

The Changing Tobacco Landscape: Implications for Women and Girls

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*The findings and conclusions in this presentation
are those of the author.*

Disclosures

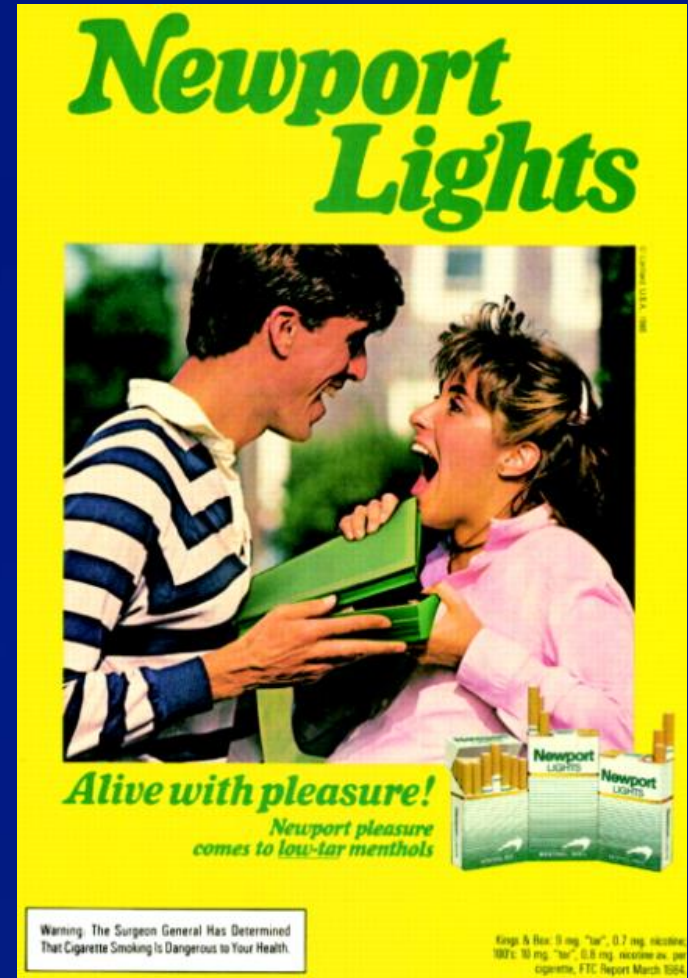
No financial disclosures

Outline

- The changing product landscape
- Patterns of tobacco use
- Industry strategies

- Health effects (pregnancy)
- Perceptions of emerging products

- Future directions



Burden of Disease from Cigarette Smoking

□ Globally

- **Smokers worldwide: 1.1 billion (increasing)**
- **Accounts for 7.7 million deaths and 200 million disability adjusted life years**

□ United States

- **13.1% of adult men smoke**
- **10.1% of adult women smoke**
- **> 200,000 women and 270,000 men die annually from smoking-related disease**
- **More female smokers than male die from CVD (>35 yo), COPD**
- **E-cigarette use in female youth now exceeds that in male youth**

□ Unique health effects in women and girls

<https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2901169-7>

Cornelius ME, Loretan CG, Jamal A, et al. Tobacco Product Use Among Adults — United States, 2021. MMWR Morb Mortal Wkly Rep 2023;72:475–483.

Changing Products

Figure 1. Tobacco Products Currently Under FDA's Authority, 2021



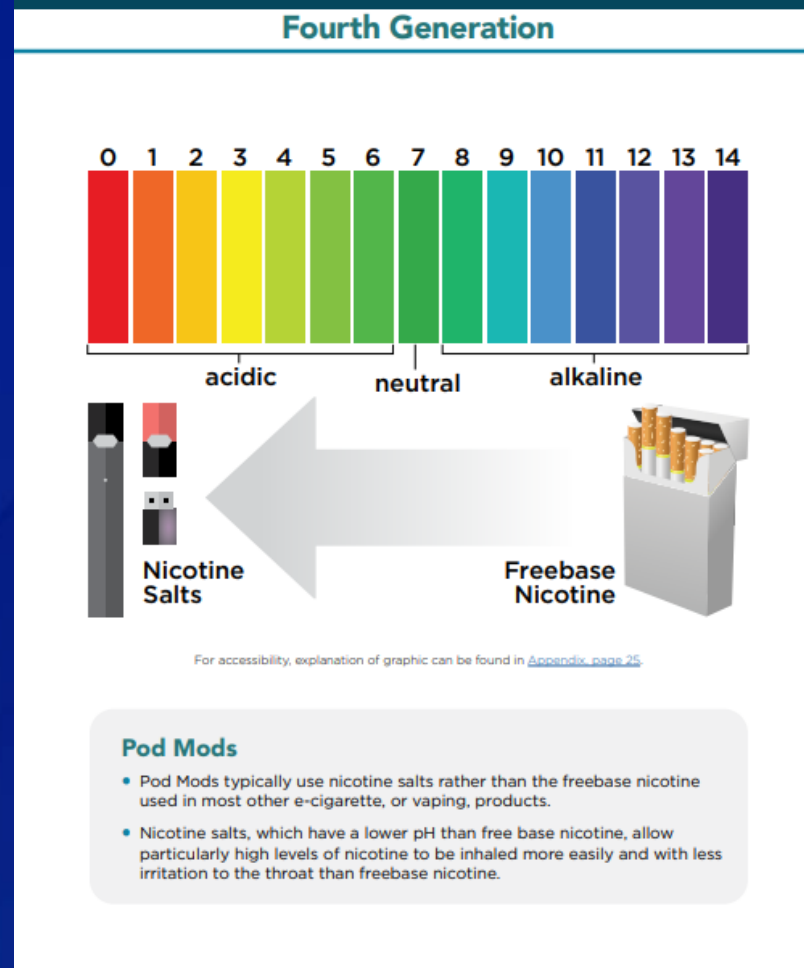
Source: Prepared by CRS with images of smokeless tobacco products, ENDS, cigars, nicotine gels, dissolvable tobacco, and pipe tobacco from FDA's website. Images of cigarettes, roll-your-own tobacco, and hookah tobacco are from Shutterstock.

Notes: Some dissolvable tobacco products can be classified as smokeless tobacco products.



https://www.everycrsreport.com/files/20190813_R45867_b21e213126430b85ccc2b9ee998442f6e7f0b67a.html#Content

