of 17,522 US adults aged ≥ 18 years.	• Dissolvable tobacco product prevalence was defined as ever use	• Dissolvable ever use = 1.6%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
NATS (Agaku 2014b)	2012-2013	The NATS was created to assess the prevalence of tobacco use, as well as the factors promoting and impeding tobacco use among adults. The 2012-2013 NATS included 60,192 non-institutionalized adults aged ≥ 18 years.	• The threshold for ever use varied by product, for instance: chewing tobacco/snuff/dip (≥20 times), snus (≥1 time), and dissolvable tobacco products (≥1 time). Then those who reported using the product every day or some days were considered current users. Because of limited sample size, all smokeless tobacco products were aggregated into a single category.	• Overall current use = 2.6% • Men = 4.8% • Women = 0.3% • 18-24 year olds = 4.4% • 25-44 year olds = 3.1% • 45-64 year olds = 2.1% • ≥ 65 years old = 1.0%
BRFSS (Nguyen 2015)	2011-2013	The Behavioral Probability Factor Surveillance System (BRFSS) is the nation's premier system of health-related telephone surveys in US adults aged ≥ 18 years.	• Smokeless tobacco use prevalence was measured as using smokeless tobacco some days of every day.	• Current smokeless tobacco use ranged from 1.4% (California and Rhode Island) to 9.8% (Wyoming) in 2011 and from 1.5% (District of Columbia and Massachusetts) to 9.4% (West Virginia) in 2013. Increases were observed in four states: Louisiana (26.7%), Montana (12.7%), South Carolina (22.2%), and West Virginia (25.3%), while declines were observed in smokeless tobacco use in two states: Ohio (-16.0%) and Tennessee (-25.0%).
Zhu et al (Zhu 2013)	2012	Cross-sectional study with a national probability sample of 10,041 participants aged ≥18 years.	• Use of snus was measured as ever use and as current use (some days or every day users).	• Overall snus ever use = 3.1% • Overall current snus use = 0.6% • Current smokers ever use = 17.3% • Current smokers current snus use = 3.2%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
Latimer et al (Latimer 2014)	2011	Online cross-sectional study including 5,028 students attending 7 public universities. Students were aged 18-24.	• Chew and snus use was defined as current use (past 30 day use).	• Chew past 30 day prevalence of use = 2.8% • Snus past 30 day prevalence of use = 1.2%
Choi et al (Choi 2013a)	2010-2011	Cross-sectional data including 2,607 young adults aged 20-28 years who participated in the Minnesota Adolescent Community Cohort Study.	• Snus use was defined as ever use and current use (past 30 day use)	• Snus ever use = 14.5% • Snus past 30 day use = 3.2%
Spangler et al (Spangler 2014)	2010	Cross-sectional study of 10,520 first year college students aged ≥ 18 years.	• Smokeless tobacco use was defined as current use (past 30 day use).	• Smokeless tobacco past 30 day use = 3.0%3
NHIS (Mazurek 2014)	2005-2010	Cross-sectional study using a nationally representative, in-person survey of the noninstitutionalized US civilian population. In 2005 and 2010, data on cigarette smoking were collected from 31,428 and 27,157 persons, respectively age ≥ 18 years.	• Current smokeless tobacco users were defined as respondents who reported having used chewing tobacco or snuff ≥20 times in their lifetime and who reported currently using chewing tobacco or snuff every day or some days.	• Smokeless tobacco current use was 2.7% in 2005 and 3.0% in 2010, the difference was not statistically significant.
Regan et al (Regan 2012)	2009	Cross-sectional mail-in study including 10,587 adults aged ≥ 18 years.	• Snus and dissolvable use was defined as ever use and current use (past 30 day use).	• Snus ever use = 12.6% • Snus past 30 day use = 4.1% • Dissolvable ever use = 3.5% • Dissolvable past 30 day use = 0.4%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Survey	Period	Study characteristics	Definitions	Prevalence
Biener et al (Biener 2011)	2008	Cross-sectional study including 4,067 adult smokers aged 18-49 years.	• Snus use was defined as ever use	• Snus ever use = 10.4%
Fu et al (Fu 2014a)	2001-2002	Cross-sectional study derived from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) including 43,093 adults aged ≥ 18 years.	• Snuff and chewing tobacco use was defined as ever use	• Snuff ever use = 2.2% • Chewing tobacco ever use = 2.5% • Dual ever use = 2.8%
Mumford et al (Mumford 2006)	1992-2002	Cross-sectional study data from the CPS-TUS including adults aged ≥ 18 years.	• Smokeless tobacco use was defined as ever use	• Ever use of smokeless tobacco has decreased from 1992 at 2.3% to 1.5% in 2002.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 32. Characteristics of studies assessing the prevalence of smokeless tobacco use in youth populations

Study	Period	Study characteristics	Definitions	Prevalence
Monitoring the Future (MTF) (Johnston 2016)	2014-2015	The MTF s an ongoing study of the behaviors, attitudes, and values of American secondary school students, college students, and young adults. Each year, a total of approximately 50,000 8th, 10th and 12th grade students are surveyed (12th graders since 1975, and 8th and 10th graders since 1991) (7).	• Current use was defined as 30-day prevalence of e-cigarette.	• Prevalence of Snus use: o 8th Grade past 30 day use = 1.9% o 10th Grade past 30 day use = 4.0% o 12th Grade past 30 day use = 5.8% • Prevalence of dissolvables use: o 8th Grade past 30 day use = 0.9% o 10th Grade past 30 day use = 1.1% o 12th Grade past 30 day use = 1.4% • Smokeless tobacco use among American young people is almost exclusively a male behavior.
Cooper et al (Cooper 2015)	2014	Participants were 13,602 6th through 12th grade students in Texas who were part of the Texas Youth Tobacco Survey.	• Chew and Snus were included • Use of smokeless tobacco in the forms of chew or snus was measured as ever use and as current use (past 30 day use).	• Overall Chew ever use = 14.4% • Overall Snus ever use = 8.9% • Chew past 30 day use = 8.6% • Snus past 30 day use = 5.17% • Chew and snus use were more common among ever users of e-cigarettes (25.1% and 15.7%) than non-users (1.6%, 0.9%).
NSDUH (Hedden S 2015)	2014	NSDUH is a face-to-face household interview survey of those aged ≥ 12 years. In 2014, screening was completed at 127,605 addresses, and 67,901 completed interviews were obtained, including 17,046 interviews from adolescents aged 12 to 17 and 50,855 interviews from adults aged 18 or older. In this section we will cover the results for adolescents aged 12-17 years.	• Smokeless tobacco use prevalence was measured as past 30 day use.	• Smokeless past 30 day use = 2.0% • The estimate for current smokeless tobacco use among adolescents in 2014 was lower than the estimates in most years from 2006 to 2010, but it was similar to the estimates in 2002 to 2005 and in 2011 to 2013.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Study	Period	Study characteristics	Definitions	Prevalence
National Youth Tobacco Survey (NYTS) (Arrazola 2015)	2013	The NYTS provides nationally representative data about middle and high school youth's tobacco-related beliefs, attitudes, behaviors, exposure to pro- and anti-tobacco influences (5). The latest dataset available is the one for 2014. Data from this survey will be presented in this report.	• In 2014, current use of e-cigarettes was assessed by the question, "During the past 30 days, on how many days did you use e-cigarettes such as Blu, 21st Century Smoke, or NJOY?", and in 2011 to 2013, such use was assessed by the question, "In the past 30 days, which [tobacco products] have you used on at least 1 day?".	• Middle school: o Chew ever use = 3.6% o Chew past 30 day use = 1.4% o Snus ever use = 1.3% o Snus past 30 day use = 0.4% o Dissovables ever use = 0.5% o Dissovables past 30 day use = N.A. • High school: o Chew ever use = 13.4% o Chew past 30 day use = 5.7% o Snus ever use = 6.2% o Snus past 30 day use = 1.8% o Dissovables ever use = 1.0% o Dissovables past 30 day use = 0.4%. o
Elfassy et al (Elfassy 2015)	2001-2013	Data from the New York City Youth Probability Behavior Survey, a cross-sectional survey which included 59,122 participants aged 14-17 years.	• Smokeless tobacco use was defined as using chewing tobacco, snuff or dip on 1 or more days in the past 30d-days.	• Smokeless tobacco use increased between 2001 and 2013 overall from 1.1% to 4.4, among non-cigarette smokers (0.2% to 1.9%) and among cigarette smokers (4.2% to 21.2%)
Camenga et al (Camenga 2014b)	2010-2011	Cross-sectional study including 1,556 students from 4 high schools.	• Chew use was defined as current use (past 30 day use).	• Overall past 30 day use = 3.0%.
Loukas et al (Loukas 2012)	2009	Cross-sectional data from the Texas Youth Tobacco Survey including adolescents in grades 6th to 12th, including 8,472.	• Snus use was defined as ever use	• Overall ever use= 7.1%

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.3.2.3.3 Determinants of use

There were 16 studies that assessed the determinants of smokeless tobacco use in US populations, and their characteristics can be found in Table 33.

Determinants of smokeless tobacco use in adult populations

There were 11 studies evaluating determinants of smokeless tobacco use in adult populations. The determinants associated with its use were: being a current smoker (Cabrera-Nguyen 2016, Choi 2013a, Fu 2014a, Kaufman 2014, Nguyen 2015, Spangler 2014), being a former smoker (Cabrera-Nguyen 2016, Choi 2013a), being male (Biener 2011, Cabrera-Nguyen 2016, Choi 2013a, Fu 2014a, Kasza 2014, Kaufman 2014, Mazurek 2014, Mumford 2006, Spangler 2014), being younger (Agaku 2014b, Biener 2011, Cabrera-Nguyen 2016, Fu 2014a, Kasza 2014, Kaufman 2014, Mazurek 2014), using e-cigarettes (Weaver 2016) or being a poly tobacco user (Cabrera-Nguyen 2016, Latimer 2014), believing that smokeless tobacco was safer or less addictive (Biener 2011, Choi 2013a, Kaufman 2014), lower education (Kasza 2014, Mazurek 2014), alcohol use (Fu 2014a, Spangler 2014), heavy smoking index (Kasza 2014), increased physical activity (Spangler 2014), being LGBT (Cabrera-Nguyen 2016) and having a mental disorder (Fu 2014a).

Inconclusive evidence was found for race (Agaku 2014b, Biener 2011, Kasza 2014, Kaufman 2014, Mazurek 2014, Mumford 2006) and for being employed fulltime (Kaufman 2014).

Determinants of smokeless tobacco use in youth populations

There were 5 studies that evaluated determinants of smokeless tobacco use in youth populations. The determinants associated with its use were: being male (Arrazola 2015, Hedden S 2015, Loukas 2012), being Caucasian or Hispanic (Hedden S 2015, Loukas 2012), using e-cigarettes (Camenga 2014b, Cooper 2015) and being older (Loukas 2012). On the other hand, being a never-smoker was associated with less risk of using smokeless tobacco (Camenga 2014b).

6.3.2.3.2.3.4 Influence on smoking (gateway effect)

There were 5 studies assessing the risk of cigarette smoking among smokeless tobacco users (O'Connor 2003, O'Connor 2005, Severson 2007, Taylor 2015, Timberlake 2009). Of the 5 studies, 1 was a cross-sectional survey (O'Connor 2005) while 4 were longitudinal studies (Table 34).

Three studies reported an increased risk of cigarette smoking in those who used smokeless tobacco, while two other studies found no difference in risk. The study by Taylor et al. (Taylor 2015) reported that non-smokers aged 20-28 years who had tried snus were more likely to become current smokers. In this study baseline non-smokers were those who had not smoked in the past

30 days and smoking was defined as having smoked in the past 30 days. The study by Severson et al. (Severson 2007) also reported an increased risk of cigarette smoking among boys in 7th to 9th grades who used smokeless tobacco. In this study, smokeless tobacco use was defined as any use in the past 30 days at baseline and smoking was defined as any ever smoking. Finally, the survey carried out by O'Connor et al. (O'Connor 2005) found that when both smokeless tobacco use and smoking status were

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

collapsed as never versus ever there was an increased risk for cigarette smoking among those who used smokeless tobacco. In this study also, smokeless tobacco use was defined as any ever use and order of product use was determined in the questionnaire.

On the other hand, the study by O'Connor et al. (O'Connor 2003), found that there was no statistically significant increased risk for cigarette smoking for smokeless tobacco users aged 12-18 years. In this study the authors differentiated between regular and sporadic smokeless tobacco use, and smoking was defined as any smoking in the past 3 days. Finally, the study by Timberlake et al. (Timberlake 2009) including 496 adolescent pairs matched through propensity scores, found that smokeless tobacco use did not predict cigarette smoking.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 33. Determinants of smokeless tobacco use in adult and youth populations in the US

Author	Population & study methods	Analyses performed	Determinants
Youth populations			
MTF(Johnston 2016)	Cross-sectional study with a total of approximately 50,000 8th, 10th and 12th grade students are surveyed (12th graders since 1975, and 8th and 10th graders since 1991) (7).	Unknown (data not shown)	Increased probability: Sex (male) Decreased probability: N.A. No difference: N.A.
NYTS (Arrazola 2015)	Of 250 schools selected for the 2013 National Youth Tobacco Survey, 187 (74.8%) participated, with a sample of 18,406 (90.7%) among 20,301 eligible students	Unknown data not shown)	Increased probability: Being Hispanic or Caucasian Sex (male) Decreased probability: N.A. No difference: N.A.
Camenga et al (Camenga 2014b)	Cross-sectional study including 1,556 students from 4 high schools.	Logistic regression analyses.	Increased probability: Using e-cigarettes (OR= 36.21, 95%CI: 12.60-104.05) Current smokers (OR= 19.55, 95%CI: 5.43-70.43) Decreased probability: Never-smokers (reference category) No difference: N.A.
Cooper et al (Cooper 2015)	Participants were 13,602 6th through 12th grade students in Texas who were part of the Texas Youth Tobacco Survey.	Chi-squared and t-test analyses.	Increased probability: Using e-cigarettes ($p<0.001$) Decreased probability: N.A. No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Loukas et al (Loukas 2012)	Cross-sectional data from the Texas Youth Tobacco Survey including adolescents in grades 6th to 12th, including 8,472.	Chi-squared and t-test analyses.	Increased probability: Sex (male) ($p<0.001$) Older age ($p<0.001$) Being Caucasian ($p<0.001$) Current smoker ($p<0.001$) Decreased probability: N.A. No difference: N.A.
Adults			
NATS (Agaku 2014b)	The 2012–2013 NATS is a stratified, national random-digit-dialed landline and cellular telephone cross-sectional study of 60,192 noninstitutionalized US adults aged ≥18 years.	Unknown (data not shown)	Increased probability: Younger age Being Caucasian or 'Other' race Decreased probability: N.A. No difference: N.A.
Latimer et al (Latimer 2014)	Online cross-sectional study including 5,028 students attending 7 public universities. Students were aged 18-24.	Unknown (data not shown).	Increased probability: Poly-tobacco user Decreased probability: N.A. No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Kaufman et al (Kaufman 2014)	Cross-sectional study using a web panel representative of the US population including 2,067 adults aged ≥ 18 years.	Chi-squared and t-test analyses.	Increased probability: Current smokers (p<0.001) Sex (male) (p<0.001) Younger age (p<0.001) Belief smokeless is less harmful (p<0.001) Decreased probability: N.A. No difference: Fulltime employment (p=0.07) Race (p=0.09) Marital status (p=0.20) Education (p=0.17)
Kasza et al (Kasza 2014)	Longitudinal study including 6,110 adult smokers aged ≥ 18 years that took part of the International Tobacco Control Four Country Survey (participants included those living in the US only)	Logistic regression analyses.	Increased probability: Sex (male) (OR= 6.03, 95%CI: 4.67-7.78) Heaviness of smoking index 4-6 (OR=1.51, 95%CI: 1.16-1.97) Decreased probability: Race other than Caucasian (OR= 0.59, 95%CI: 0.44-0.80) ↑ Education (OR= 0.53, 95%CI: 0.37-0.74) ↑ Age (for 55 +) (OR= 0.09, 95%CI: 0.06-0.14) No difference: Income (OR= 1.31, 95%CI: 0.86-1.99) Have intention to quit (OR= 0.83, 95%CI: 0.68-1.02)
Spangler et al (Spangler 2014)	Cross-sectional study of 10,520 first year college students aged ≥ 18 years.	Logistic regression analyses.	Increased probability: Current smokers (OR = 5.5; 95% CI: 4.21–7.10) Sex (male) (OR= 11.6; 95% CI: 8.16–16.59). Any use of alcohol (OR = 4.8; 95% CI: 3.62–6.43) Increased physical activity (OR = 1.5; 95% CI: 1.07–2.01). Decreased probability: N.A. No difference: N.A.