Changing Products: E-cigarettes



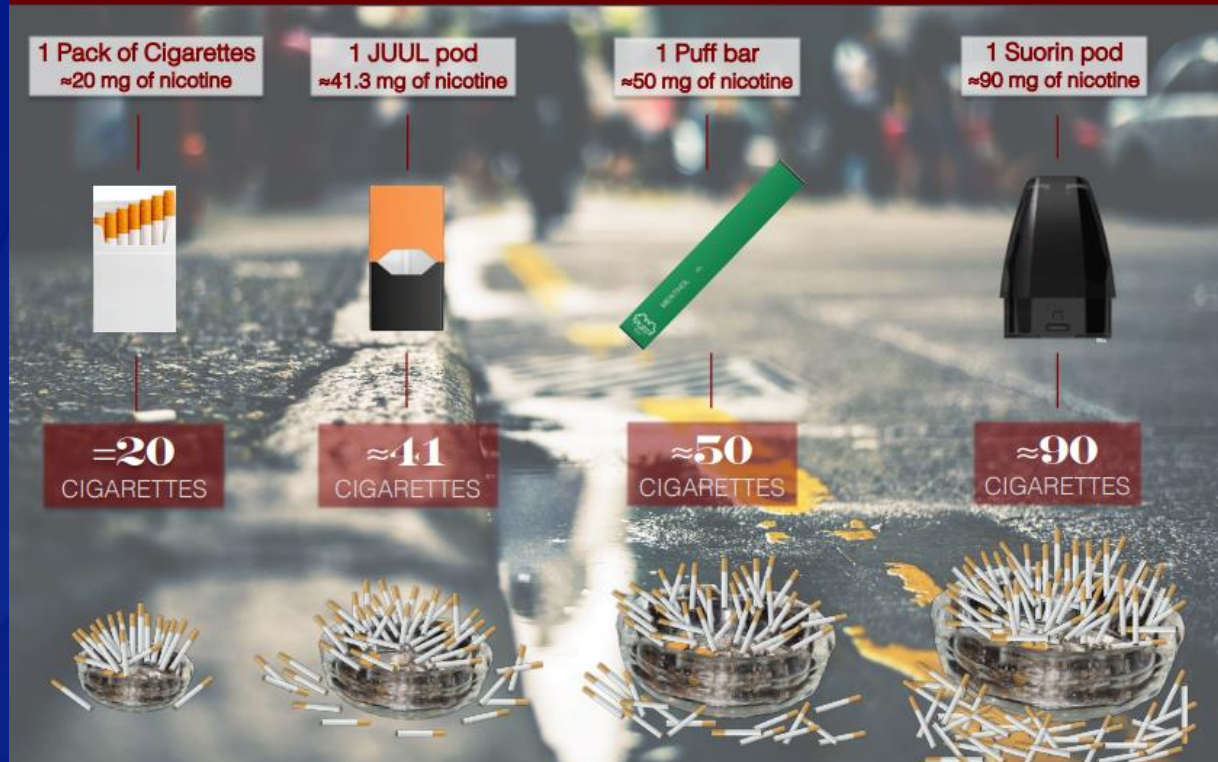
https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdfs/ecigarette-or-vaping-products-visual-dictionary-508.pdf

Changing Products

Cigs in a Pod



tobaccopreventiontoolkit.stanford.edu



- <https://med.stanford.edu/tobaccopreventiontoolkit/curriculum-decision-maker/by-module/E-Cigs.html>

Trends in US E-cigarette Unit Sales by Nicotine Strength 2017-2022

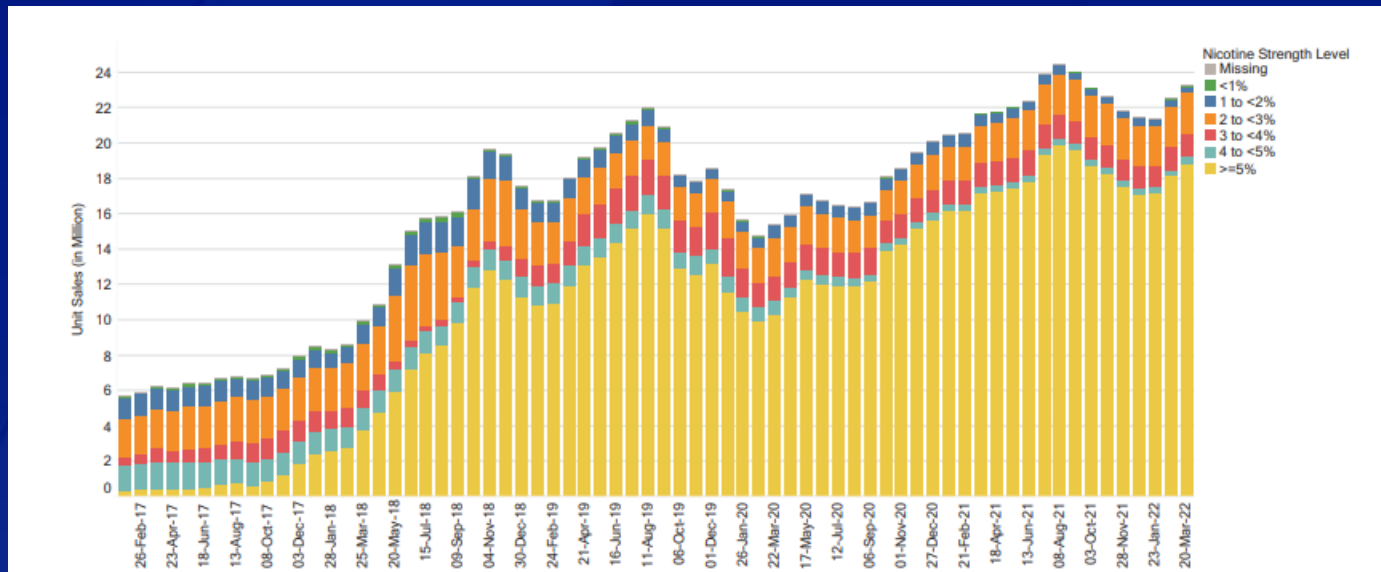
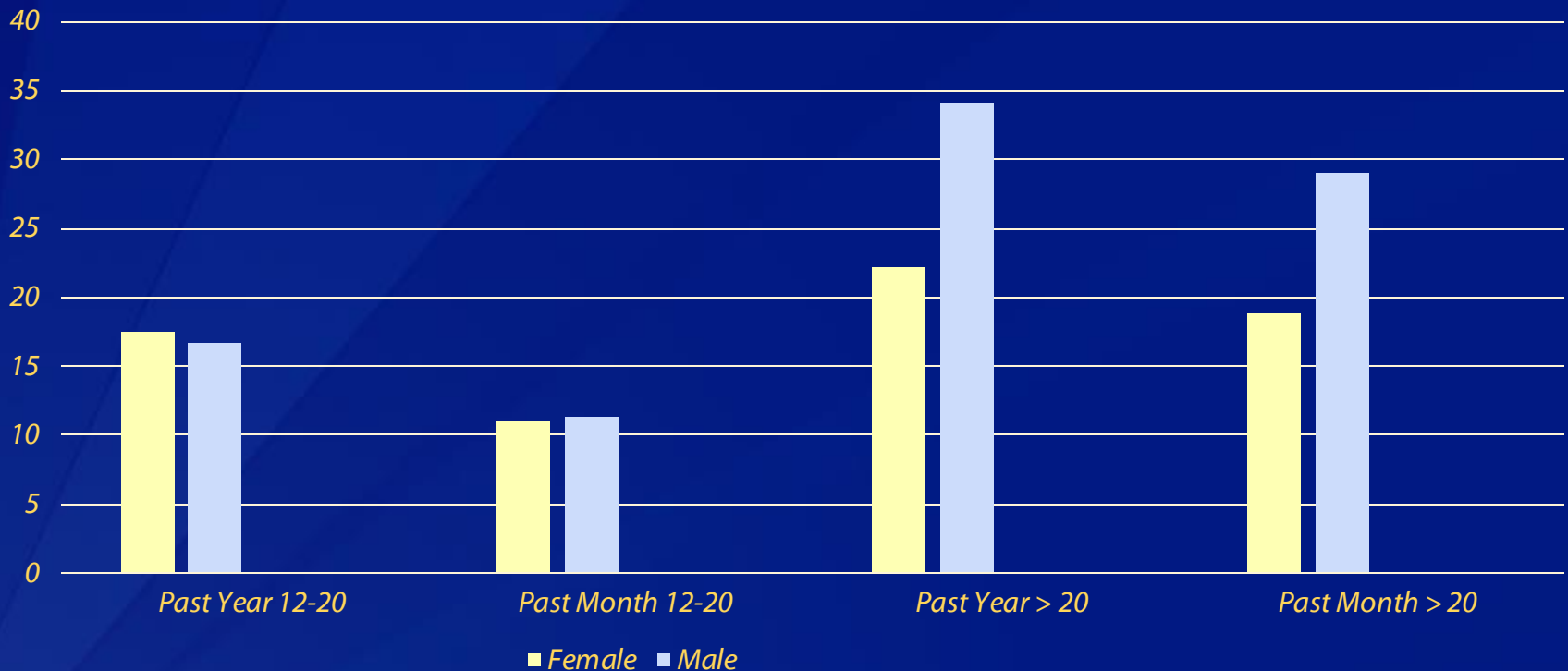


Figure 1. Total e-cigarette unit sales^a by nicotine strength^b, United States^c, 2017–2022^d.^aRetail sales data were obtained from Information Resources, Inc (IRI) for convenience stores, gas stations, grocery stores, drugstores/pharmacies, mass merchandiser outlets, club stores, dollar stores, and military sales; data from the Internet and vape shops were not collected. Unit sales were summed in 4-week periods. To account for variations in product type when summing unit sales, all units were standardized to reflect the most common package size: a standardized unit was equal to: Five prefilled cartridges/pods; one disposable device; or one e-liquid bottle.^bNicotine strength information was available in the data for 92.6% of the Universal Product Codes. Products with missing nicotine strength (7.4%) were searched online and identified. Nicotine strength level was categorized into five mutually exclusive categories: <1%; 1% to <2%; 2% to <3%; 3% to <4%; 4% to <5%; ≥5%.^cData were included from the 48 continental states (excluding Alaska and Hawaii) and Washington, DC.^dEach bar in the figure represents a 4-week aggregate interval.

Fatma Romeh M Ali, Elizabeth L Seaman, Elisha Crane, et al. Trends in US E-cigarette Sales and Prices by Nicotine Strength, Overall and by Product and Flavor Type, 2017–2022, *Nicotine & Tobacco Research*, Volume 25, Issue 5, May 2023, Pages 1052–1056.

US Prevalence of Tobacco Use or Vaping 2021

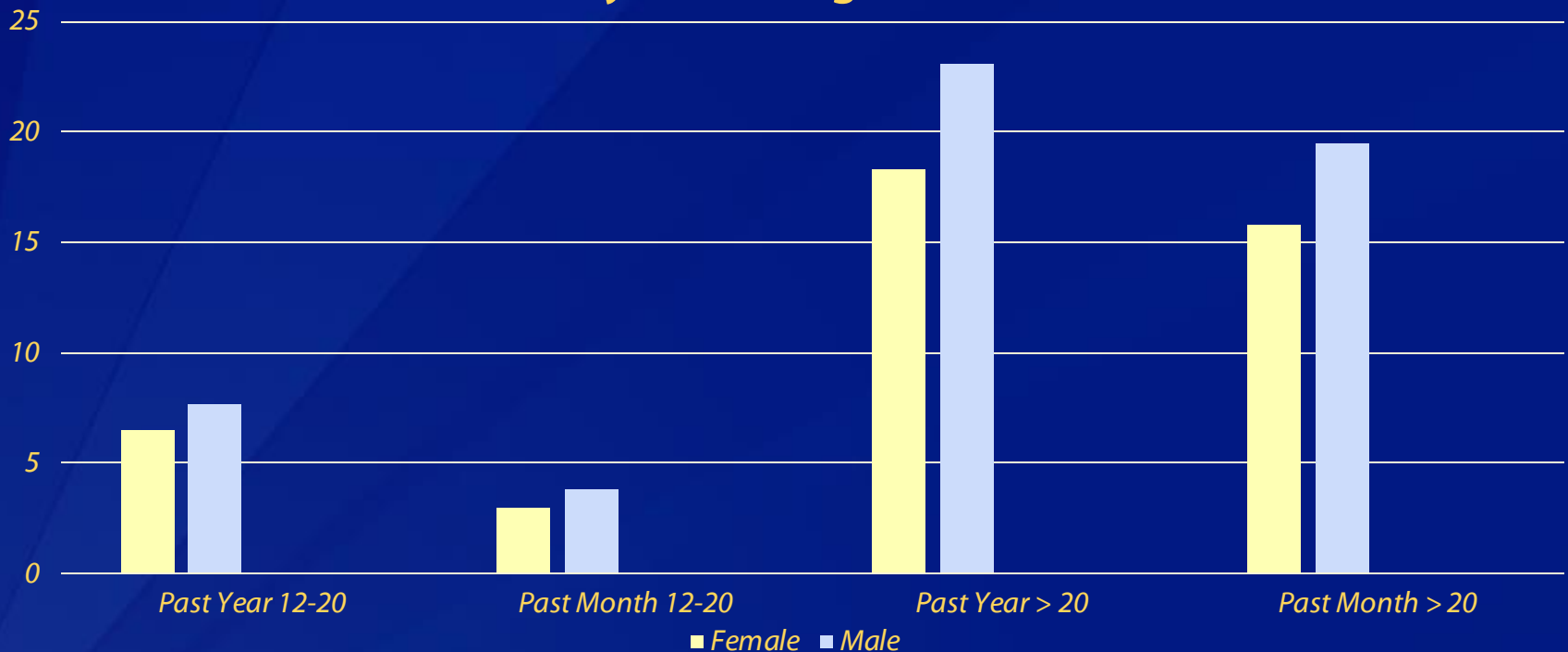
Percentage past and current tobacco use or vaping by sex and age, NSDUH 2021



NSDUH—<https://www.samhsa.gov/data/report/2021-nsduh-detailed-tables>

US Prevalence of Cigarette Smoking 2021

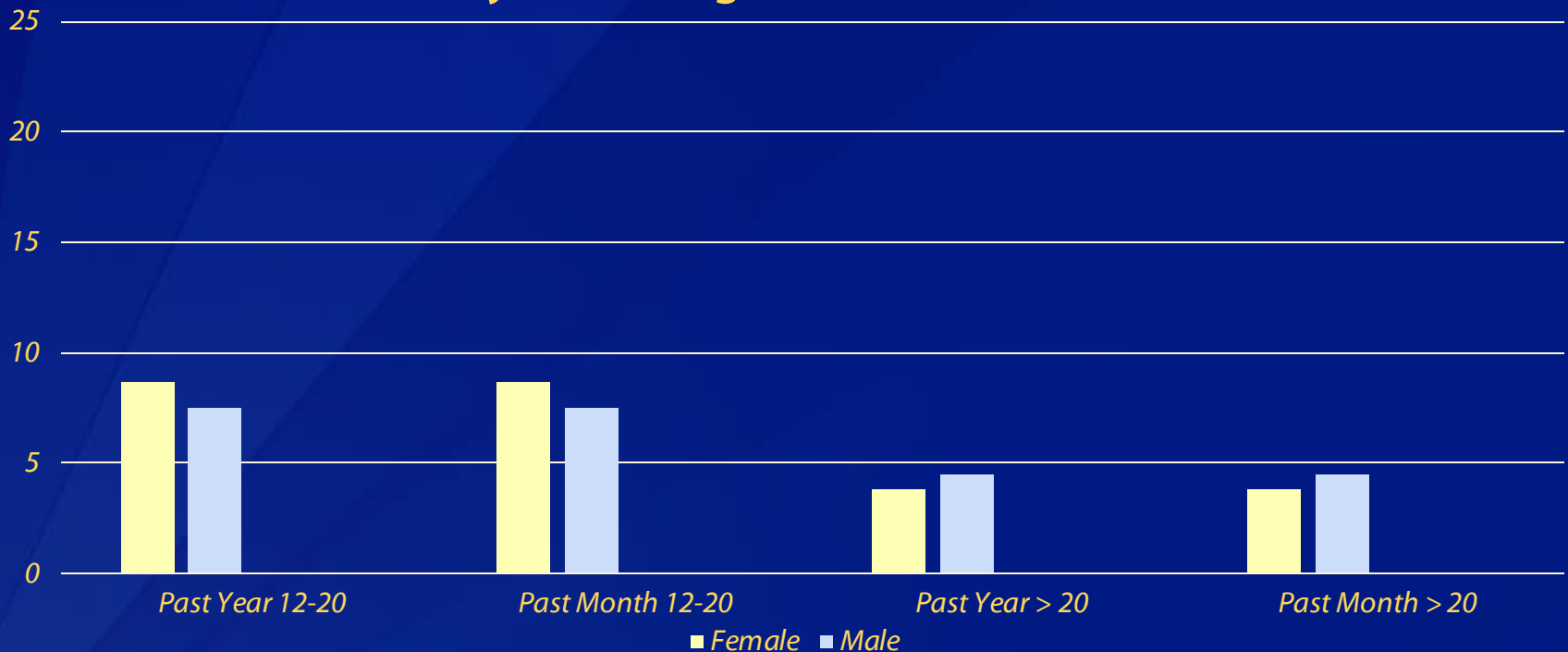
Percentage past and current cigarette smoking by sex and age, NSDUH 2021