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Fu et al (Fu 2014a)	Cross-sectional study derived from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) including 43,093 adults aged ≥ 18 years.	Chi-squared and t-test analyses.	Increased probability: Panic or specific phobia disorders (p<0.05) Alcohol use disorder(p<0.05) Younger age (p<0.05) Current smoker (p<0.05) Sex (male) (p<0.05) Decreased probability: Urbanicity (p<0.05) No difference: Income (P>0.05)
Mumford et al (Mumford 2006)	Cross-sectional study data from the CPS-TUS including adults aged ≥ 18 years.	Unknown (data not shown)	Increased probability: Sex (male) Being Caucasian Older age Decreased probability: N.A. No difference: N.A.
Choi et al (Choi 2013a)	Cross-sectional data including 2,607 young adults aged 20-28 years who participated in the Minnesota Adolescent Community Cohort Study.	Logistic regression analyses.	Increased probability: Sex (male) (OR= 9.59, 95%CI: 6.80-13.53) Current smokers (OR=4.60, 95%CI: 3.32-6.37) Former smokers (OR= 2.68, 95%CI: 1.82-3.94) Belief snus is less addictive (OR= 1.67, 95%CI: 1.22-2.29) Belief snus helps quit (OR= 2.05, 95%CI: 1.50-2.81) Decreased probability: Education (enrolled or graduated from ≥ 4 years of college) (OR= 1.03, 95%CI: 0.73-1.47) No difference: Age (20-24 years) (OR= 1.24, 95%CI: 0.94-1.63) Being 'other' ethnicity (OR= 0.66, 95%CI: 0.40-1.08)

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Analyses performed	Determinants
Cabrera-Nguyen et al (Cabrera-Nguyen 2016)	Cross-sectional study using a nationally representative sample of 17,522 US adults aged ≥ 18 years.	Logistic regression analyses	Increased probability: Current smokers (OR = 20.00, 95% CI: 10.35-38.60) Former smokers (OR = 3.51, 95% CI: 1.58-7.76) Sex (male) (OR = 2.24,95% CI: 1.66-3.02) Younger age (For every 1-year increase in age the odds of DTP ever use was 5% less likely) ($p \leq 0.001$). Being LGBT (OR = 1.66, 95% CI: 1.18-2.34). Poly-tobacco user (OR = 4.04, 95% CI: 2.18-7.49). Decreased probability: N.A. No difference: N.A.
NHIS (Mazurek 2014)	Cross-sectional study using a nationally representative, in-person survey of the noninstitutionalized US civilian population. In 2005 and 2010, data on cigarette smoking were collected from 31,428 and 27,157 persons, respectively age ≥ 18 years.	Unknown (data not shown)	Increased probability: Adults aged 25-44 years old Sex (male) Being Caucasian Lower education Living in the South Decreased probability: N.A. No difference: N.A.
Biener et al (Biener 2011)	Cross-sectional study including 4,067 adult smokers aged 18-49 years.		Increased probability: Intention to quit (OR= 2.37, 95%CI: 1.12-5.00) Being Caucasian (OR=2.02, 95%CI: 1.07-3.83) Younger age (OR=9.46, 95%CI: 5.21-7.19) Sex (male) (OR= 4.00, 95%CI: 2.22-7.19) Decreased probability: N.A. No difference: Education (OR= 1.62, 95%CI: 0.99-2.66) Home smoking ban (OR= 1.19, 95%CI: 0.67-2.10)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 34. Studies evaluating the probability of initiation of cigarette smoking in smokeless tobacco users

Study	Period	Study characteristics	Probability of cigarette smoking	Comments
Taylor et al (Taylor 2015)	2010-2012	Cohort study of 2,184 participants aged 20-28 years of the Minnesota Adolescent Community Cohort	Non-smokers who had tried snus were subsequently more likely than those who had not tried snus to become current smokers (OR= 1.79, 95%CI: 1.01-3.14).	Non-smokers at baseline were those who had not smoked in the past 30 days. Current smoking at follow-up were those who had smoked in the last 30 days. Snus was defined as any type of use.
O'Connor et al (O'Connor 2005)	2005	Survey of 7,952 male participants aged 22-34 years, users of smokeless tobacco.	When both smokeless tobacco and smoking status were collapsed as never versus ever, the RR for smoking given smokeless tobacco use was 1.7 (95%CI : 1.6-1.9)	Definition of smokeless tobacco was defined as ever using snuff. Order of product use was determined accordingly.
Timberlake et al (Timberlake 2009)	2001-2002	Longitudinal study of 496 adolescent pairs matched through propensity score.	Prior to matching, the unadjusted probability of becoming a daily smoker was significantly greater for smokeless tobacco users compared to non-users (RR ranged from 1.3-2.0) but after pairing individuals on propensity score there was no evidence for an increased probability of smoking among smokeless tobacco users.	
Severson et al (Severson 2007)	1994-1999	Longitudinal survey of 2,263 boys in grades 7 to 9 that were followed-up 2 years later in 9th to 11th grade.	The odds ratio for the association of smokeless tobacco use with weekly smoking after 2 years was = 2.6 (95%CI : 1.5-4.5)	Definition of smokeless tobacco use was any use in the past 30 days and smoking was defined as weekly smoking or having smoked at least 1 puff last week.
O'connor et al (O'Connor 2003)	1989	Longitudinal survey reanalysis of data from the TAPS survey including 2,683 males aged 12-18 years who were not smokers at baseline.	Regular smokeless tobacco use did not predict smoking after adjusting for psychosocial variables (OR= 1.68, 95%CI : 0.83-3.41).	Authors differentiated regular smokeless from sporadic smokeless tobacco use. Smoking was defined as smoking in the past 30 days.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.3.2.3.5 Influence on cessation and relapse

There were 3 studies that assessed the probability of smoking cessation in those using smokeless tobacco (Kasza 2014, Kozlowski 2003, Messer 2008) (Table 35). All studies included adult populations, and none of them reported smokeless tobacco use in youth. Two of the studies reported no increased probability of smoking cessation in those who used smokeless tobacco compared to those who did not use it (Kasza 2014, Messer 2008). On the other hand, the study by Kozlowski et al. (Kozlowski 2003) found that those who had used cigarettes before moist snuff were more likely to have quit smoking than cigarette-only users.

6.3.2.3.2.3.6 Discussion

The prevalence of current use of smokeless tobacco is the US population is low in both adults (Mumford 2006) and youth (Arrazola 2015, Johnston 2016), and these rates have decreased in the past 10 years (Mumford 2006). Rates have been shown to vary by state (Nguyen 2015) as well by product type, as the use of snus and chew is higher than the prevalence of use of dissolvable tobacco (Fu 2014a, Regan 2012, Weaver 2016). Additionally, the prevalence of current smokeless tobacco use is much higher in men than in women (Agaku 2014b) and among current smokers than never smokers in both adults and youth populations (Cooper 2015, Elfassy 2015, Zhu 2013). The determinants of use are similar among adults and youth populations and they include being male (as previously noted), being a smoker or former smoker or using e-cigarettes (Cabrera-Nguyen 2016, Camenga 2014b, Choi 2013a, Cooper 2015) and being younger for adults or older for youths (Agaku 2014b, Loukas 2012).

Studies assessing the probability of cigarette smoking initiation in those who use smokeless tobacco found conflicting results. Three studies found an increased risk of cigarette smoking initiation (O'Connor 2005, Severson 2007, Taylor 2015), while two studies found no association (O'Connor 2003, Timberlake 2009). Interestingly 1 of the studies that found an association for the majority of smokeless tobacco ever users (66%), 2000 National Household Survey on Drug Abuse (NHSDA),identified them as being non-causal users (users that smoked before using smokeless tobacco). For these individuals, smokeless tobacco use cannot have caused them to smoke and when non-causal users were removed, smokeless tobacco was a minor predictor of current smoking which is likely due to linked experimentation (O'Connor 2005). Additionally, the definition of smokeless tobacco use and smoking were vague in these three studies, as smokeless tobacco use was defined as any use (or ever use) and smoking was defined as past 30-day use in 1 study (Taylor 2015) and as ever smoker in another (Severson 2007). The study by O'Connor et al. (O'Connor 2005) included smokers who reported having used smokeless tobacco before baseline and therefore was not truly longitudinal or could assess causality. On the other hand, the study by Timberlake et al. (Timberlake 2009) used propensity score matching to study the influence of smokeless tobacco use on cigarette smoking initiation. Before the propensity scores were applied, there seemed to be a relationship; however, this relationship disappeared after the propensity scores were introduced. It is important to note that this procedure dramatically reduced the sample size from 18,924 to 496 pairs. Finally, there did not appear to be an association between smokeless tobacco use and the probability of cessation.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 35. Studies evaluating the probability of cigarette smoking cessation in smokeless tobacco users

Study	Period	Study characteristics	Probability of quitting in e-cigarette users	Comments
Messer et al (Messer 2008)	2010-2011	Participants of the Tobacco Use Supplement to the Current Population Survey including 26,760 cigarette smokers and 675 concurrently used smokeless tobacco. Participants were aged ≥ 18 years.	Compared to those who do not use smokeless tobacco, users were more likely than exclusive smokers (OR= 1.33, 95%CI : 1.15-1.53).	
Kasza et al (Kasza 2014)	2001-2011	Longitudinal study including 6,110 adult smokers aged ≥ 18 years that took part of the International Tobacco Control Four Country Survey (participants included those living in the US only)	There was no association of smokeless tobacco use and smoking cessation (OR= 0.77, 95%CI : 0.27-1.60).	
Koylowski et al (Kozlowski 2003)	1987-1988	Data from the Cancer Control Supplement to the 1987 NHIS of 2,614 males aged 23-34.	Of those who had ever used smokeless tobacco with or without cigarettes, 77.2% were classifiable as non-gateways users in that 35% had only used smokeless tobacco and 42.2% had used cigarettes first. And those who had used cigarettes before moist snuff were 2.1 times more likely to have quit smoking (95CI : 1.2-6.4) than cigarette-only users	

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

There are several types of smokeless tobacco products that can be used orally or nasally (Melikian 2009). Available evidence suggests that adverse health consequences of smokeless tobacco use vary by specific type, and the use of specific types of smokeless tobacco is strongly associated with geography and culture. Epidemiologic evidence also suggests that the use of smokeless tobacco product can cause cancer in humans particularly for pancreatic cancer. Snus – a type of smokeless cigarette- however, contains less toxicants than cigarette smoke, and a harm reduction option would be to propose the use of smokeless tobacco as a sort of nicotine replacement therapy (Melikian 2009). Deterrents of this approach argue that the use of smokeless tobacco could lead to cigarette smoking; however, there is little to no evidence for this 'gateway' effect of smokeless tobacco. What is more, evidence from Sweden shows that since 1980 snus consumption has increased dramatically, and smoking has declined among Swedish men. Additionally, although the prevalence of tobacco use has remained the approximately the same, while smoking prevalence has declined (Rodu 2003) tobacco-related mortality in Sweden is among the lowest in the developed world.

6.3.2.3.2.4 Conclusions

The use of smokeless tobacco in the US is mainly a male habit, and the prevalence of use of these types of products is very low. There does not seem to be a relationship between the use of smokeless tobacco and either initiation or cessation of cigarette smoking.

6.3.2.3.3 Dual or poly-tobacco use

6.3.2.3.3.1 Search strategies

Articles retrieved through the previously disclosed search strategies that included information on the prevalence of dual or poly-tobacco use in the US population are summarized in this section.

6.3.2.3.3.2 Prevalence of dual or poly-tobacco use

There were 13 publications reporting data from 10 original studies assessing the prevalence of dual or poly-tobacco use in the US population. Out of these 13 publications 6 included adult populations (Backinger 2008, Enofe 2014, McMillen 2012, Miller 2014, Rath 2012, Sung 2016), 5 included youth populations (Agaku 2013, Arrazola 2015, Gilreath 2016, Kaufman 2015, Saunders 2012), 1 included mixed populations (Soneji 2016) and 1 included both populations analyzed separately (Fix 2014). Their characteristics can be found in Table 36.

6.3.2.3.3.2.1 Dual and poly-tobacco use in adult populations

There were 7 studies reporting prevalence of dual or poly-tobacco use in adult populations (Backinger 2008, Enofe 2014, Fix 2014, McMillen 2012, Miller 2014, Rath 2012). Out of these 7 studies, 4 reported results from nationally representative surveys (Backinger 2008, Fix 2014, McMillen 2012, Sung 2016) while 3 reported results from young adult or college aged populations (Enofe 2014, Miller 2014, Rath 2012).

Dual use was assessed in 2 studies (McMillen 2012, Miller 2014). The study by Miller et al. (Miller 2014), which was based on a sample of college students with a mean age of 19.2 years reported that the prevalence of dual use (cigarettes plus smokeless tobacco) was 5.7% in men and 1.1% in women, while the study by Mc Millen et al. (McMillen 2012), which was based on a nationally representative sample, reported that the dual use prevalence of cigarettes plus another product in daily smokers was: for snus

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

12.9%, hookah 12.9%, dissolvable tobacco 0.9% and e-cigarettes 6.2%. They also reported that the prevalence of dual product use of cigarettes plus another product in non-daily smokers was: for snus 4.1%, hookah 26%, dissolvable tobacco 2.7% and e-cigarettes 8.2%.