NSDUH—<https://www.samhsa.gov/data/report/2021-nsduh-detailed-tables>

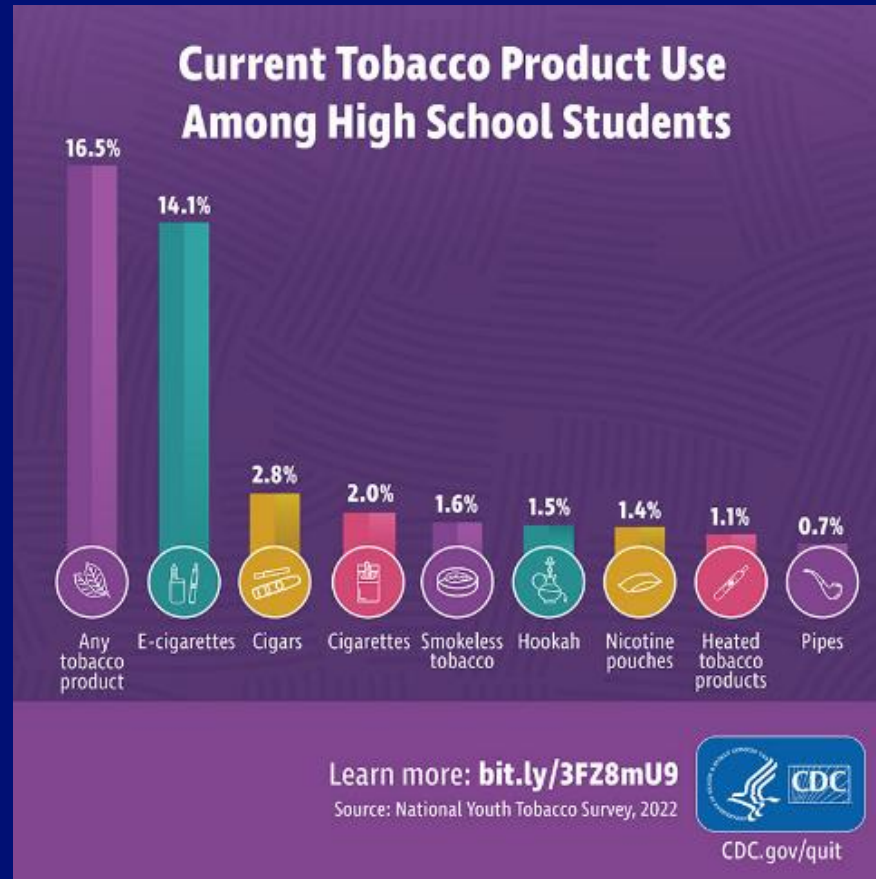
US Prevalence of Nicotine Vaping 2021

Percentage past and current vaping
by sex and age, NSDUH 2021



NSDUH—<https://www.samhsa.gov/data/report/2021-nsduh-detailed-tables>

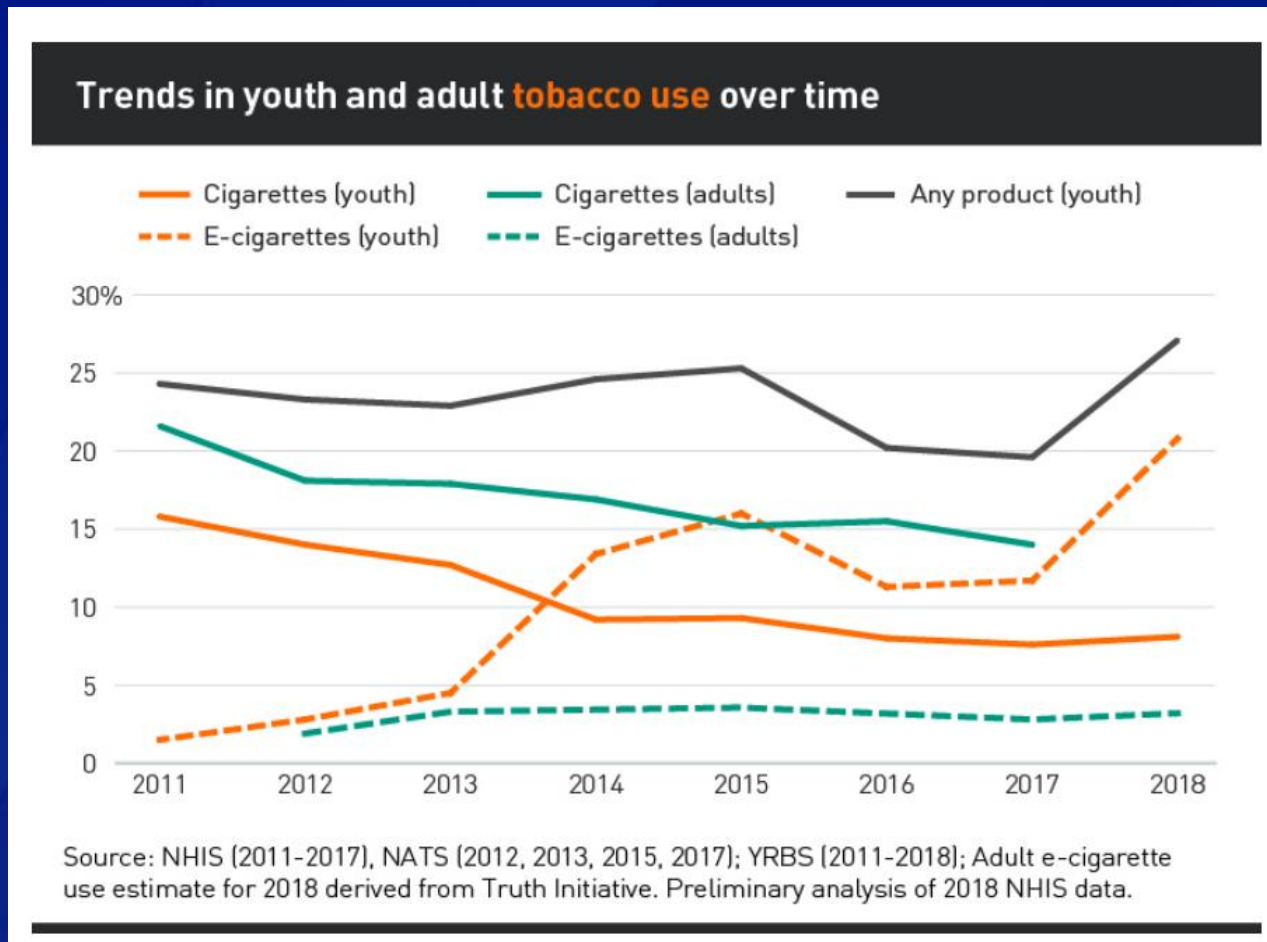
Youth Tobacco Use NYTS 2022



*“Current use” is determined by respondents indicating that they have used a tobacco product on at least 1 day during the past 30 days.

In 2022, “any tobacco product” includes electronic cigarettes, cigarettes, cigars, smokeless tobacco (including chewing tobacco, snuff, dip, snus, and dissolvable tobacco), pipe tobacco, bidis, hookah, heated tobacco products, and nicotine pouches.

Trends in Tobacco Use 2011-2018



<https://truthinitiative.org/research-resources/tobacco-industry-marketing/spinning-new-tobacco-industry-how-big-tobacco-trying>

Women Who Smoke in Pregnancy are Less Likely to Disclose

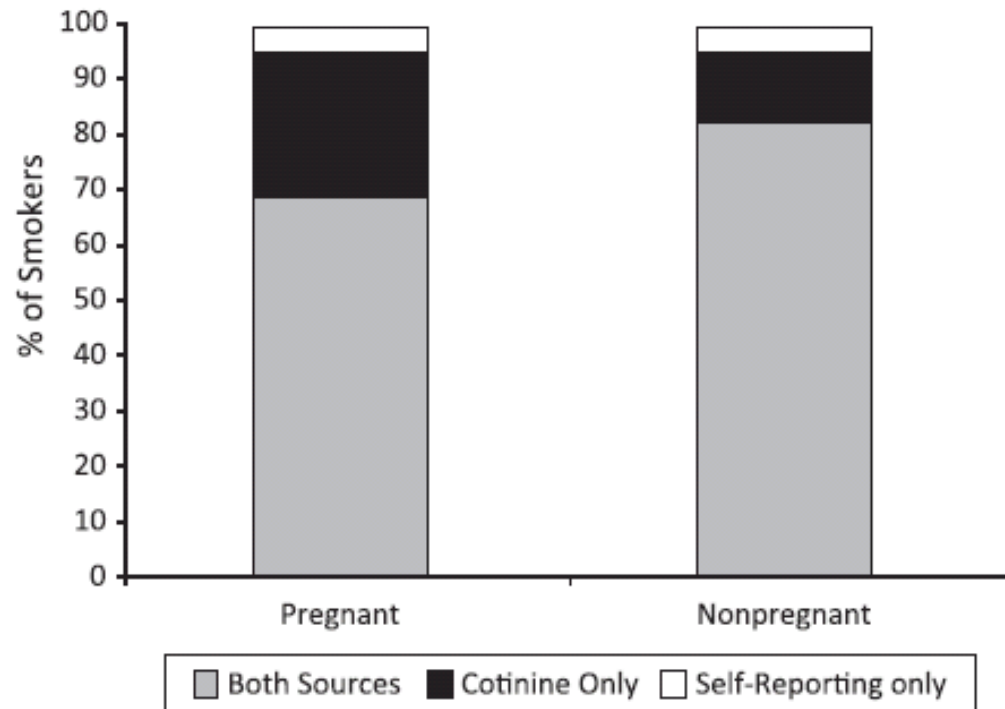
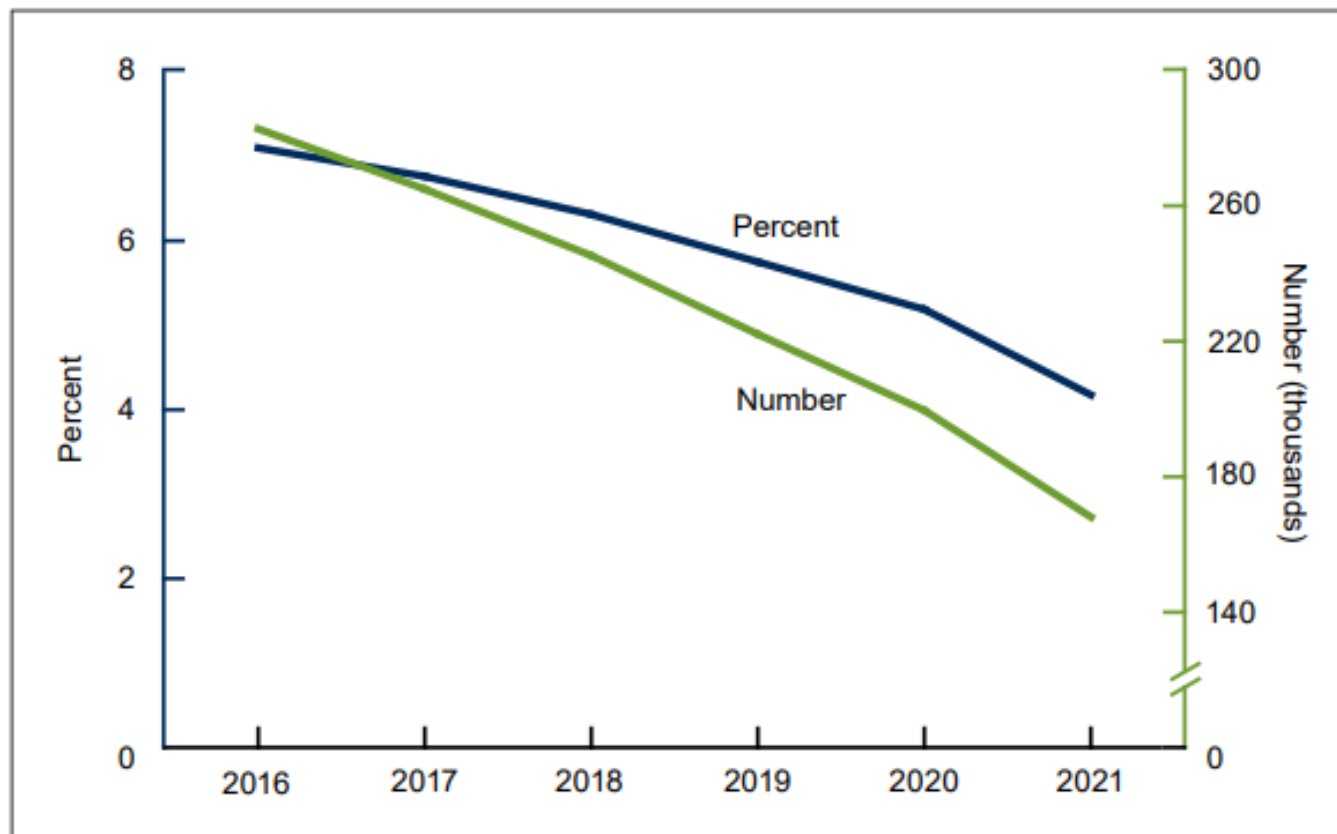


Figure 1. Method of determination of smoking status among women 18–44 years of age in the National Health and Nutrition Examination Survey, 1999–2006.

Dietz P, Homa D, England L, et al. Estimates of nondisclosure of cigarette smoking among pregnant and non-pregnant women of reproductive age in the United States. *Amer J Epidemiol* 2011; 173(3):355-9.

Pregnancy and Smoking 2016-2021

Figure 1. Number and percentage of mothers who smoked cigarettes during pregnancy: United States, 2016–2021



NOTES: Significant declining trends in numbers and rates from 2016 to 2021 ($p < 0.05$). Access data table for Figure 1 at: <https://www.cdc.gov/nchs/data/databriefs/db458-tables.pdf#1>.

SOURCE: National Center for Health Statistics, National Vital Statistics System, Natality.

Pregnancy and Cessation

- **Smoking cessation rates are high (~ 50%)**
- **Most women quit on their own before or in early pregnancy (~ 1/3 pregnancies are unintended)**
- **Quitting is associated with strong beliefs about the dangers of smoking**
- **~ Half of women who quit relapse by 2-6 mos pp**

Tong VT, Dietz PM, Morrow B, et al. Trends in smoking before, during, and after pregnancy--Pregnancy Risk Assessment Monitoring System, United States, 40 sites, 2000-2010. *MMWR Surveill Summ.* 2013 Nov 8;62(6):1-19.

Kia F, Tosun N, Carlson S, Allen S. Examining characteristics associated with quitting smoking during pregnancy and relapse postpartum. *Addict Behav.* 2018 Mar;78:114-119.

Allen AM, Jung AM, Lemieux AM, et al. Stressful life events are associated with perinatal cigarette smoking. *Prev Med.* 2019 Jan;118:264-271.

Jones M, Lewis S, Parrott S *et al.* Re-starting smoking in the postpartum period after receiving a smoking cessation intervention: a systematic review. *Addiction* 2016.

Kurti AN, Redner R, Bunn JY, Tang K, et al. Examining the relationship between pregnancy and quitting use of tobacco products in a U.S. national sample of women of reproductive age. *Prev Med.* 2018 Dec;117:52-60.