Poly-tobacco use was assessed in 5 studies (Backinger 2008, Enofe 2014, Fix 2014, Rath 2012, Sung 2016). The study by Rath et al. (Rath 2012) and Enofe et al. (Enofe 2014) both reported results from young adults. The study by Rath et al. (Rath 2012) reported a prevalence of poly-tobacco use of cigarettes plus other products of 7% (overall). In those aged 18-24 years, the prevalence was 6% and in those aged 25-34 years it was 7%. Additionally, the prevalence was higher in men (7%) than women (1%). The study by Enofe et al. (Enofe 2014) reported the prevalence of use of alternative tobacco products in daily smokers (17.8%) and non-daily smokers (38.8%).

There were 3 studies that reported poly-tobacco use prevalence from nationally representative samples. The study by Backinger et al. (Backinger 2008) reported the prevalence of poly-tobacco use in current cigarette smokers (1.2%). Daily smokers had a slightly higher prevalence (0.9%) than non-daily smokers (0.3%). The study by Sung et al. (Sung 2016), reporting results from the NHIS found that among current cigarette users, poly-tobacco use prevalence was 7.6%; among cigar users it was 51.1%; among chewing tobacco users it was 51.9%; and among snuff users it was 44.7%. Finally, the study by Fix et al. (Fix 2014), reporting results from the NSDUH, found that the prevalence of poly-tobacco use in the past 12 months was 28.6% in those aged 18-25 years and 17.4% in those aged 26 years or older, while the prevalence of 30-day use in those aged 18-25 years was 23.7% and in those aged 26 or older was 9.9%. They also reported that men had a higher prevalence of poly-tobacco use (17.8%) than women (6.8%).

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 36. Prevalence of dual and poly-tobacco use

Author	Population & study methods	Prevalence of dual or poly tobacco use
Gilreath et al (Gilreath 2016)	Data from 2,097 11th- and 12th-grade participants in the Southern California Children's Health Study were collected via self-report in 2014. Participants who reported current product use were classified as current users of that product. Those who reported use of more than 1 product were classified as poly-tobacco users.	Poly-tobacco experimenters: 13.9% Poly-tobacco users: 5.6%
Sung et al (Sung 2016)	Data was pooled from the 1998, 2000, 2005 and 2010 Cancer Control Supplements of the NHIS which included 123,399 adults ≥ 18 years of age. Poly-tobacco use was defined as currently using two or more tobacco products.	**Poly-tobacco use:** Poly-tobacco use among cigarette smokers: 7.6% Poly-tobacco use among cigar users: 51.1% Poly-tobacco use chewing tobacco users: 51.9% Poly-tobacco use among snuff users: 44.7%
Arrazola et al (Arrazola 2015)	Data from the NYTS 2011-2014. Sample sizes and overall response rates for 2011, 2012, and 2013 were 18,866 (72.7%), 24,658 (73.6%), and 18,406 (67.8%), respectively. Participants were asked about current (past 30-day) use of cigarettes, cigars (defined as cigars, cigarillos, or little cigars), smokeless tobacco (defined as chewing tobacco, snuff, or dip), e-cigarettes, hookahs, pipes, snus, dissolvable tobacco (dissolvables), and bidis. Current use for each product was defined as using a product on ≥1 day during the past 30 days. Tobacco use was categorized as "any tobacco product use," defined as use of 1 or more tobacco products and "≥2 tobacco product use," defined as use of two or more tobacco products.	**Use of 2 or more tobacco products:** Male: 3.8% Female 2.4% Non-Hispanic Caucasian: 2.5% Non-Hispanic African American: 2.0% Hispanic: 5.0%
Kaufman et al (Kaufman 2015)	Data from cross sectional study Add Health including 20,774 male and female adolescents in grades 7 through 12. Information on smokeless tobacco use was asked as "During the past 30 days, on how many days have you used chewing tobacco or snuff?" Responses were dichotomized to indicate use (yes or no) for each wave. For cigarette smoking, at each wave participants were asked, "During the past 30 days, on how many days did you smoke cigarettes?" Responses were dichotomized to indicate use (yes or no) for each wave.	**Dual us of cigarettes and smokeless tobacco:** Total 7.2% Male: 12.3% Female: 2.2% Caucasian: 9.5% African American: 2.9% Native American: 5.9% Asian: 3.0% West: 4.8% Midwest: 9.1% South: 7.5% North East: 7.9%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Prevalence of dual or poly tobacco use
Enofe et al (Enofe 2014)	Cross sectional online study among students aged 18-25 years attending 6 Southeastern US colleges. To assess smoking status, students were asked: "In the past 30 days, on how many days did you smoke a cigarette (even a puff)?" They also were asked: "Have you ever smoked cigarettes daily, that is, at least 1 cigarette every day for 30 days?" Students were considered current smokers if they reported smoking at least once in the past 30 days. Among the current smokers, students were categorized as daily smokers if they reported smoking on all 30 days versus nondaily smokers. The alternative tobacco products assessed in the survey were chewing tobacco, snuff, dip, cigars, little cigars, cigarillos, water pipe tobacco (hookah), snus, and electronic cigars.	Use of alternative tobacco products among daily cigarette smokers: 17.8% Use of alternative tobacco products among non-daily cigarette smokers: 38.8%
Soneji et al (Soneji 2014)	Web-based cross sectional study including 1,596 16-26 year olds. Assessment of current (past 30 days) multiple tobacco product use was based on respondents' self-reported answers to the following question, "For each of the tobacco products listed below tell us if you used it in the last 30 days?" The tobacco products included: chewing tobacco, cigarettes, dip, dissolvables, e-cigarettes, hookah, large or premium cigars, little filtered cigars, medium cigars or cigarillos, snuff and snus. Single users were current users of only 1 tobacco product, a 'dual user' was a current user of two tobacco products and a 'multiple user' was a current user of three or more tobacco products.	Any dual use: 7% Multiple tobacco product use: 6%
Fix et al (Fix 2014)	Data from the NSDUH survey (from 2002-2011). Use of tobacco products was assessed in terms of use in the 12 months prior to the survey including subjects aged 12 and above. Participants were also asked about their use of cigarettes, cigars, and smokeless tobacco within the past 12 months.	**Last 12 month poly-tobacco use (2011):** Male: 30.4% Female: 12.3% 12-17 year olds: 39.9% 18-25 years: 28.6% 26 years or older: 17.4% **Past 30 day poly-tobacco use (2011):** Male: 17.8% Female: 6.8% 12-17 year olds: 29.0% 18-25 years: 23.7% 26 years or older: 9.9%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Prevalence of dual or poly tobacco use
Miller et al (Miller 2014)	Cross sectional survey of college students including 1,242 subjects (53.5% female and 46.5% male) with a mean age of 19.2 years. No definition of dual user was given.	**Dual user of cigarettes and smokeless tobacco:** Male: 7.5% Female: 1.1%
Agaku et al (Agaku 2013)	Data from the 2011 NYTS including subjects from US middle and high school students both female and male. Current use of any combustible tobacco product was defined as use of at least 1 of the following projects on ≥ 1 days during the past 30 days: cigarettes, cigars, bidis, kreteks, pipes and water pipes. The same questions were asked about smokeless tobacco.	**Use of any smokeless tobacco product plus a combustible product:** Overall: 4.0% 9-11 years: 2.0% 12-14 years: 2.0% 15-17 years: 5.4% ≥ 18 years: 7.8%
Saunders & Geletko (Saunders 2012)	Data from the 2004, 2006 and 2009 NTYS including 37'175,806 male and female participants aged 14-17 years. Current use cigarettes in combination with 1 other tobacco product (smokeless tobacco, cigars, pipes, bidis or kreteks) was assessed.	**Dual use of cigarette smokers plus:** Smokeless tobacco: 18.0% Cigars: 38.7% Pipes: 12.3% Bidis: 8.9% Kreteks: 9.9%
Rath et al (Rath 2012)	Data from the Legacy Young Adult Cohort Study including 4,215 subjects aged 18-34 years. Tobacco use was assessed with measures of ever tobacco use, first tobacco product tried, past 30-day use, every day or someday use, and number of cigarettes smoked per day. Tobacco use was categorized as respondents who reported current "every day" or "some days" use of cigarettes or tobacco products. Categories included "cigarettes only," "cigarettes and other tobacco products," and "other tobacco products only." Individuals who reported no current tobacco product use, including those who never used a product, were classified as "neither." Individuals who reported using both cigarettes and other tobacco products "every day" or "some days" were classified as dual users.	**Current poly-tobacco use (cigarettes and other tobacco products):** Overall: 7.0% 18-24 years: 6.0% 25-34 years: 7.0% Male: 7.0% Female: 1.0%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Prevalence of dual or poly tobacco use
McMillen et al	Data from the Social Climate Survey of Tobacco Control which is a nationally representative annual cross sectional study which included 1,504 respondents and an additional 2,272 panelists who were randomly drawn from a probability panel. To assess current cigarette smoking status of respondents, respondents were asked, "Have you smoked at least 100 cigarettes in your entire life?" Respondents who reported that they had were then asked, "Do you now smoke cigarettes every day, some days, or not at all?" Respondents who reported that they have smoked at least 100 cigarettes and now smoke every day or some days were categorized as daily and non-daily smokers; respondents who had not smoked at least 100 cigarettes were categorized as never smokers; and respondents who reported that they have smoked at least 100 cigarettes, but no longer smokers were categorized as former smokers. One set of items assessed lifetime use of emerging tobacco products. Which of the following products have you tried, even just once? (1) Smokeless tobacco, (2) snus, such as Camel or Marlboro snus, (3) roll-your-own cigarettes, (4) smoking tobacco from a waterpipe, (5) dissolvable tobacco products, (6) electronic cigarettes or E-cigarettes. Respondents who had tried a product were asked if they had used that product in the past 30 days. Those who had were considered to be current users.	**Dual use of cigarettes plus another product in daily smokers:** Snus: 12.9% Waterpipe: 12.9% Dissolvable tobacco: 0.9% e-cigarettes: 6.2% **Dual use of cigarettes plus another product in non-daily smokers:** Snus: 4.1% Waterpipe: 26.0% Dissolvable tobacco: 2.7% e-cigarettes: 8.2%

(Table continues)

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Author	Population & study methods	Prevalence of dual or poly tobacco use
Backinger et al (Backinger 2008)	Cross sectional data from the 1995/1996, 1998, 2000 and 2001/02 Tobacco Use Supplements to the Current Population Survey (TUS-CPS) ran by the US Department of Commerce.552, 804 male and female participants aged 18 or older. The CPS uses a multistage probability sample design to collect data on a monthly basis from about 50,000 households and interviews were conducted in person and by telephone using computer assisted interviewing technology. The Tobacco Use Supplement (TUS) is conducted in conjunction with the CPS every three years. Measures of cigarette smoking status, frequency of smoking, and other tobacco use were assessed using the TUS-CPS. Never smokers were respondents who indicated that they smoked fewer than 100 cigarettes in their entire life. Respondents who smoked at least 100 cigarettes in their lifetime were asked, "Do you now smoke cigarettes every day, some days, or not at all?" Current cigarette smokers were defined as those who reported smoking every day or some days at the time of their interview. Intermittent smokers were defined as current smokers who reported smoking some days at the time of their interview. Daily smokers were current smokers who indicated that they smoked every day at the time of their interview.	**Use of cigarettes plus any other products (combined surveys 1995-2002):** Current cigarette smokers: 1.2% Daily cigarette smokers: 0.9% Intermittent cigarette smokers: 0.3%
Bombard et al (Bombard 2008)	Data from 50,000 participants from 6th-12th grade of the 2002-2004 NYTS. Current cigarette smokers were respondents who indicated using cigarettes during the previous 30 days, and we defined current poly-tobacco users as current cigarette smokers who reported also using cigars, smokeless tobacco, pipes, bidis, and/or kreteks during the previous 30 days.	**Poly-tobacco use:** Cigarette-only use: 53.9% Cigarettes plus 1product: 26.4% Cigarettes plus 2 products: 19.7%

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.3.3.2.2 Dual and poly-tobacco use in youth populations

There were 6 publications reporting prevalence of dual or poly-tobacco use in youth populations (Agaku 2013, Arrazola 2015, Fix 2014, Gilreath 2016, Kaufman 2015, Saunders 2012). Only 1 study reported results from a non-nationally representative sample, which consisted of students from the 11th and12th grades in Southern California. This study reported that the prevalence of poly-tobacco experimentation was 13.9%, while the prevalence of poly-tobacco use was 5.6% (Gilreath 2016).

Dual use was assessed in 2 publications (Kaufman 2015, Saunders 2012). The study by Saunders et al. (Saunders 2012) using data from the 2009 NYTS reported that dual use of cigarettes plus another product ranged from 8.9% to 38.7%. The rate with concomitant smokeless tobacco use was 18%, cigar use 38.7%, pipe use 12.3%, bidis use 8.9% and kreteks use 9.9%. The study by Kaufman et al. (Kaufman 2015), using data from the Add Health study including 7th-12th grade students, reported a dual use overall prevalence of 7.2%. The prevalence was higher in men (12.3%) than in women (2.2%) and it was also higher in Caucasians (9.5%), followed by Native Americans (5.9%), Asians (3%) and was lowest among African Americans (2.9%).

Poly-tobacco use was reported by 3 publications. Arrazola et al. (Arrazola 2015) and Agaku et al. (Agaku 2013) reported rates from the NYTS 2014 and 2011 respectively, while Fix et al. (Fix 2014) reported results from the NSDUH. In the NYTS 2014 (Arrazola 2015) the current use of 2 or more tobacco or nicotine containing products was 3.8% in men and 2.4% in women, and the prevalence was higher among Hispanics (5%) than Caucasians (2.5%) or African-Americans (2%). The NYTS from 2011 (Agaku 2013) reported an overall prevalence of poly-tobacco use of 4% with prevalence varying by age groups from 2% in those aged either 9-11 years or 12-14 years to 5.8% in those aged 15-17 years and 7.8% in students aged 18 or older. Finally, the study by Fix et al. (Fix 2014) reported that among those aged 12-17 years the prevalence of last 12 months poly-tobacco use was 39.9% while the past 30-day prevalence was 29%.

6.3.2.3.3.2.3 Dual and poly-tobacco use in mixed populations

The only study assessing prevalence of dual or poly-tobacco use was Soneji et al. (Soneji 2016), who reported results of past 30-day use from a sample of participants aged 16-26 years. Any dual use prevalence was 7%, and poly-tobacco use prevalence was 6%.

6.3.2.3.3.3 Discussion

There were 13 publications that assessed the prevalence of dual or poly-tobacco use in diverse populations. The use of dual or multiple types of tobacco or nicotine containing products was mainly reported in those who smoked cigarettes. It was more common in Caucasians and men, and it varied by the definition of use (ever use or current use).