Kim S. Changes in Multiple and Different Tobacco Product Use Behaviors in Women Before and During Pregnancy: An Analysis of Longitudinal Population Assessment of Tobacco and Health Data. *Am J Prev Med.* 2020 Oct;59(4):588-592.

Pregnancy and E-cigarettes

■ PRAMS 2019

- Before pregnancy e-cigarette use
 - Total use (dual + e-cigs) 4.3%
 - E-cigarette only 1.6% (1.5-1.9)
 - Dual use 2.6% (2.4-2.9)
- During pregnancy e-cigarette use:
 - Total use (dual + e-cigs) 1.3%
 - E-cigarette only 0.6% (0.5-0.7)
 - Dual use 0.7% (0.5-0.8)

■ 2016 – 2019

- Dual use was stable at 0.7%
- E-cigarette only use increased from 0.4% to 0.6%

Head SK, Zaganjor I, Kofie JN, Sawdey MD, Cullen KA. Patterns and Trends in Use of Electronic Nicotine Delivery Systems Before and During Pregnancy: Pregnancy Risk Assessment Monitoring System, United States, 2016-2019. J Community Health. 2022

Pregnancy and E-cigarettes

- **E-cigarette use was associated with**
 - Younger age (< 20 years: **13.4% before, 3.6% during**)
 - White race
 - \leq HS education, \leq FPL
 - Mistimed or unintended pregnancy
 - Pre-pregnancy use of alcohol, cigarettes
- **Cessation rates vary by cigarette use**
 - Dual users: **46.3%** (95% CI 41.5 – 51.1)
 - E-cigs only **82.2%** (95% CI 76.9 – 86.5)
 - Cigarettes only **55.0%** (95% CI 52.7 – 57.2)

Head SK, Zaganjor I, Kofie JN, Sawdey MD, Cullen KA. Patterns and Trends in Use of Electronic Nicotine Delivery Systems Before and During Pregnancy: Pregnancy Risk Assessment Monitoring System, United States, 2016-2019. J Community Health. 2022

Tobacco Cessation Interventions



U.S. Preventive Services
TASK FORCE

JAMA. 2021;325(3):265-279.
doi:10.1001/jama.2020.25019

Recommendation Summary

Population	Recommendation	Grade
Nonpregnant adults	The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and US Food and Drug Administration (FDA)--approved pharmacotherapy for cessation to nonpregnant adults who use tobacco.	A
Pregnant persons	The USPSTF recommends that clinicians ask all pregnant persons about tobacco use, advise them to stop using tobacco, and provide behavioral interventions for cessation to pregnant persons who use tobacco.	A
Pregnant persons	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy interventions for tobacco cessation in pregnant persons.	I



ACOG

The American College of
Obstetricians and Gynecologists

“Use of NRT should be considered only after a detailed discussion with the patient of the known risks of continued smoking, the possible risks of NRT, and need for close supervision. If NRT is used, it should be with the clear resolve of the patient to quit smoking.”

Tobacco and nicotine cessation during pregnancy. ACOG Committee Opinion No. 807. American College of Obstetricians and Gynecologists. Obstet Gynecol 2020;135:e221–9.

Industry Strategies Before 2006-2007

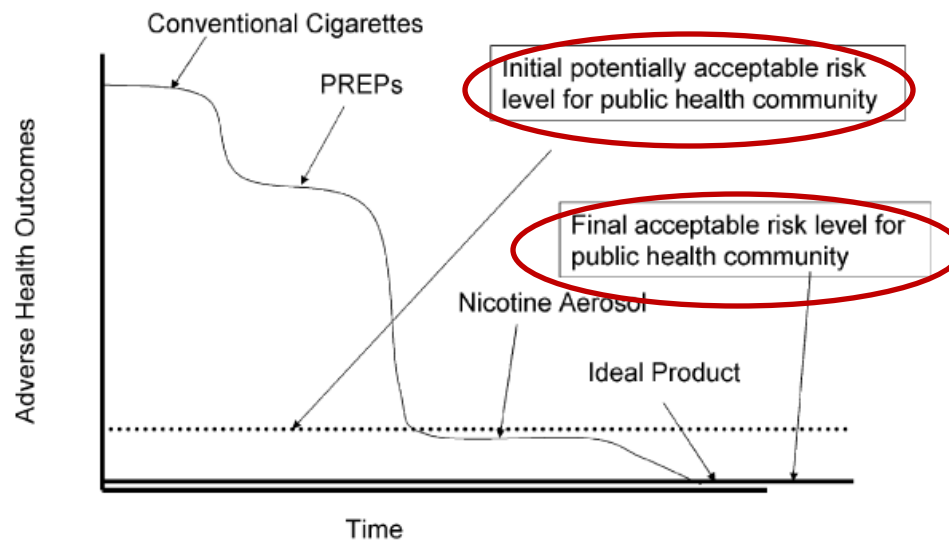
- From 1950s: “safer” cigarettes
- 1980s
 - “Socially acceptable” cigarettes (women)
 - Increasing threat regarding health effects of SHS (MCH)
 - Undermined the scientific evidence on SHS
 - Later introduced oral products for women (lozenges)
 - Began promoting benefits of nicotine (mood, cognition)
- 1990s: recognized NRT as a business opportunity
 - “If Anyone Is Going to Take Away Our Business It Should Be Us”*
- 1999: began to co-opt “Harm Reduction”
- Inadequate regulatory framework



Ling PM, Glantz SA. Tobacco company strategies to identify and promote the benefits of nicotine. *Tob Control*. 2019 May;28(3):289-296.
Apollonio D, Glantz SA. Tobacco Industry Research on Nicotine Replacement Therapy: "If Anyone Is Going to Take Away Our Business It Should Be Us". *Am J Public Health*. 2017 Oct;107(10):1636-1642.
Peeters S, Gilmore AB. Understanding the emergence of the tobacco industry's use of the term tobacco harm reduction in order to inform public health policy. *Tobacco Control* 2015;24:182-189

Continuum of Risk Framework Industry Perspective

Potential Impact of Smoking and Nicotine Addiction



ACS-BD-NicotineAddictionConsensus-
12.12.03

DRAFT – For discussion
Purposes only

15

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Continuum of Risk Framework

More toxic

**Combusted products/
conventional cigarettes**

**Non-combusted tobacco
products**

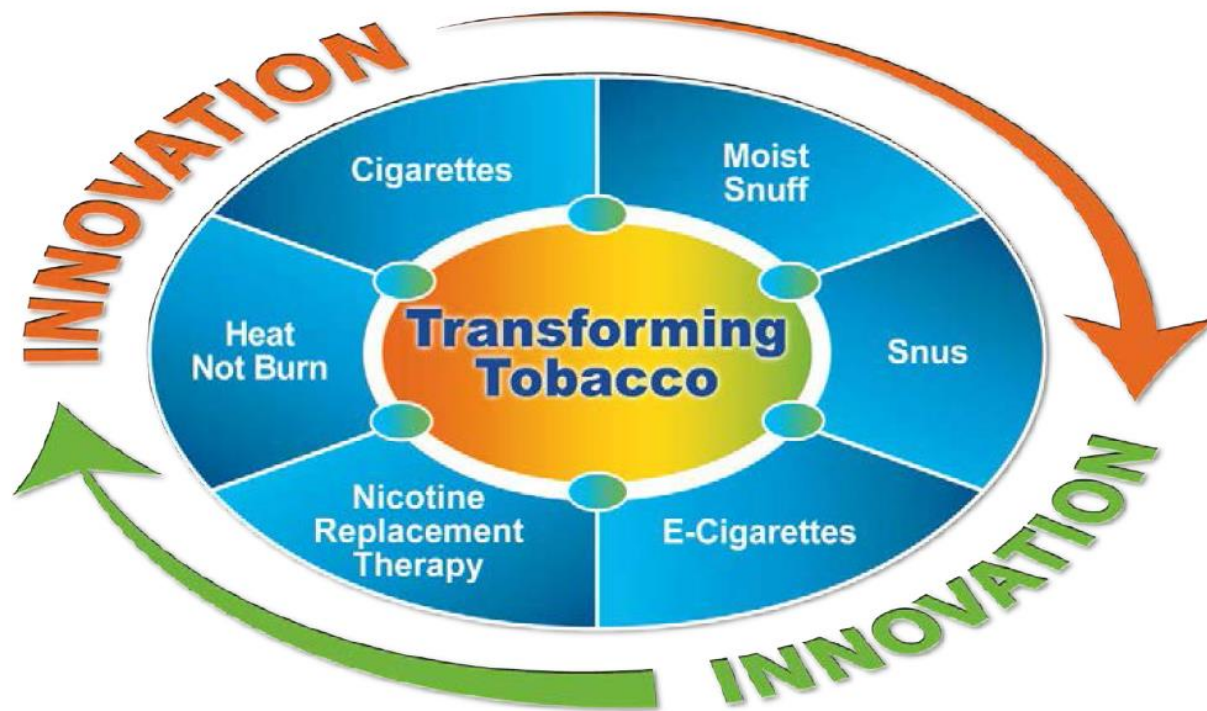
Less toxic

Nicotine only products

No nicotine use



Innovation Across Categories



Oral Tobacco Product Ads Targeting Women



Ultra Discreet Satisfaction
Oral Hygiene Friendly



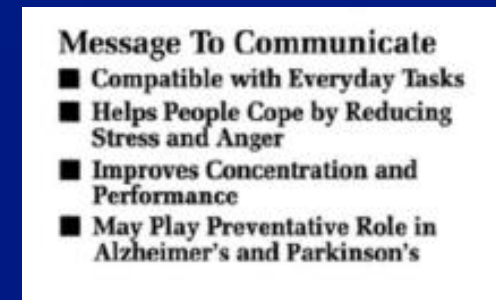
<https://www.businessinsider.com/reynolds-rolls-out-nicotine-lozenges-revel-2019-3>

Unger JB, Barker J, Cruz TB, Leventhal AM, Pentz MA. Lucy-Novel Flavored Nicotine Gum, Lozenges, and Pouches: Are They Misleading Consumers? *Subst Use Misuse*. 2022;57(8):1328-1331.

Industry Strategies to Promote Nicotine

Starting in the 1980s

- **Funded studies of the benefits of nicotine on cognition, performance, and mood**
 - **Used outcomes accessible to the public (driving, flying a plane)**
- **Implemented PR campaign comparing nicotine to socially acceptable substances (caffeine) while disputing 1989 SGR finding that nicotine is addictive**



Positive aspects of smoking
RJ Reynolds Records. 1994

Ling PM, Glantz SA. Tobacco company strategies to identify and promote the benefits of nicotine. *Tob Control*. 2019 May;28(3):289-296.

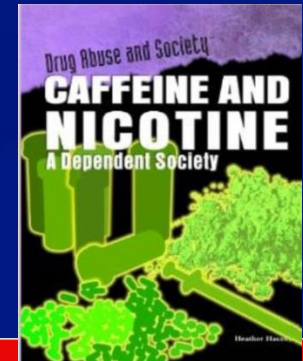
Thursday, March 21, 2013

Nicotine Increases Exercise Endurance

Similarity of Nicotine and Caffeine

	Nicotine	Caffeine
Source	Plant alkaloid	Plant alkaloid
CNS	Stimulant	Stimulant

In my lectures on tobacco harm reduction I compare the properties of nicotine with those of caffeine (see slides at left). Despite some obvious differences, the drugs have remarkably similar effects. I have just found a study from 2006 showing that "...nicotine administration during moderate-intensity exercise delays fatigue, with a significant improvement of 17% [$\pm 7\%$] in time to exhaustion. This observation is similar to observations of the effects of caffeine supplementation." (Available at the journal *Experimental Physiology* [here](#)).

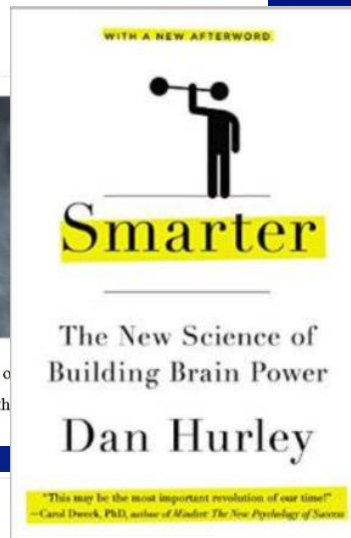


5 Things You Didn't Know Could Make You Smarter

#2. Cigarettes



Apparently some "scientists" have decided that smoking doesn't have lots of those folks opposed to cancer and offending people. But it seems that, in the end, nicotine has some beneficial effect on the brain.



HEALTH & HEALTHCARE

A Nicotine Patch a Day Keeps the Cognitive Impairment Away

by Jennifer Gibson, PharmD | February 6, 2012

MENU

TIME

Subscribe

These 5 Things Will Make You Smarter

3) Performance enhancing drugs for your brain

No, they're not anabolic steroids. It's caffeine, sugar and nicotine. Coffee and nicotine make you smarter.

Smarter: The New Science of Building Brain Power
 "...nicotine—free of its noxious host, tobacco, and delivered instead by chewing gum or transdermal patch—may prove to be a weirdly, improbably effective cognitive enhancer and treatment for a variety of neurological disorders...Plus it has been associated with weight loss. With few known safety risks. Nicotine? Yes, nicotine."

NRT as a Business Opportunity

coated
nicotine gum

NDC 11873-532-78

nicotine polacrilex gum,
4 mg (nicotine)
stop smoking aid

Compare to active ingredient
in Nicorette® Gum*

Includes User's Guide

FOR THOSE WHO SMOKE THEIR FIRST
CIGARETTE WITHIN 30 MINUTES
OF WAKING UP

If you smoke your first cigarette
MORE THAN 30 MINUTES after waking up,
use Nicotine Polacrilex Gum, 2 mg



ACTUAL
SIZE

4
mg

MINT
FLAVOR

100
SUGAR FREE
PIECES

up&up

100 PIECES, 4 mg EACH



one less **CIGARETTE**,
one more **VICTORY.**

That's how ZONNIC NICOTINE GUM helps you quit.

FIND OUT MORE.



**GREAT
TASTE**



Three delicious flavors
to match your mood:

Fruity Citrus
Refreshing Mint
Cooling Cherry Ice

LUCY

**USE
ANYWHERE**

Lucy Nicotine Gum is
a discreet way to deliver
nicotine...



...no matter
where you are.

LUCY

- Kostygina G, England L, Ling P, "New Product Marketing Blurs the Line Between Nicotine Replacement Therapy and Smokeless Tobacco Products", *American Journal of Public Health* 106, 7 (2016): pp. 1219-1222.
- Unger JB, Barker J, Cruz TB, Leventhal AM, Pentz MA. Lucy-Novel Flavored Nicotine Gum, Lozenges, and Pouches: Are They Misleading Consumers? *Subst Use Misuse*. 2022;57(8):1328-1331.

Health Effects of Smoking

- Smoking damages every organ in the body
 - Dysmenorrhea
 - More severe menopausal symptoms
 - Earlier menopause
 - Increased risk of osteoporosis
 - Increased time to conception
 - ART: lower success rates, twice as many cycles of in vitro fertilization to achieve conception.

THE TOBACCO BODY World Health Organization

Tobacco is deadly in any form. Smoked tobacco products, including cigarettes, contain over 7000 chemicals, including at least 250 chemicals known to be toxic or to cause cancer. Use of combustible tobacco products can result in various – sometimes fatal – health problems. Exposure to second-hand smoke has also been implicated in a variety of health outcomes, including death. Some tobacco products contain even more chemicals than traditional tobacco products and are harmful to health. Linking tobacco smokers to at least 10 years of life on average. Globally, over 22 000 people die from tobacco use or second-hand smoke exposure every day – one person every 4 seconds. Tobacco use affects almost all organs of the human body. Some of the health effects are depicted below – from head to toe.