As cigarette smoking has decreased, literature obtained from our search showed that use of smokeless tobacco has decreased as well (Mumford 2006), whereas the use of e-cigarettes has increased, although this increase might be leveling off (Johnston 2016). Along with e-cigarettes, other new tobacco products have entered the US market, namely, Swedish snus in 2006 and dissolvable tobacco in 2008 (Agaku 2013). Although these new products are lower in tobacco specific nitrosamine content as well as biomarkers of exposure to harmful and potentially harmful tobacco constituents (HPHCs) than cigarettes (Agaku 2013), the relatively lower risk of tobacco-related diseases compared to cigarettes

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

at a population level might depend upon whether these novel products are used exclusively (not as part as dual use) by those who would have otherwise been smoking (Agaku 2013). For this reason it is important to evaluate the frequency of dual and poly-tobacco (or nicotine) use.

The study of dual or poly-tobacco use is challenging because of the lack of a consistent definition (Klesges 2011); hence, it is difficult to interpret the data from the different studies that were retrieved as they used different definitions of current use (current every day or some days or past 30-day use).

In general, dual or poly-tobacco use is more common in adult than youth populations, in males, and it seems to primarily apply to cigarette smokers.

6.3.2.3.3.4 Conclusion

Dual and poly-tobacco use is more common in adults, among cigarette smokers and males.

6.3.2.4 General discussion

The aim of these literature searches was to understand and summarize the prevalence of use of cigarettes, e-cigarettes and smokeless tobacco products in the overall US population as well is subgroups such as adults, youth and specific populations; as well as to gain insight into the prevalence of patterns of dual or multiple product use. Articles retrieved relevant to cigarette smoking show that the prevalence of current smoking has decreased dramatically during the past 40 years; since 2005 it has declined from 20.9% to 16.8% in adults according to the NHIS (Jamal 2015). The prevalence of cigarette smoking in adults reported by nationally representative surveys ranges from 16.8% (Jamal 2015) to 19% (Agaku 2014b) (those who had smoked 100 cigarettes or more in their lifetime and currently smoked either every day or some days) depending on the survey reporting these values, while in youth the prevalence of smoking (mostly measured by past 30-day cigarette smoking) ranges from 2.5% in middle school students to 10% in high school students (Arrazola 2015). There was also evidence that the prevalence of smoking was higher among certain populations such as: those living under the poverty level (26.3%) (Jamal 2015), those in the LGBT community (23.9%-42.1%) (Agaku 2014a, Jamal 2015, Tami-Maury 2015), those living with mental illnesses (44%-73.1%) (Dickerson 2013, Glasheen 2014, Kotov 2010) and HIV + patients (37.6%-54%) (Mamary 2002, Mdodo 2015). These rates will need to be monitored once THS is marketed. Another finding from the literature review is that most cigarette smoking initiation will occur prior to 26 years of age (99% of initiation) (Gray 2015), additionally, it can take up to 2 years to progress from early experimentation to established smoking (Ramo 2015a), for these reasons, these age groups will need to be of particular attention in post-marketing surveillance.

The rates of smokeless tobacco use have seen a similar effect as those from cigarette smoking, the prevalence has either decreased (among youth) (Hedden S 2015) or remained stable (in adults) (Nguyen 2015), while the prevalence of e-cigarette use has increased in the last few years since their introduction in the US market although its use appears to be leveling off in certain youth groups (Johnston 2016). The effect of e-cigarettes or smokeless tobacco products on cigarette smoking initiation was also studied, the evidence up to date does not seem to suggest that either e-cigarettes or smokeless tobacco product use have an adverse impact on cigarette smoking rates, either

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

uptake of cessation (Al-Delaimy 2015, Cardenas 2016, Christensen 2014, Kalkhoran 2016, Kasza 2014, Kozlowski 2003, Leventhal 2015, Messer 2008, O'Connor 2003, O'Connor 2005, Popova 2013, Primack 2015, Severson 2007, Taylor 2015, Timberlake 2009, Wills 2016).

Finally, the studies evaluating cessation from and relapse to cigarette smoking show that although combination therapy is effective in inducing quitting for certain lengths of time (mostly up to 6 months), relapse is the most common result after a quit attempt (Piasecki 2002). Furthermore, observational studies report continuous abstinence rates (or quit rates) ranging from 6.2%-6.4% , the latter being a cumulative rate for cessation seen in a cohort with 9-10 years of follow-up. These will also need to be monitored during post-market surveillance. This information, paired with the fact that around one-third of smokers do not want to quit smoking at all (Centers for Disease 2016g), opens the door for the introduction of new tobacco or nicotine containing products that could replace cigarettes while reducing exposure to harmful and potential harmful smoke constituents (Hatsukami 2012).

6.3.2.5 General conclusions

According to the FDA's MRTPA guidance, in order to be able to market new tobacco products as MRTPs, they must "demonstrate that [they] meet a series of rigorous criteria and will benefit the health of the population as a whole" (FDA (Food and Drug Administration) 2012). Hatsukami et al. (Hatsukami 2012) point out that in order for these products to have an effect on population harm, the potential MRTP should not only have reduced toxicity but also must possess appeal as well as consumer acceptability. Based on the overall tobacco use experience in the US, including trends over time, an adverse impact of THS appears to be unlikely; but will still need to be monitored.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.2.6 References

Abar CC, Jackson KM, Colby SM, Barnett NP. Common and unique parenting predictors of adolescent tobacco and alcohol use. Addictive behaviors. 2014; 39(10):1528-32.

Abrams DB, Herzog TA, Emmons KM, Linnan L. Stages of change versus addiction: a replication and extension. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2000; 2(3):223-9.

Abrantes AM, Bloom EL, Strong DR, Riebe D, Marcus BH, Desaulniers J, Fokas K, Brown RA. A preliminary randomized controlled trial of a behavioral exercise intervention for smoking cessation. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(8):1094-103.

Agaku IT, Ayo-Yusuf OA, Vardavas CI, Alpert HR, Connolly GN. Use of conventional and novel smokeless tobacco products among US adolescents. Pediatrics. 2013; 132(3):e578-86.

Agaku IT, King BA, Dube SR, Centers for Disease C, Prevention. Current cigarette smoking among adults - United States, 2005-2012. MMWR Morbidity and mortality weekly report. 2014a; 63(2):29-34.

Agaku IT, King BA, Husten CG, Bunnell R, Ambrose BK, Hu SS, Holder-Hayes E, Day HR, Centers for Disease C, Prevention. Tobacco product use among adults--United States, 2012-2013. MMWR Morbidity and mortality weekly report. 2014b; 63(25):542-7.

Al-Delaimy WK, Myers MG, Leas EC, Strong DR, Hofstetter CR. E-cigarette use in the past and quitting behavior in the future: a population-based study. American journal of public health. 2015; 105(6):1213-9.

Albers AB, Biener L, Siegel M, Cheng DM, Rigotti N. Household smoking bans and adolescent antismoking attitudes and smoking initiation: findings from a longitudinal study of a Massachusetts youth cohort. American journal of public health. 2008; 98(10):1886-93.

Alcala HE, Albert SL, Ortega AN. E-cigarette use and disparities by race, citizenship status and language among adolescents. Addictive behaviors. 2016; 57:30-4.

Allem JP, Forster M, Neiberger A, Unger JB. Characteristics of emerging adulthood and e-cigarette use: Findings from a pilot study. Addictive behaviors. 2015; 50:40-4.

Allen SS, Bade T, Hatsukami D, Center B. Craving, withdrawal, and smoking urges on days immediately prior to smoking relapse. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2008; 10(1):35-45.

Amato MS, Boyle RG, Levy D. How to define e-cigarette prevalence? Finding clues in the use frequency distribution. Tobacco control. 2016; 25(e1):e24-9.

Amrock SM, Zakhar J, Zhou S, Weitzman M. Perception of e-cigarette harm and its correlation with use among U.S. adolescents. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(3):330-6.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Arrazola RA, Singh T, Corey CG, Husten CG, Neff LJ, Apelberg BJ, Bunnell RE, Choiniere CJ, King BA, Cox S, McAfee T, Caraballo RS, Centers for Disease C, Prevention. Tobacco use among middle and high school students - United States, 2011-2014. MMWR Morbidity and mortality weekly report. 2015; 64(14):381-5.

Backinger CL, Fagan P, O'Connell ME, Grana R, Lawrence D, Bishop JA, Gibson JT. Use of other tobacco products among U.S. adult cigarette smokers: prevalence, trends and correlates. Addictive behaviors. 2008; 33(3):472-89.

Baer JS, Kamarck T, Lichtenstein E, Ransom CC, Jr. Prediction of smoking relapse: analyses of temptations and transgressions after initial cessation. Journal of consulting and clinical psychology. 1989; 57(5):623-7.

Baldwin AS, Rothman AJ, Hertel AW, Linde JA, Jeffery RW, Finch EA, Lando HA. Specifying the determinants of the initiation and maintenance of behavior change: an examination of self-efficacy, satisfaction, and smoking cessation. Health psychology : official journal of the Division of Health Psychology, American Psychological Association. 2006; 25(5):626-34.

Barnett TE, Soule EK, Forrest JR, Porter L, Tomar SL. Adolescent Electronic Cigarette Use: Associations With Conventional Cigarette and Hookah Smoking. American journal of preventive medicine. 2015; 49(2):199-206.

Barrington-Trimis JL, Berhane K, Unger JB, Cruz TB, Huh J, Leventhal AM, Urman R, Wang K, Howland S, Gilreath TD, Chou CP, Pentz MA, McConnell R. Psychosocial Factors Associated With Adolescent Electronic Cigarette and Cigarette Use. Pediatrics. 2015; 136(2):308-17.

Barrington-Trimis JL, Samet JM, McConnell R. Flavorings in electronic cigarettes: an unrecognized respiratory health hazard? Jama. 2014; 312(23):2493-4.

Berg CJ. Preferred flavors and reasons for e-cigarette use and discontinued use among never, current, and former smokers. International journal of public health. 2016; 61(2):225-36.

Berg CJ, Barr DB, Stratton E, Escoffery C, Kegler M. Attitudes toward E-Cigarettes, Reasons for Initiating E-Cigarette Use, and Changes in Smoking Behavior after Initiation: A Pilot Longitudinal Study of Regular Cigarette Smokers. Open journal of preventive medicine. 2014; 4(10):789-800.

Berg CJ, Haardoerfer R, Escoffery C, Zheng P, Kegler M. Cigarette users' interest in using or switching to electronic nicotine delivery systems for smokeless tobacco for harm reduction, cessation, or novelty: a cross-sectional survey of US adults. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(2):245-55.

Bernat DH, Klein EG, Forster JL. Smoking initiation during young adulthood: a longitudinal study of a population-based cohort. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2012; 51(5):497-502.

Bhatnagar A, Whitsel LP, Ribisl KM, Bullen C, Chaloupka F, Piano MR, Robertson RM, McAuley T, Goff D, Benowitz N, American Heart Association Advocacy Coordinating Committee CoC, Stroke Nursing CoCC, Council on Quality of C,

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Outcomes R. Electronic cigarettes: a policy statement from the American Heart Association. Circulation. 2014; 130(16):1418-36.

Biener L, Hamilton WL, Siegel M, Sullivan EM. Individual, social-normative, and policy predictors of smoking cessation: a multilevel longitudinal analysis. American journal of public health. 2010; 100(3):547-54.

Biener L, McCausland K, Curry L, Cullen J. Prevalence of trial of snus products among adult smokers. American journal of public health. 2011; 101(10):1874-6.

Bilal U, Fernandez E, Beltran P, Navas-Acien A, Bolumar F, Franco M. Validation of a method for reconstructing historical rates of smoking prevalence. American journal of epidemiology. 2014; 179(1):15-9.

Bohnert KM, Rios-Bedoya CF, Breslau N. Parental monitoring at age 11 and smoking initiation up to age 17 among Blacks and Whites: a prospective investigation. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2009; 11(12):1474-8.

Bolt DM, Piper ME, Theobald WE, Baker TB. Why two smoking cessation agents work better than one: role of craving suppression. Journal of consulting and clinical psychology. 2012; 80(1):54-65.

Bombard JM, Rock VJ, Pederson LL, Asman KJ. Monitoring polytobacco use among adolescents: do cigarette smokers use other forms of tobacco? Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2008; 10(11):1581-9.

Bostean G, Trinidad DR, McCarthy WJ. E-Cigarette Use Among Never-Smoking California Students. American journal of public health. 2015; 105(12):2423-5.

Boyko EJ, Trone DW, Peterson AV, Jacobson IG, Littman AJ, Maynard C, Seelig AD, Crum-Cianflone NF, Bricker JB. Longitudinal Investigation of Smoking Initiation and Relapse Among Younger and Older US Military Personnel. American journal of public health. 2015; 105(6):1220-9.

Breland A, Soule E, Lopez A, Ramoa C, El-Hellani A, Eissenberg T. Electronic cigarettes: what are they and what do they do? Annals of the New York Academy of Sciences. 2016.

Breland AB, Spindle T, Weaver M, Eissenberg T. Science and electronic cigarettes: current data, future needs. Journal of addiction medicine. 2014; 8(4):223-33.

Bricker JB, Bush T, Zbikowski SM, Mercer LD, Heffner JL. Randomized trial of telephone-delivered acceptance and commitment therapy versus cognitive behavioral therapy for smoking cessation: a pilot study. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(11):1446-54.

Bricker JB, Liu J, Comstock BA, Peterson AV, Kealey KA, Marek PM. Social cognitive mediators of adolescent smoking cessation: results from a large randomized intervention trial. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors. 2010; 24(3):436-45.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Brook JS, Marcus SE, Zhang C, Stimmel MA, Balka EB, Brook DW. Adolescent attributes and young adult smoking cessation behavior. Substance use & misuse. 2010; 45(13):2172-84.

Buller DB, Halperin A, Severson HH, Borland R, Slater MD, Bettinghaus EP, Tinkelman D, Cutter GR, Woodall WG. Effect of nicotine replacement therapy on quitting by young adults in a trial comparing cessation services. Journal of public health management and practice : JPHMP. 2014; 20(2):E7-E15.

Burton D, Chakravorty B, Weeks K, Flay BR, Dent C, Stacy A, Sussman S. Outcome of a tobacco use cessation randomized trial with high-school students. Substance use & misuse. 2009; 44(7):965-80.

Bush TM, Levine MD, Magnusson B, Cheng Y, Chen X, Mahoney L, Miles L, Zbikowski SM. Impact of baseline weight on smoking cessation and weight gain in quitlines. Annals of behavioral medicine : a publication of the Society of Behavioral Medicine. 2014; 47(2):208-17.

Cabrera-Nguyen EP, Cavazos-Rehg P, Krauss M, Kim Y, Emery S. Awareness and Use of Dissolvable Tobacco Products in the United States. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016; 18(5):857-63.

Cahall EJ. Assisting with tobacco cessation. Journal of vascular nursing : official publication of the Society for Peripheral Vascular Nursing. 2004; 22(4):117-23; quiz 24-5.

Camenga DR, Delmerico J, Kong G, Cavallo D, Hyland A, Cummings KM, Krishnan-Sarin S. Trends in use of electronic nicotine delivery systems by adolescents. Addictive behaviors. 2014a; 39(1):338-40.

Camenga DR, Kong G, Cavallo DA, Liss A, Hyland A, Delmerico J, Cummings KM, Krishnan-Sarin S. Alternate tobacco product and drug use among adolescents who use electronic cigarettes, cigarettes only, and never smokers. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2014b; 55(4):588-91.

Caraballo RS, Kruger J, Asman K, Pederson L, Widome R, Kiefe CI, Hitsman B, Jacobs DR, Jr. Relapse among cigarette smokers: the CARDIA longitudinal study - 1985-2011. Addictive behaviors. 2014; 39(1):101-6.

Cardenas VM, Breen PJ, Compadre CM, Delongchamp RR, Barone CP, Phillips MM, Wheeler JG. The smoking habits of the family influence the uptake of e-cigarettes in US children. Annals of epidemiology. 2015; 25(1):60-2.

Cardenas VM, Evans VL, Balamurugan A, Faramawi MF, Delongchamp RR, Wheeler JG. Use of electronic nicotine delivery systems and recent initiation of smoking among US youth. International journal of public health. 2016; 61(2):237-41.

Carvajal SC, Granillo TM. A prospective test of distal and proximal determinants of smoking initiation in early adolescents. Addictive behaviors. 2006; 31(4):649-60.

Catley D, Goggin K, Harris KJ, Richter KP, Williams K, Patten C, Resnicow K, Ellerbeck EF, Bradley-Ewing A, Lee HS, Moreno JL, Grobe JE. A Randomized

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Trial of Motivational Interviewing: Cessation Induction Among Smokers With Low Desire to Quit. American journal of preventive medicine. 2016; 50(5):573-83.

Census US. Current Population Survey (CPS) 2016. Available from: http://www.census.gov/programs-surveys/cps/about.html.

Centers for Disease C. Behavioral Risk Factor Surveillance System (BRFSS). 2016a.

Centers for Disease C. Monitoring the Future: National Survey Results on Drug Use 1975-2015. 2016b.

Centers for Disease C. National Adult Tobacco Survey (NATS) 2016c. Available from: http://www.cdc.gov/tobacco/data_statistics/surveys/nats/index.htm.

Centers for Disease C. National Health and Nutrition Examination Survey (NHANES) 2016d. Available from: http://www.cdc.gov/nchs/nhanes.htm.

Centers for Disease C. National Health Interview Survey 2016e [cited 2016 April 19th]. Available from: http://www.cdc.gov/nchs/nhis/index.htm.

Centers for Disease C. National Youth Tobacco Survey (NYTS) 2016f. Available from: http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/index.htm.

Centers for Disease C. Smoking and Tobacco use 2016g [cited 2016 12 April 2016]. Available from: http://www.cdc.gov/tobacco/index.htm.

Centers for Disease C. Smoking and Tobacco use Surveys 2016h. Available from: http://www.cdc.gov/tobacco/data_statistics/surveys/.

Centers for Disease C. Youth Risk Behavior Surveillance System (YRBSS) 2016i. Available from: http://www.cdc.gov/healthyyouth/data/yrbs/index.htm.

Centers for Disease C. Youth Tobacco Survey (YTS) 2016j. Available from: http://www.cdc.gov/tobacco/data_statistics/surveys/yts/index.htm.

Chengappa KN, Perkins KA, Brar JS, Schlicht PJ, Turkin SR, Hetrick ML, Levine MD, George TP. Varenicline for smoking cessation in bipolar disorder: a randomized, double-blind, placebo-controlled study. The Journal of clinical psychiatry. 2014; 75(7):765-72.

Cherrington A, Williams JH, Foster PP, Coley HL, Kohler C, Allison JJ, Kiefe CI, Volkman JE, Houston TK. Narratives to enhance smoking cessation interventions among African-American smokers, the ACCE project. BMC research notes. 2015; 8:567.

Choi K, Forster J. Awareness, perceptions and use of snus among young adults from the upper Midwest region of the USA. Tobacco control. 2013a; 22(6):412-7.

Choi K, Forster J. Characteristics associated with awareness, perceptions, and use of electronic nicotine delivery systems among young US Midwestern adults. American journal of public health. 2013b; 103(3):556-61.

Choi K, Forster JL. Beliefs and experimentation with electronic cigarettes: a prospective analysis among young adults. American journal of preventive medicine. 2014; 46(2):175-8.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Choi WS, Harris KJ, Okuyemi K, Ahluwalia JS. Predictors of smoking initiation among college-bound high school students. Annals of behavioral medicine : a publication of the Society of Behavioral Medicine. 2003; 26(1):69-74.

Christensen T, Welsh E, Faseru B. Profile of e-cigarette use and its relationship with cigarette quit attempts and abstinence in Kansas adults. Preventive medicine. 2014; 69:90-4.

Cobb CO, Graham AL. Use of non-assigned interventions in a randomized trial of internet and telephone treatment for smoking cessation. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014a; 16(10):1289-97.

Cobb LK, McAdams-DeMarco MA, Huxley RR, Woodward M, Koton S, Coresh J, Anderson CA. The association of spousal smoking status with the ability to quit smoking: the Atherosclerosis Risk in Communities Study. American journal of epidemiology. 2014b; 179(10):1182-7.

Collins BN, Wileyto EP, Patterson F, Rukstalis M, Audrain-McGovern J, Kaufmann V, Pinto A, Hawk L, Niaura R, Epstein LH, Lerman C. Gender differences in smoking cessation in a placebo-controlled trial of bupropion with behavioral counseling. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2004; 6(1):27-37.

Cook JW, Collins LM, Fiore MC, Smith SS, Fraser D, Bolt DM, Baker TB, Piper ME, Schlam TR, Jorenby D, Loh WY, Mermelstein R. Comparative effectiveness of motivation phase intervention components for use with smokers unwilling to quit: a factorial screening experiment. Addiction. 2016; 111(1):117-28.

Cooper M, Case KR, Loukas A. E-cigarette use among Texas youth: Results from the 2014 Texas Youth Tobacco Survey. Addictive behaviors. 2015; 50:173-7.

Covey LS, Botello-Harbaum M, Glassman AH, Masmela J, LoDuca C, Salzman V, Fried J. Smokers' response to combination bupropion, nicotine patch, and counseling treatment by race/ethnicity. Ethnicity & disease. 2008; 18(1):59-64.

Covey LS, Weissman J, LoDuca C, Duan N. A comparison of abstinence outcomes among gay/bisexual and heterosexual male smokers in an intensive, non-tailored smoking cessation study. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2009; 11(11):1374-7.

Cox LS, Nollen NL, Mayo MS, Choi WS, Faseru B, Benowitz NL, Tyndale RF, Okuyemi KS, Ahluwalia JS. Bupropion for smoking cessation in African American light smokers: a randomized controlled trial. Journal of the National Cancer Institute. 2012; 104(4):290-8.

Croghan IT, Hurt RD, Ebbert JO, Croghan GA, Polk OD, Stella PJ, Novotny PJ, Sloan J, Loprinzi CL. Racial differences in smoking abstinence rates in a multicenter, randomized, open-label trial in the United States. Zeitschrift fur Gesundheitswissenschaften = Journal of public health. 2010; 18(1):59-68.

Culhane MA, Schoenfeld DA, Barr RS, Cather C, Deckersbach T, Freudenreich O, Goff DC, Rigotti NA, Evins AE. Predictors of early abstinence in smokers with schizophrenia. The Journal of clinical psychiatry. 2008; 69(11):1743-50.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Dal Cin S, Stoolmiller M, Sargent JD. Exposure to smoking in movies and smoking initiation among black youth. American journal of preventive medicine. 2013; 44(4):345-50.

Dale LC, Glover ED, Sachs DP, Schroeder DR, Offord KP, Croghan IT, Hurt RD. Bupropion for smoking cessation : predictors of successful outcome. Chest. 2001; 119(5):1357-64.

Dalton MA, Beach ML, Adachi-Mejia AM, Longacre MR, Matzkin AL, Sargent JD, Heatherton TF, Titus-Ernstoff L. Early exposure to movie smoking predicts established smoking by older teens and young adults. Pediatrics. 2009; 123(4):e551-8.

Daza P, Cofta-Woerpel L, Mazas C, Fouladi RT, Cinciripini PM, Gritz ER, Wetter DW. Racial and ethnic differences in predictors of smoking cessation. Substance use & misuse. 2006; 41(3):317-39.

Dickerson F, Stallings CR, Origoni AE, Vaughan C, Khushalani S, Schroeder J, Yolken RH. Cigarette smoking among persons with schizophrenia or bipolar disorder in routine clinical settings, 1999-2011. Psychiatric services. 2013; 64(1):44-50.

Distefan JM, Gilpin EA, Choi WS, Pierce JP. Parental influences predict adolescent smoking in the United States, 1989-1993. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 1998; 22(6):466-74.

Doran N, Khoddam R, Sanders PE, Schweizer CA, Trim RS, Myers MG. A prospective study of the Acquired Preparedness Model: the effects of impulsivity and expectancies on smoking initiation in college students. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors. 2013; 27(3):714-22.

Dutra SJ, Stoeckel LE, Carlini SV, Pizzagalli DA, Evins AE. Varenicline as a smoking cessation aid in schizophrenia: effects on smoking behavior and reward sensitivity. Psychopharmacology. 2012; 219(1):25-34.

Ebbert JO, Hatsukami DK, Croghan IT, Schroeder DR, Allen SS, Hays JT, Hurt RD. Combination varenicline and bupropion SR for tobacco-dependence treatment in cigarette smokers: a randomized trial. Jama. 2014; 311(2):155-63.

Elfassy T, Yi SS, Kansagra SM. Trends in cigarette, cigar, and smokeless tobacco use among New York City public high school youth smokers, 2001-2013. Preventive medicine reports. 2015; 2:488-91.

Enofe N, Berg CJ, Nehl EJ. Alternative tobacco use among college students: who is at highest risk? American journal of health behavior. 2014; 38(2):180-9.

Evins AE, Cather C, Culhane MA, Birnbaum A, Horowitz J, Hsieh E, Freudenreich O, Henderson DC, Schoenfeld DA, Rigotti NA, Goff DC. A 12-week double-blind, placebo-controlled study of bupropion sr added to high-dose dual nicotine replacement therapy for smoking cessation or reduction in schizophrenia. Journal of clinical psychopharmacology. 2007; 27(4):380-6.

Evins AE, Cather C, Pratt SA, Pachas GN, Hoeppner SS, Goff DC, Achtyes ED, Ayer D, Schoenfeld DA. Maintenance treatment with varenicline for smoking cessation in

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

patients with schizophrenia and bipolar disorder: a randomized clinical trial. Jama. 2014; 311(2):145-54.

Evins AE, Culhane MA, Alpert JE, Pava J, Liese BS, Farabaugh A, Fava M. A controlled trial of bupropion added to nicotine patch and behavioral therapy for smoking cessation in adults with unipolar depressive disorders. Journal of clinical psychopharmacology. 2008; 28(6):660-6.

Fallin A, Goodin A, Lee YO, Bennett K. Smoking characteristics among lesbian, gay, and bisexual adults. Preventive medicine. 2015; 74:123-30.

Fallin A, Lee YO, Bennett K, Goodin A. Smoking Cessation Awareness and Utilization Among Lesbian, Gay, Bisexual, and Transgender Adults: An Analysis of the 2009-2010 National Adult Tobacco Survey. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016; 18(4):496-500.

Farrelly MC, Kamyab K, Nonnemaker J, Crankshaw E, Allen JA. Movie smoking and youth initiation: parsing smoking imagery and other adult content. PloS one. 2012; 7(12):e51935.

Farsalinos KE, Polosa R. Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review. Therapeutic advances in drug safety. 2014a; 5(2):67-86.

Farsalinos KE, Spyrou A, Tsimopoulou K, Stefopoulos C, Romagna G, Voudris V. Nicotine absorption from electronic cigarette use: comparison between first and new-generation devices. Scientific reports. 2014b; 4:4133.

FDA (Food and Drug Administration). Guidance for industry - Modified risk tobacco product applications - Draft Guidance. 2012.

Fix BV, O'Connor RJ, Vogl L, Smith D, Bansal-Travers M, Conway KP, Ambrose B, Yang L, Hyland A. Patterns and correlates of polytobacco use in the United States over a decade: NSDUH 2002-2011. Addictive behaviors. 2014; 39(4):768-81.

Flay BR, Hu FB, Siddiqui O, Day LE, Hedeker D, Petraitis J, Richardson J, Sussman S. Differential influence of parental smoking and friends' smoking on adolescent initiation and escalation of smoking. Journal of health and social behavior. 1994; 35(3):248-65.

Fletcher JM, Sindelar JL. The Effects of Family Stressors on Substance Use Initiation in Adolescence. Review of economics of the household. 2012; 10(1):99-114.

Fridberg DJ, Cao D, Grant JE, King AC. Naltrexone improves quit rates, attenuates smoking urge, and reduces alcohol use in heavy drinking smokers attempting to quit smoking. Alcoholism, clinical and experimental research. 2014; 38(10):2622-9.

Frieden TJ, HW; Stephens, JW; Thacker, SB; Zaza, S. Quitting Smoking Among Adults - United States, 2001-20102011.

Friedman AS. How does electronic cigarette access affect adolescent smoking? Journal of health economics. 2015; 44:300-8.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Fritz DJ, Hardin SB, Gore PA, Jr., Bram D. A computerized smoking cessation intervention for high school smokers. Pediatric nursing. 2008; 34(1):13-7.

Fu Q, Vaughn MG, Wu LT, Heath AC. Psychiatric correlates of snuff and chewing tobacco use. PloS one. 2014a; 9(12):e113196.

Fu SS, van Ryn M, Sherman SE, Burgess DJ, Noorbaloochi S, Clothier B, Taylor BC, Schlede CM, Burke RS, Joseph AM. Proactive tobacco treatment and population-level cessation: a pragmatic randomized clinical trial. JAMA internal medicine. 2014b; 174(5):671-7.

Gamarel KE, Kahler CW, Lee JH, Reisner SL, Mereish EH, Matthews AK, Operario D. Sexual orientation disparities in smoking vary by sex and household smoking among US adults: Findings from the 2003-2012 National Health and Nutrition Examination Surveys. Preventive medicine. 2016; 82:1-6.

Garcia-Rodriguez O, Secades-Villa R, Florez-Salamanca L, Okuda M, Liu SM, Blanco C. Probability and predictors of relapse to smoking: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug and alcohol dependence. 2013; 132(3):479-85.

Gariti P, Lynch K, Alterman A, Kampman K, Xie H, Varillo K. Comparing smoking treatment programs for lighter smokers with and without a history of heavier smoking. Journal of substance abuse treatment. 2009; 37(3):247-55.

Garvey AJ, Bliss RE, Hitchcock JL, Heinold JW, Rosner B. Predictors of smoking relapse among self-quitters: a report from the Normative Aging Study. Addictive behaviors. 1992; 17(4):367-77.

Gilman SE, Rende R, Boergers J, Abrams DB, Buka SL, Clark MA, Colby SM, Hitsman B, Kazura AN, Lipsitt LP, Lloyd-Richardson EE, Rogers ML, Stanton CA, Stroud LR, Niaura RS. Parental smoking and adolescent smoking initiation: an intergenerational perspective on tobacco control. Pediatrics. 2009; 123(2):e274-81.

Gilreath TD, Leventhal A, Barrington-Trimis JL, Unger JB, Cruz TB, Berhane K, Huh J, Urman R, Wang K, Howland S, Pentz MA, Chou CP, McConnell R. Patterns of Alternative Tobacco Product Use: Emergence of Hookah and E-cigarettes as Preferred Products Amongst Youth. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2016; 58(2):181-5.

Giovenco DP, Lewis MJ, Delnevo CD. Factors associated with e-cigarette use: a national population survey of current and former smokers. American journal of preventive medicine. 2014; 47(4):476-80.

Glasheen C, Hedden SL, Forman-Hoffman VL, Colpe LJ. Cigarette smoking behaviors among adults with serious mental illness in a nationally representative sample. Annals of epidemiology. 2014; 24(10):776-80.

Glover ED, Laflin MT, Schuh KJ, Schuh LM, Nides M, Christen AG, Glover PN, Strnad JV. A randomized, controlled trial to assess the efficacy and safety of a transdermal delivery system of nicotine/mecamylamine in cigarette smokers. Addiction. 2007; 102(5):795-802.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Gokbayrak NS, Paiva AL, Blissmer BJ, Prochaska JO. Predictors of relapse among smokers: transtheoretical effort variables, demographics, and smoking severity. Addictive behaviors. 2015; 42:176-9.

Goldade K, Choi K, Bernat DH, Klein EG, Okuyemi KS, Forster J. Multilevel predictors of smoking initiation among adolescents: findings from the Minnesota Adolescent Community Cohort (MACC) study. Preventive medicine. 2012; 54(3-4):242-6.

Goodwin RD, Kim JH, Weinberger AH, Taha F, Galea S, Martins SS. Symptoms of alcohol dependence and smoking initiation and persistence: a longitudinal study among US adults. Drug and alcohol dependence. 2013; 133(2):718-23.

Gray KM, Carpenter MJ, Baker NL, Hartwell KJ, Lewis AL, Hiott DW, Deas D, Upadhyaya HP. Bupropion SR and contingency management for adolescent smoking cessation. Journal of substance abuse treatment. 2011; 40(1):77-86.

Gray KM, McClure EA, Baker NL, Hartwell KJ, Carpenter MJ, Saladin ME. An exploratory short-term double-blind randomized trial of varenicline versus nicotine patch for smoking cessation in women. Addiction. 2015; 110(6):1027-34.

Green KJ, Hunter CM, Bray RM, Pemberton M, Williams J. Peer and role model influences for cigarette smoking in a young adult military population. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2008; 10(10):1533-41.

Halpern SD, French B, Small DS, Saulsgiver K, Harhay MO, Audrain-McGovern J, Loewenstein G, Brennan TA, Asch DA, Volpp KG. Randomized trial of four financial-incentive programs for smoking cessation. The New England journal of medicine. 2015; 372(22):2108-17.

Hampson SE, Andrews JA, Severson HH, Barckley M. Prospective Predictors of Novel Tobacco and Nicotine Product Use in Emerging Adulthood. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2015; 57(2):186-91.

Hanson K, Allen S, Jensen S, Hatsukami D. Treatment of adolescent smokers with the nicotine patch. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2003; 5(4):515-26.

Harrell PT, Simmons VN, Pineiro B, Correa JB, Menzie NS, Meltzer LR, Unrod M, Brandon TH. E-cigarettes and expectancies: why do some users keep smoking? Addiction. 2015; 110(11):1833-43.

Harris KJ, Okuyemi KS, Catley D, Mayo MS, Ge B, Ahluwalia JS. Predictors of smoking cessation among African-Americans enrolled in a randomized controlled trial of bupropion. Preventive medicine. 2004; 38(4):498-502.

Harte CB, Proctor SP, Vasterling JJ. Prospective examination of cigarette smoking among Iraq-deployed and nondeployed soldiers: prevalence and predictive characteristics. Annals of behavioral medicine : a publication of the Society of Behavioral Medicine. 2014; 48(1):38-49.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Hatsukami DK, Biener L, Leischow SJ, Zeller MR. Tobacco and nicotine product testing. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2012; 14(1):7-17.

Hedden S KJ, Lipari R, Medley G, Tice P. Behavioral Health Trends in the United States: Results from the 2014 National Survey on Drug Use and Health2015. Available from: samhsa.gov.

Heffner JL, Lee TC, Arteaga C, Anthenelli RM. Predictors of post-treatment relapse to smoking in successful quitters: pooled data from two phase III varenicline trials. Drug and alcohol dependence. 2010; 109(1-3):120-5.

Hickman NJ, 3rd, Delucchi KL, Prochaska JJ. A population-based examination of cigarette smoking and mental illness in Black Americans. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2010; 12(11):1125-32.

Hitsman B, Borrelli B, McChargue DE, Spring B, Niaura R. History of depression and smoking cessation outcome: a meta-analysis. Journal of consulting and clinical psychology. 2003; 71(4):657-63.

Horn K, Dino G, Kalsekar I, Massey CJ, Manzo-Tennant K, McGloin T. Exploring the relationship between mental health and smoking cessation: a study of rural teens. Prevention science : the official journal of the Society for Prevention Research. 2004; 5(2):113-26.

Horton JL, Phillips CJ, White MR, LeardMann CA, Crum-Cianflone NF. Trends in new U.S. Marine Corps accessions during the recent conflicts in Iraq and Afghanistan. Military medicine. 2014; 179(1):62-70.

Huang J, Kim Y, Vera L, Emery SL. Electronic Cigarettes Among Priority Populations: Role of Smoking Cessation and Tobacco Control Policies. American journal of preventive medicine. 2016; 50(2):199-209.

Hughes JR, Carpenter MJ, Naud S. Do point prevalence and prolonged abstinence measures produce similar results in smoking cessation studies? A systematic review. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2010; 12(7):756-62.

Hughes JR, Marcy TW, Naud S. Interest in treatments to stop smoking. Journal of substance abuse treatment. 2009; 36(1):18-24.

Hughes JR, Peters EN, Naud S. Relapse to smoking after 1 year of abstinence: a meta-analysis. Addictive behaviors. 2008; 33(12):1516-20.

Hughes JR, Solomon LJ, Naud S, Fingar JR, Helzer JE, Callas PW. Natural history of attempts to stop smoking. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(9):1190-8.

Husky MM, Mazure CM, Paliwal P, McKee SA. Gender differences in the comorbidity of smoking behavior and major depression. Drug and alcohol dependence. 2008; 93(1-2):176-9.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Jackson C, Brown JD, L'Engle KL. R-rated movies, bedroom televisions, and initiation of smoking by white and black adolescents. Archives of pediatrics & adolescent medicine. 2007; 161(3):260-8.

Jackson C, Dickinson D. Enabling parents who smoke to prevent their children from initiating smoking: results from a 3-year intervention evaluation. Archives of pediatrics & adolescent medicine. 2006; 160(1):56-62.

Jackson C, Henriksen L. Do as I say: parent smoking, antismoking socialization, and smoking onset among children. Addictive behaviors. 1997; 22(1):107-14.

Jamal A, Agaku IT, O'Connor E, King BA, Kenemer JB, Neff L. Current cigarette smoking among adults--United States, 2005-2013. MMWR Morbidity and mortality weekly report. 2014; 63(47):1108-12.

Jamal A, Homa DM, O'Connor E, Babb SD, Caraballo RS, Singh T, Hu SS, King BA. Current cigarette smoking among adults - United States, 2005-2014. MMWR Morbidity and mortality weekly report. 2015; 64(44):1233-40.

Japuntich SJ, Zehner ME, Smith SS, Jorenby DE, Valdez JA, Fiore MC, Baker TB, Gustafson DH. Smoking cessation via the internet: a randomized clinical trial of an internet intervention as adjuvant treatment in a smoking cessation intervention. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2006; 8 Suppl 1:S59-67.

Javitz HS, Swan GE, Lerman C. The dynamics of the urge-to-smoke following smoking cessation via pharmacotherapy. Addiction. 2011; 106(10):1835-45.

Joffe A, McNeely C, Colantuoni E, An MW, Wang W, Scharfstein D. Evaluation of school-based smoking-cessation interventions for self-described adolescent smokers. Pediatrics. 2009; 124(2):e187-94.

Johnston LOM, PM.; Bachman, JG., et al. Monitoring the Future national survey results on drug use, 1975–2013: Volume I, Secondary school students. Ann Arbor: Institute for Social Research, The University of Michigan. 2014.

Johnston LOM, PM.; Miech, RA, Bachman, JG & Schulenberg, JE. Monitoring the Future national survey results on drug use, 1975-2015: Overview, key findings on adolescent drug use.2016.

Jordan JN, McElroy JA, Everett KD. Smoking initiation, tobacco product use, and secondhand smoke exposure among general population and sexual minority youth, Missouri, 2011-2012. Preventing chronic disease. 2014; 11:E113.

Kahler CW, Spillane NS, Day AM, Cioe PA, Parks A, Leventhal AM, Brown RA. Positive Psychotherapy for Smoking Cessation: A Pilot Randomized Controlled Trial. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(11):1385-92.

Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. The Lancet Respiratory medicine. 2016; 4(2):116-28.

Kandel D. Stages in adolescent involvement in drug use. Science. 1975; 190(4217):912-4.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Kann L, Kinchen S, Shanklin SL, Flint KH, Kawkins J, Harris WA, Lowry R, Olsen EO, McManus T, Chyen D, Whittle L, Taylor E, Demissie Z, Brener N, Thornton J, Moore J, Zaza S, Centers for Disease C, Prevention. Youth risk behavior surveillance--United States, 2013. MMWR supplements. 2014; 63(4):1-168.

Kasza KA, Bansal-Travers M, O'Connor RJ, Compton WM, Kettermann A, Borek N, Fong GT, Cummings KM, Hyland AJ. Cigarette smokers' use of unconventional tobacco products and associations with quitting activity: findings from the ITC-4 U.S. cohort. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(6):672-81.

Kaufman AR, Land S, Parascandola M, Augustson E, Backinger CL. Tobacco use transitions in the United States: The National Longitudinal Study of Adolescent Health. Preventive medicine. 2015; 81:251-7.

Kaufman AR, Mays D, Koblitz AR, Portnoy DB. Judgments, awareness, and the use of snus among adults in the United States. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(10):1404-8.

Kendzor DE, Businelle MS, Reitzel LR, Castro Y, Vidrine JI, Mazas CA, Cinciripini PM, Lam CY, Adams CE, Correa-Fernandez V, Cano MA, Wetter DW. The influence of discrimination on smoking cessation among Latinos. Drug and alcohol dependence. 2014; 136:143-8.

Kessler DA. Nicotine addiction in young people. The New England journal of medicine. 1995; 333(3):186-9.

Kiefe CI, Williams OD, Lewis CE, Allison JJ, Sekar P, Wagenknecht LE. Ten-year changes in smoking among young adults: are racial differences explained by socioeconomic factors in the CARDIA study? American journal of public health. 2001; 91(2):213-8.

Killen JD, Fortmann SP. Craving is associated with smoking relapse: findings from three prospective studies. Experimental and clinical psychopharmacology. 1997; 5(2):137-42.

King BA, Patel R, Nguyen KH, Dube SR. Trends in awareness and use of electronic cigarettes among US adults, 2010-2013. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(2):219-27.

Kinnunen T, Korhonen T, Garvey AJ. Role of nicotine gum and pretreatment depressive symptoms in smoking cessation: twelve-month results of a randomized placebo controlled trial. International journal of psychiatry in medicine. 2008; 38(3):373-89.

Klein EG, Forster JL, Erickson DJ. Longitudinal predictors of stopping smoking in young adulthood. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2013; 53(3):363-7.

Klesges RC, Ebbert JO, Morgan GD, Sherrill-Mittleman D, Asfar T, Talcott WG, Debon M. Impact of differing definitions of dual tobacco use: implications for studying dual use and a call for operational definitions. Nicotine & tobacco research :

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

official journal of the Society for Research on Nicotine and Tobacco. 2011; 13(7):523-31.

Knight C, Howard P, Baker CL, Marton JP. The cost-effectiveness of an extended course (12+12 weeks) of varenicline compared with other available smoking cessation strategies in the United States: an extension and update to the BENESCO model. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2010; 13(2):209-14.

Kobus K. Peers and adolescent smoking. Addiction. 2003; 98 Suppl 1:37-55.

Kotov R, Guey LT, Bromet EJ, Schwartz JE. Smoking in schizophrenia: diagnostic specificity, symptom correlates, and illness severity. Schizophrenia bulletin. 2010; 36(1):173-81.

Kozlowski LT, O'Connor RJ, Edwards BQ, Flaherty BP. Most smokeless tobacco use is not a causal gateway to cigarettes: using order of product use to evaluate causation in a national US sample. Addiction. 2003; 98(8):1077-85.

Krall EA, Garvey AJ, Garcia RI. Smoking relapse after 2 years of abstinence: findings from the VA Normative Aging Study. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2002; 4(1):95-100.

Kravitz-Wirtz N. A discrete-time analysis of the effects of more prolonged exposure to neighborhood poverty on the risk of smoking initiation by age 25. Social science & medicine. 2016; 148:79-92.

Krishnan-Sarin S, Morean ME, Camenga DR, Cavallo DA, Kong G. E-cigarette Use Among High School and Middle School Adolescents in Connecticut. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(7):810-8.

Latimer LA, Batanova M, Loukas A. Prevalence and harm perceptions of various tobacco products among college students. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(5):519-26.

Lechner WV, Tackett AP, Grant DM, Tahirkheli NN, Driskill LM, Wagener TL. Effects of duration of electronic cigarette use. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(2):180-5.

Lee PN. Appropriate and inappropriate methods for investigating the "gateway" hypothesis, with a review of the evidence linking prior snus use to later cigarette smoking. Harm reduction journal. 2015; 12:8.

Leventhal AM, Strong DR, Kirkpatrick MG, Unger JB, Sussman S, Riggs NR, Stone MD, Khoddam R, Samet JM, Audrain-McGovern J. Association of Electronic Cigarette Use With Initiation of Combustible Tobacco Product Smoking in Early Adolescence. Jama. 2015; 314(7):700-7.

Lillard DR, Plassmann V, Kenkel D, Mathios A. Who kicks the habit and how they do it: socioeconomic differences across methods of quitting smoking in the USA. Social science & medicine. 2007; 64(12):2504-19.

Lipkus IM, Barefoot JC, Williams RB, Siegler IC. Personality measures as predictors of smoking initiation and cessation in the UNC Alumni Heart Study. Health

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

psychology : official journal of the Division of Health Psychology, American Psychological Association. 1994; 13(2):149-55.

Little MA, Derefinko KJ, Bursac Z, Ebbert JO, Colvin L, Talcott GW, Hryshko-Mullen AS, Richey PA, Klesges RC. Prevalence and Correlates of Tobacco and Nicotine Containing Product Use in a Sample of United States Air Force Trainees. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016; 18(4):416-23.

Loukas A, Batanova M, Fernandez A, Agarwal D. Changes in use of cigarettes and non-cigarette alternative products among college students. Addictive behaviors. 2015; 49:46-51.

Loukas A, Batanova MD, Velazquez CE, Lang WJ, Sneden GG, Pasch KE, Karn SS, Robertson TR. Who uses snus? A study of Texas adolescents. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2012; 14(5):626-30.

Lukowski AV, Morris CD, Young SE, Tinkelman D. Quitline Outcomes for Smokers in 6 States: Rates of Successful Quitting Vary by Mental Health Status. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(8):924-30.

Mahabee-Gittens EM, Khoury JC, Huang B, Dorn LD, Ammerman RT, Gordon JS. The Protective Influence of Family Bonding on Smoking Initiation in Adolescents by Racial/Ethnic and Age Subgroups. Journal of child & adolescent substance abuse. 2011; 20(3):270-87.

Mahabee-Gittens EM, Xiao Y, Gordon JS, Khoury JC. Continued importance of family factors in youth smoking behavior. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2012; 14(12):1458-66.

Mahabee-Gittens EM, Xiao Y, Gordon JS, Khoury JC. The dynamic role of parental influences in preventing adolescent smoking initiation. Addictive behaviors. 2013; 38(4):1905-11.

Mamary EM, Bahrs D, Martinez S. Cigarette smoking and the desire to quit among individuals living with HIV. AIDS patient care and STDs. 2002; 16(1):39-42.

Mathur C, Stigler MH, Erickson DJ, Perry CL, Forster JL. Transitions in smoking behavior during emerging adulthood: a longitudinal analysis of the effect of home smoking bans. American journal of public health. 2014; 104(4):715-20.

Matthews AK, Li CC, Kuhns LM, Tasker TB, Cesario JA. Results from a community-based smoking cessation treatment program for LGBT smokers. Journal of environmental and public health. 2013; 2013:984508.

Matthews AK, Riley BB, Everett B, Hughes TL, Aranda F, Johnson T. A longitudinal study of the correlates of persistent smoking among sexual minority women. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(9):1199-206.

Mazurek JM, Syamlal G, King BA, Castellan RM, Division of Respiratory Disease Studies NIfOS, Health CDC. Smokeless tobacco use among working adults -

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

United States, 2005 and 2010. MMWR Morbidity and mortality weekly report. 2014; 63(22):477-82.

McMillen R, Maduka J, Winickoff J. Use of emerging tobacco products in the United States. Journal of environmental and public health. 2012; 2012:989474.

McMillen RC, Gottlieb MA, Shaefer RM, Winickoff JP, Klein JD. Trends in Electronic Cigarette Use Among U.S. Adults: Use is Increasing in Both Smokers and Nonsmokers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014.

Mdodo R, Frazier EL, Dube SR, Mattson CL, Sutton MY, Brooks JT, Skarbinski J. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States: cross-sectional surveys. Annals of internal medicine. 2015; 162(5):335-44.

Melikian A, Hoffman, D. Smokeless tobacco: a gateway to smoking or a way away from smoking. Biomarkers. 2009; 14:85-9.

Merzel CR, Isasi CR, Strizich G, Castaneda SF, Gellman M, Maisonet Giachello AL, Lee DJ, Penedo FJ, Perreira KM, Kaplan RC. Smoking cessation among U.S. Hispanic/Latino adults: Findings from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). Preventive medicine. 2015; 81:412-9.

Messer K, Mills AL, White MM, Pierce JP. The effect of smoke-free homes on smoking behavior in the U.S. American journal of preventive medicine. 2008; 35(3):210-6.

Miller MB, Lechner WV, Meier E, Tucker RP, Wiener JL. Dual tobacco use among college students: contexts of use, self-perceptions, and attitudes toward quitting. Substance use & misuse. 2014; 49(6):700-7.

Moadel AB, Bernstein SL, Mermelstein RJ, Arnsten JH, Dolce EH, Shuter J. A randomized controlled trial of a tailored group smoking cessation intervention for HIV-infected smokers. Journal of acquired immune deficiency syndromes. 2012; 61(2):208-15.

Morean ME, Kong G, Camenga DR, Cavallo DA, Carroll KM, Pittman B, Krishnan-Sarin S. Contingency management improves smoking cessation treatment outcomes among highly impulsive adolescent smokers relative to cognitive behavioral therapy. Addictive behaviors. 2015; 42:86-90.

Mumford EA, Levy DT, Gitchell JG, Blackman KO. Smokeless tobacco use 1992-2002: trends and measurement in the Current Population Survey-Tobacco Use Supplements. Tobacco control. 2006; 15(3):166-71.

Muramoto ML, Leischow SJ, Sherrill D, Matthews E, Strayer LJ. Randomized, double-blind, placebo-controlled trial of 2 dosages of sustained-release bupropion for adolescent smoking cessation. Archives of pediatrics & adolescent medicine. 2007; 161(11):1068-74.

Murphy JM, Mahoney MC, Hyland AJ, Higbee C, Cummings KM. Disparity in the use of smoking cessation pharmacotherapy among Medicaid and general population smokers. Journal of public health management and practice : JPHMP. 2005; 11(4):341-5.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Nakajima M, al'Absi M. Predictors of risk for smoking relapse in men and women: a prospective examination. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors. 2012; 26(3):633-7.

Nguyen K, Marshall L, Hu S, Neff L, Centers for Disease C, Prevention. State-specific prevalence of current cigarette smoking and smokeless tobacco use among adults aged >/=18 years - United States, 2011-2013. MMWR Morbidity and mortality weekly report. 2015; 64(19):532-6.

Nitzkin JL. The case in favor of E-cigarettes for tobacco harm reduction. International journal of environmental research and public health. 2014; 11(6):6459-71.

Nollen NL, Cox LS, Nazir N, Ellerbeck EF, Owen A, Pankey S, Thompson N, Ahluwalia JS. A pilot clinical trial of varenicline for smoking cessation in black smokers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2011; 13(9):868-73.

Nordstrom BL, Kinnunen T, Utman CH, Krall EA, Vokonas PS, Garvey AJ. Predictors of continued smoking over 25 years of follow-up in the normative aging study. American journal of public health. 2000; 90(3):404-6.

O'Connor RJ, Flaherty BP, Quinio Edwards B, Kozlowski LT. Regular smokeless tobacco use is not a reliable predictor of smoking onset when psychosocial predictors are included in the model. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2003; 5(4):535-43.

O'Connor RJ, Kozlowski LT, Flaherty BP, Edwards BQ. Most smokeless tobacco use does not cause cigarette smoking: results from the 2000 National Household Survey on Drug Abuse. Addictive behaviors. 2005; 30(2):325-36.

Ordonez JE, Kleinschmidt KC, Forrester MB. Electronic cigarette exposures reported to Texas poison centers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(2):209-11.

Pachas GN, Cather C, Pratt SA, Hoeppner B, Nino J, Carlini SV, Achtyes ED, Lando H, Mueser KT, Rigotti NA, Goff DC, Evins AE. Varenicline for Smoking Cessation in Schizophrenia: Safety and Effectiveness in a 12-Week, Open-Label Trial. Journal of dual diagnosis. 2012; 8(2):117-25.

Paek HJ, Kim S, Hove T, Huh JY. Reduced harm or another gateway to smoking? source, message, and information characteristics of E-cigarette videos on YouTube. Journal of health communication. 2014; 19(5):545-60.

Patnode CD, O'Connor E, Whitlock EP, Perdue LA, Soh C. Primary Care Relevant Interventions for Tobacco Use Prevention and Cessation in Children and Adolescents: A Systematic Evidence Review for the US Preventive Services Task Force. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. ed. Rockville (MD): 2012. p.

Pearson JL, Richardson A, Niaura RS, Vallone DM, Abrams DB. e-Cigarette awareness, use, and harm perceptions in US adults. American journal of public health. 2012; 102(9):1758-66.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Peiper N, Rodu B. Evidence of sex differences in the relationship between current tobacco use and past-year serious psychological distress: 2005-2008 National Survey on Drug Use and Health. Social psychiatry and psychiatric epidemiology. 2013; 48(8):1261-71.

Pentz MA, Shin H, Riggs N, Unger JB, Collison KL, Chou CP. Parent, peer, and executive function relationships to early adolescent e-cigarette use: a substance use pathway? Addictive behaviors. 2015; 42:73-8.

Peterson AV, Jr., Kealey KA, Mann SL, Marek PM, Ludman EJ, Liu J, Bricker JB. Group-randomized trial of a proactive, personalized telephone counseling intervention for adolescent smoking cessation. Journal of the National Cancer Institute. 2009; 101(20):1378-92.

Physicians RCo. RCP statement on e-cigarettes2014 May 27th 2016.

Piasecki TM, Fiore MC, McCarthy DE, Baker TB. Have we lost our way? The need for dynamic formulations of smoking relapse proneness. Addiction. 2002; 97(9):1093-108.

Pineiro B, Correa JB, Simmons VN, Harrell PT, Menzie NS, Unrod M, Meltzer LR, Brandon TH. Gender differences in use and expectancies of e-cigarettes: Online survey results. Addictive behaviors. 2016; 52:91-7.

Piper ME, Fiore MC, Smith SS, Fraser D, Bolt DM, Collins LM, Mermelstein R, Schlam TR, Cook JW, Jorenby DE, Loh WY, Baker TB. Identifying effective intervention components for smoking cessation: a factorial screening experiment. Addiction. 2016; 111(1):129-41.

Piper ME, Smith SS, Schlam TR, Fiore MC, Jorenby DE, Fraser D, Baker TB. A randomized placebo-controlled clinical trial of 5 smoking cessation pharmacotherapies. Archives of general psychiatry. 2009; 66(11):1253-62.

Pokhrel P, Little MA, Fagan P, Muranaka N, Herzog TA. Electronic cigarette use outcome expectancies among college students. Addictive behaviors. 2014; 39(6):1062-5.

Popova L, Ling PM. Alternative tobacco product use and smoking cessation: a national study. American journal of public health. 2013; 103(5):923-30.

Porter L, Duke J, Hennon M, Dekevich D, Crankshaw E, Homsi G, Farrelly M. Electronic Cigarette and Traditional Cigarette Use among Middle and High School Students in Florida, 2011-2014. PloS one. 2015; 10(5):e0124385.

Prevention CfDCa. Types of Smokeless Tobacco 2016 [June 1st 2016]. Available from: http://www.cdc.gov/tobacco/data_statistics/fact_sheets/smokeless/use_us/types/index.htm.

Prevention CfDCa. Youth and Tobacco Use2015. Available from: http://www.cdc.gov/tobacco/data_statistics/fact_sheets/youth_data/tobacco_use/.

Primack BA, Soneji S, Stoolmiller M, Fine MJ, Sargent JD. Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults. JAMA pediatrics. 2015; 169(11):1018-23.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Prochaska JJ, Benowitz NL. The Past, Present, and Future of Nicotine Addiction Therapy. Annual review of medicine. 2016; 67:467-86.

Puckett M, Neri A, Thompson T, Underwood JM, Momin B, Kahende J, Zhang L, Stewart SL, Centers for Disease C, Prevention. Tobacco cessation among users of telephone and web-based interventions--four states, 2011-2012. MMWR Morbidity and mortality weekly report. 2015; 63(51):1217-21.

Pulvers K, Hayes RB, Scheuermann TS, Romero DR, Emami AS, Resnicow K, Olendzki E, Person SD, Ahluwalia JS. Tobacco Use, Quitting Behavior, and Health Characteristics Among Current Electronic Cigarette Users in a National Tri-Ethnic Adult Stable Smoker Sample. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(9):1085-95.

Rafful C, Garcia-Rodriguez O, Wang S, Secades-Villa R, Martinez-Ortega JM, Blanco C. Predictors of quit attempts and successful quit attempts in a nationally representative sample of smokers. Addictive behaviors. 2013; 38(4):1920-3.

Rajesh V, Diamond PM, Spitz MR, Wilkinson AV. Smoking Initiation Among Mexican Heritage Youth and the Roles of Family Cohesion and Conflict. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2015; 57(1):24-30.

Ramo DE, Thrul J, Chavez K, Delucchi KL, Prochaska JJ. Feasibility and Quit Rates of the Tobacco Status Project: A Facebook Smoking Cessation Intervention for Young Adults. Journal of medical Internet research. 2015a; 17(12):e291.

Ramo DE, Young-Wolff KC, Prochaska JJ. Prevalence and correlates of electronic-cigarette use in young adults: findings from three studies over five years. Addictive behaviors. 2015b; 41:142-7.

Rass O, Pacek LR, Johnson PS, Johnson MW. Characterizing use patterns and perceptions of relative harm in dual users of electronic and tobacco cigarettes. Experimental and clinical psychopharmacology. 2015; 23(6):494-503.

Rath JM, Villanti AC, Abrams DB, Vallone DM. Patterns of tobacco use and dual use in US young adults: the missing link between youth prevention and adult cessation. Journal of environmental and public health. 2012; 2012:679134.

Reed MB, McCabe C, Lange JE, Clapp JD, Shillington AM. The relationship between alcohol consumption and past-year smoking initiation in a sample of undergraduates. The American journal of drug and alcohol abuse. 2010; 36(4):202-7.

Reed MB, Wang R, Shillington AM, Clapp JD, Lange JE. The relationship between alcohol use and cigarette smoking in a sample of undergraduate college students. Addictive behaviors. 2007; 32(3):449-64.

Regan AK, Dube SR, Arrazola R. Smokeless and flavored tobacco products in the U.S.: 2009 Styles survey results. American journal of preventive medicine. 2012; 42(1):29-36.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Regan AK, Promoff G, Dube SR, Arrazola R. Electronic nicotine delivery systems: adult use and awareness of the 'e-cigarette' in the USA. Tobacco control. 2013; 22(1):19-23.

Regan S, Reid ZZ, Kelley JH, Reyen M, Korotkin M, Japuntich SJ, Viana JC, Levy DE, Rigotti NA. Smoking Status Confirmation by Proxy: Validation in a Smoking Cessation Trial. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016; 18(1):34-40.

Reidpath DD, Davey TM, Kadirvelu A, Soyiri IN, Allotey P. Does one cigarette make an adolescent smoker, and is it influenced by age and age of smoking initiation? Evidence of association from the U.S. Youth Risk Behavior Surveillance System (2011). Preventive medicine. 2014; 59:37-41.

Reitzel LR, Langdon KJ, Nguyen NT, Zvolensky MJ. Financial strain and smoking cessation among men and women within a self-guided quit attempt. Addictive behaviors. 2015; 47:66-9.

Rodu B, Stegmayr B, Nasic S, Cole P, Asplund K. Evolving patterns of tobacco use in northern Sweden. Journal of internal medicine. 2003; 253(6):660-5.

Rojewski AM, Toll BA, O'Malley SS. Menthol cigarette use predicts treatment outcomes of weight-concerned smokers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(1):115-9.

Rose JE, Behm FM. Combination treatment with varenicline and bupropion in an adaptive smoking cessation paradigm. The American journal of psychiatry. 2014; 171(11):1199-205.

Roth MT, Andrus MR, Westman EC. Outcomes from an outpatient smoking-cessation clinic. Pharmacotherapy. 2005; 25(2):279-88.

Sachs-Ericsson N, Schmidt NB, Zvolensky MJ, Mitchell M, Collins N, Blazer DG. Smoking cessation behavior in older adults by race and gender: the role of health problems and psychological distress. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2009; 11(4):433-43.

Samet JM. Smoking cessation: benefits versus risks of using pharmacotherapy to quit. Circulation. 2014; 129(1):8-10.

Saunders C, Geletko K. Adolescent cigarette smokers' and non-cigarette smokers' use of alternative tobacco products. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2012; 14(8):977-85.

Scherrer JF, Xian H, Pan H, Pergadia ML, Madden PA, Grant JD, Sartor CE, Haber JR, Jacob T, Bucholz KK. Parent, sibling and peer influences on smoking initiation, regular smoking and nicotine dependence. Results from a genetically informative design. Addictive behaviors. 2012; 37(3):240-7.

Schlam TR, Fiore MC, Smith SS, Fraser D, Bolt DM, Collins LM, Mermelstein R, Piper ME, Cook JW, Jorenby DE, Loh WY, Baker TB. Comparative effectiveness of intervention components for producing long-term abstinence from smoking: a factorial screening experiment. Addiction. 2016; 111(1):142-55.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Schmidt L, Reidmohr A, Harwell TS, Helgerson SD. Prevalence and reasons for initiating use of electronic cigarettes among adults in Montana, 2013. Preventing chronic disease. 2014; 11:E204.

Schmitz JM, Stotts AL, Mooney ME, Delaune KA, Moeller GF. Bupropion and cognitive-behavioral therapy for smoking cessation in women. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2007; 9(6):699-709.

Schneider S, Diehl K. Vaping as a Catalyst for Smoking? An Initial Model on the Initiation of Electronic Cigarette Use and the Transition to Tobacco Smoking Among Adolescents. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015.

Schnoll RA, Goelz PM, Veluz-Wilkins A, Blazekovic S, Powers L, Leone FT, Gariti P, Wileyto EP, Hitsman B. Long-term nicotine replacement therapy: a randomized clinical trial. JAMA internal medicine. 2015; 175(4):504-11.

Schoenborn CA, Gindi RM. Electronic Cigarette Use Among Adults: United States, 2014. NCHS data brief. 2015; (217):1-8.

Services. USDoHaH. The Health consequences of smoking. A report of the Surgeon general.2004.

Severson HH, Forrester KK, Biglan A. Use of smokeless tobacco is a risk factor for cigarette smoking. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2007; 9(12):1331-7.

Shen X, Bachyrycz A, Anderson JR, Tinker D, Raisch DW. Quitting patterns and predictors of success among participants in a tobacco cessation program provided by pharmacists in New Mexico. Journal of managed care & specialty pharmacy. 2014; 20(6):579-87.

Shopland DR, Anderson CM, Burns DM. Association between home smoking restrictions and changes in smoking behaviour among employed women. Journal of epidemiology and community health. 2006; 60 Suppl 2:44-50.

Slopen N, Kontos EZ, Ryff CD, Ayanian JZ, Albert MA, Williams DR. Psychosocial stress and cigarette smoking persistence, cessation, and relapse over 9-10 years: a prospective study of middle-aged adults in the United States. Cancer causes & control : CCC. 2013; 24(10):1849-63.

Smith SS, McCarthy DE, Japuntich SJ, Christiansen B, Piper ME, Jorenby DE, Fraser DL, Fiore MC, Baker TB, Jackson TC. Comparative effectiveness of 5 smoking cessation pharmacotherapies in primary care clinics. Archives of internal medicine. 2009; 169(22):2148-55.

Soneji S, Sargent J, Tanski S. Multiple tobacco product use among US adolescents and young adults. Tobacco control. 2016; 25(2):174-80.

Soneji S, Sargent J, Tanski S. Multiple tobacco product use among US adolescents and young adults. Tobacco control. 2014.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Song AV, Morrell HE, Cornell JL, Ramos ME, Biehl M, Kropp RY, Halpern-Felsher BL. Perceptions of smoking-related risks and benefits as predictors of adolescent smoking initiation. American journal of public health. 2009; 99(3):487-92.

Spangler J, Song E, Pockey J, Sutfin EL, Reboussin BA, Wagoner K, Wolfson M. Correlates of smokeless tobacco use among first year college students. Health education journal. 2014; 73(6):693-701.

Spillane NS, Muller CJ, Noonan C, Goins RT, Mitchell CM, Manson S. Sensation-seeking predicts initiation of daily smoking behavior among American Indian high school students. Addictive behaviors. 2012; 37(12):1303-6.

Stanton CA, Papandonatos GD, Shuter J, Bicki A, Lloyd-Richardson EE, de Dios MA, Morrow KM, Makgoeng SB, Tashima KT, Niaura RS. Outcomes of a Tailored Intervention for Cigarette Smoking Cessation Among Latinos Living With HIV/AIDS. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(8):975-82.

Staten RR, Noland M, Rayens MK, Hahn E, Dignan M, Ridner SL. Social influences on cigarette initiation among college students. American journal of health behavior. 2007; 31(4):353-62.

Stead LF, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, Lancaster T. Nicotine replacement therapy for smoking cessation. The Cochrane database of systematic reviews. 2012; 11:CD000146.

Stewart DW, Cano MA, Correa-Fernandez V, Spears CA, Li Y, Waters AJ, Wetter DW, Vidrine JI. Lower health literacy predicts smoking relapse among racially/ethnically diverse smokers with low socioeconomic status. BMC public health. 2014; 14:716.

Stratton K, Shetty P, Wallace R, Bondurant S. Clearing the smoke: the science base for tobacco harm reduction--executive summary. Tobacco control. 2001; 10(2):189-95.

Sung HY, Wang Y, Yao T, Lightwood J, Max W. Polytobacco Use of Cigarettes, Cigars, Chewing Tobacco, and Snuff Among US Adults. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016; 18(5):817-26.

Sutfin EL, McCoy TP, Morrell HE, Hoeppner BB, Wolfson M. Electronic cigarette use by college students. Drug and alcohol dependence. 2013; 131(3):214-21.

Sutfin EL, Reboussin BA, Debinski B, Wagoner KG, Spangler J, Wolfson M. The Impact of Trying Electronic Cigarettes on Cigarette Smoking by College Students: A Prospective Analysis. American journal of public health. 2015; 105(8):e83-9.

Swan GE, Jack LM, Curry S, Chorost M, Javitz H, McAfee T, Dacey S. Bupropion SR and counseling for smoking cessation in actual practice: predictors of outcome. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2003; 5(6):911-21.

Tami-Maury I, Lin MT, Lapham HL, Hong JH, Cage C, Shete S, Gritz ER. A pilot study to assess tobacco use among sexual minorities in Houston, Texas. The American

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions. 2015; 24(5):391-5.

Taylor N, Choi K, Forster J. Snus use and smoking behaviors: preliminary findings from a prospective cohort study among US Midwest young adults. American journal of public health. 2015; 105(4):683-5.

Tercyak KP, Rodriguez D, Audrain-McGovern J. High school seniors' smoking initiation and progression 1 year after graduation. American journal of public health. 2007; 97(8):1397-8.

Thomas JL, Bengtson JE, Wang Q, Luo X, Marigi E, Ghidei W, Ahluwalia JS. Abstinence rates among college cigarette smokers enrolled in a randomized clinical trial evaluating Quit and Win contests: The impact of concurrent hookah use. Preventive medicine. 2015; 76:20-5.

Timberlake DS, Huh J, Lakon CM. Use of propensity score matching in evaluating smokeless tobacco as a gateway to smoking. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2009; 11(4):455-62.

Titus-Ernstoff L, Dalton MA, Adachi-Mejia AM, Longacre MR, Beach ML. Longitudinal study of viewing smoking in movies and initiation of smoking by children. Pediatrics. 2008; 121(1):15-21.

Torres OV, O'Dell LE. Stress is a principal factor that promotes tobacco use in females. Progress in neuro-psychopharmacology & biological psychiatry. 2016; 65:260-8.

Trumbo CW, Harper R. Use and perception of electronic cigarettes among college students. Journal of American college health : J of ACH. 2013; 61(3):149-55.

Tseng TY, Ostroff JS, Campo A, Gerard M, Kirchner T, Rotrosen J, Shelley D. A Randomized Trial Comparing the Effect of Nicotine Versus Placebo Electronic Cigarettes on Smoking Reduction Among Young Adult Smokers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016.

Tucker JS, Edelen MO, Go MH, Pollard MS, Green HD, Jr., Kennedy DP. Resisting Smoking When a Best Friend Smokes: Do Intrapersonal and Contextual Factors Matter? Journal of research on adolescence : the official journal of the Society for Research on Adolescence. 2012; 22(1):113-22.

Tworek C, Schauer GL, Wu CC, Malarcher AM, Jackson KJ, Hoffman AC. Youth tobacco cessation: quitting intentions and past-year quit attempts. American journal of preventive medicine. 2014; 47(2 Suppl 1):S15-27.

Vakkalanka JP, Hardison LS, Jr., Holstege CP. Epidemiological trends in electronic cigarette exposures reported to U.S. Poison Centers. Clinical toxicology. 2014; 52(5):542-8.

Vanable PA, Carey MP, Carey KB, Maisto SA. Smoking among psychiatric outpatients: relationship to substance use, diagnosis, and illness severity. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors. 2003; 17(4):259-65.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Varghese M, Sheffer C, Stitzer M, Landes R, Brackman SL, Munn T. Socioeconomic disparities in telephone-based treatment of tobacco dependence. American journal of public health. 2014; 104(8):e76-84.

Vickerman KA, Schauer GL, Malarcher AM, Zhang L, Mowery P, Nash CM. Quitline Use and Outcomes among Callers with and without Mental Health Conditions: A 7-Month Follow-Up Evaluation in Three States. BioMed research international. 2015a; 2015:817298.

Vickerman KA, Zhang L, Malarcher A, Mowery P, Nash C. Cessation Outcomes Among Quitline Callers in Three States During a National Tobacco Education Campaign. Preventing chronic disease. 2015b; 12:E110.

Vickers KS, Thomas JL, Patten CA, Mrazek DA. Prevention of tobacco use in adolescents: review of current findings and implications for healthcare providers. Current opinion in pediatrics. 2002; 14(6):708-12.

Vidrine DJ, Kypriotakis G, Li L, Arduino RC, Fletcher FE, Tami-Maury I, Gritz ER. Mediators of a smoking cessation intervention for persons living with HIV/AIDS. Drug and alcohol dependence. 2015; 147:76-80.

Voorhees CC, Ye C, Carter-Pokras O, MacPherson L, Kanamori M, Zhang G, Chen L, Fiedler R. Peers, tobacco advertising, and secondhand smoke exposure influences smoking initiation in diverse adolescents. American journal of health promotion : AJHP. 2011; 25(3):e1-11.

Walker JF, Loprinzi PD. Longitudinal examination of predictors of smoking cessation in a national sample of U.S. adolescent and young adult smokers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2014; 16(6):820-7.

Walton KM, Abrams DB, Bailey WC, Clark D, Connolly GN, Djordjevic MV, Eissenberg TE, Fiore MC, Goniewicz ML, Haverkos L, Hecht SS, Henningfield JE, Hughes JR, Oncken CA, Postow L, Rose JE, Wanke KL, Yang L, Hatsukami DK. NIH electronic cigarette workshop: developing a research agenda. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015; 17(2):259-69.

Weaver SR, Majeed BA, Pechacek TF, Nyman AL, Gregory KR, Eriksen MP. Use of electronic nicotine delivery systems and other tobacco products among USA adults, 2014: results from a national survey. International journal of public health. 2016; 61(2):177-88.

Webb MS, de Ybarra DR, Baker EA, Reis IM, Carey MP. Cognitive-behavioral therapy to promote smoking cessation among African American smokers: a randomized clinical trial. Journal of consulting and clinical psychology. 2010; 78(1):24-33.

Weinberger AH, Reutenauer EL, Jatlow PI, O'Malley SS, Potenza MN, George TP. A double-blind, placebo-controlled, randomized clinical trial of oral selegiline hydrochloride for smoking cessation in nicotine-dependent cigarette smokers. Drug and alcohol dependence. 2010; 107(2-3):188-95.

Weiss JW, Mouttapa M, Cen S, Johnson CA, Unger J. Longitudinal effects of hostility, depression, and bullying on adolescent smoking initiation. The Journal of

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

adolescent health : official publication of the Society for Adolescent Medicine. 2011; 48(6):591-6.

White HR, Jarrett N, Valencia EY, Loeber R, Wei E. Stages and sequences of initiation and regular substance use in a longitudinal cohort of black and white male adolescents. Journal of studies on alcohol and drugs. 2007; 68(2):173-81.

White HR, Pandina RJ, Chen PH. Developmental trajectories of cigarette use from early adolescence into young adulthood. Drug and alcohol dependence. 2002; 65(2):167-78.

Williams M, Villarreal A, Bozhilov K, Lin S, Talbot P. Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. PloS one. 2013; 8(3):e57987.

Wills TA, Knight R, Sargent JD, Gibbons FX, Pagano I, Williams RJ. Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control. 2016.

Wills TA, Knight R, Williams RJ, Pagano I, Sargent JD. Risk factors for exclusive e-cigarette use and dual e-cigarette use and tobacco use in adolescents. Pediatrics. 2015; 135(1):e43-51.

Wills TA KR, Sargent JD, Gibbons FX, Pagano I, Williams RJ. Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control. 2016; 0:1-6.

Yeomans K, Payne KA, Marton JP, Merikle EP, Proskorovsky I, Zou KH, Li Q, Willke RJ. Smoking, smoking cessation and smoking relapse patterns: a web-based survey of current and former smokers in the US. International journal of clinical practice. 2011; 65(10):1043-54.

Zablocki RW, Edland SD, Myers MG, Strong DR, Hofstetter CR, Al-Delaimy WK. Smoking ban policies and their influence on smoking behaviors among current California smokers: a population-based study. Preventive medicine. 2014; 59:73-8.

Zhu SH, Gamst A, Lee M, Cummins S, Yin L, Zoref L. The use and perception of electronic cigarettes and snus among the U.S. population. PloS one. 2013; 8(10):e79332.

Zvolensky MJ, Bakhshaie J, Sheffer C, Perez A, Goodwin RD. Major depressive disorder and smoking relapse among adults in the United States: a 10-year, prospective investigation. Psychiatry research. 2015; 226(1):73-7.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.