DISEASES CAUSED BY ALL FORMS OF TOBACCO

HEART ATTACK, STROKE, AND OTHER CARDIOVASCULAR DISEASES

ORAL CANCER AND OTHER ORAL DISEASES

THROAT CANCER

OTHER CANCERS

FETAL DEATH

REDUCED FETAL GROWTH, LOW BIRTH WEIGHT AND PRETERM DELIVERY

WEAKENED IMMUNE SYSTEM

WEAR BONES

Skin Damage

DISEASES CAUSED BY TOBACCO SMOKE

LUNG CANCER

ASTHMA

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

TUBERCULOSIS

OTHER RESPIRATORY ILLNESSES AND REDUCED LUNG FUNCTION

TYPE 2 DIABETES

DEMENTIA

REDUCED FERTILITY IN MEN AND WOMEN

ERECTILE DYSFUNCTION

SUDDEN INFANT DEATH SYNDROME

Menstruation and Menopause

BIRTH DEFECTS

VISION LOSS

HEARING LOSS

GASTROINTESTINAL DISEASES

WEAKENED IMMUNE SYSTEM

WEAR BONES

Skin Damage

BENEFITS OF QUITTING

It is never too late to quit. The cessation of tobacco use has the potential to reduce the risk of many of these diseases significantly and, in some cases, to reduce risk to that of a person who has never smoked. For more information, please visit: www.who.int/tobacco

12 hours Carbon monoxide levels in your blood drop to normal

20 minutes Your heart rate drops

1 to 9 months Your coughing and phlegm go away

1 year Your risk of coronary heart disease is cut in half

5 years Your stroke risk is reduced to that of a non-smoker

10 years Your lung cancer death rate is about half that of a smoker. Your risk of cancer of the mouth, throat, esophagus, bladder, kidney and pancreas are halved.

15 years Your risk of cardiovascular disease is cut in half

Health Effects of Smoking during Pregnancy

- **Stillbirth**
- **Preterm delivery**
- **PPROM**
- **LBW (<2500 grams)**
- **IUGR**
- **Perinatal mortality**
- **Placenta previa**
- **Placental abruption**
- **Preeclampsia (reduced risk)**
- **Altered lung development**
- **Neuroteratogen**
- **SIDS**
- **Ectopic pregnancy**
- **Orofacial clefts**

USDHHS. The Health Consequences of smoking—50 Years of progress: A Report of the Surgeon General. Atlanta, GA: USDHHS, CDC, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.

USDHHS. E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General. Atlanta, GA: USDHHS, CDC, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2016.

Pregnancy and Smoking: Potential Long-term Effects on Offspring

- ❑ Internalizing and externalizing behavior problems**
- ❑ Conduct disorder**
- ❑ Aggressive behavior**
- ❑ ADHD**
- ❑ Mood disorders**
- ❑ SUDs**
- ❑ Chronic medical problems including hypertension and obesity**

Establishing causality is challenging

Parker SE, Collett BR, Speltz ML, Werler MM. Prenatal smoking and childhood behavior problems: is the association mediated by birth weight? *J Dev Orig Health Dis.* 2016 Jun;7(3):273-281

How Do We Study the Health Effects of Nicotine?

- **Animal studies**
- **Studies of the health effects of nicotine product use (cohort studies of Swedish male snus users to understand health effects of NRT)**
- **Synthesize data from animal models of nicotine exposure and human studies of cigarette smoking**

The Role of Nicotine in Human Development



- Nicotine binds to receptors called nicotinic acetylcholine receptors, nAChRs
- nAChRs present *very* early in development
- nAChRs expression increases in the developing nervous system during critical periods of neuronal development

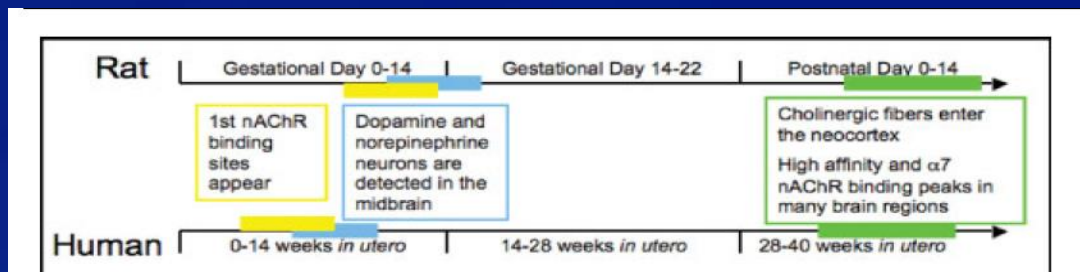


Figure 2. Comparison of the timetables for neural development in rat and human. Most of the developmental events that occur in the third trimester in human occur during the first two postnatal weeks in rat.

The Role of Nicotine in Development



- ❑ **nAChR binding in normal cellular development**
 - **Promote neural cell replication, initiate switch from neural cell replication to differentiation**
 - **Initiate, terminate axogenesis and synaptogenesis, evoke or retard apoptosis, enable migration of specific cell populations**
- ❑ **Nicotine can “hijack” developmental processes**
 - **Triggers apoptosis, reduces the number of neuronal cells, impairs synaptogenesis, causes abnormal switch from neuronal proliferation to differentiation**
 - **Prenatal exposure results in lower total brain DNA in offspring (reduction in total cell number)**
 - **Damage and cell loss intensify in the postnatal period, even after discontinuation of exposure**

Slotkin TA. Fetal nicotine or cocaine exposure: which one is worse? J Pharmacol Exp Ther. 1998;285:931–945.

Studies of Outcomes in Smokeless Tobacco Users

Support that nicotine

- **Has minor contributions to fetal growth restriction**
- **Does not reduce risk of preeclampsia (may increase)**
- **Increases the risk of**
 - **Infant apnea**
 - **SIDS and SUID, post-neonatal mortality**
 - **Oral cleft defects**
 - **Preterm delivery**
 - **Stillbirth**
- **Alters autonomic cardiac regulation/autonomic instability at 1-2 months; increased arterial stiffness higher SBP at 5-6 yrs**

Sweden

Most studies of pregnancy outcomes use the country's Medical Birth Register

- **Snus added in 1999 (3 months before pregnancy and current daily use)**
- **Captures nearly all live and stillbirths**
 - **~75,000 singleton live births/yr**
- **Women enter prenatal care early (~15 weeks)**
- **Gestational age dating by early US (~17 wks)**
- **Linked to ICD-10 codes**
- **Smoking: 1-9 or 10+ cigarettes/day**



Sweden: Preterm Birth

Live singleton births, 1999-2009

PTB < 37 weeks gestation (n=33,172)

Tobacco Use Before/Early Pregnancy	Crude OR, 95% CI	Adjusted OR, 95% CI
No tobacco use	Reference	Reference
Snus user /non-user	1.01 (0.92, 1.10)	0.92 (0.84, 1.01)
Snus user /snus user	1.34 (1.22, 1.48)	1.29 (1.17, 1.43)
Smoker/non-smoker	1.02 (0.99, 1.06)	0.90 (0.87, 0.94)
Smoker/smoker	1.43 (1.38, 1.48)	1.30 (1.25, 1.36)

***Adjusted for maternal BMI, age, parity, education, partner.**

Baba S, Wikström AK, Stephansson O, Cnattingius S. Influence of smoking and snuff cessation on risk of preterm birth. Eur J Epidemiol. 2012 Apr;27(4):297-304.

Sweden: Preeclampsia

- Live singleton births in Sweden 1999-2006
- N=612,000

Tobacco Use in Early Pregnancy	Term Preeclampsia		Preterm Preeclampsia	
	N	Adjusted OR*	N	Adjusted OR*
No tobacco use	11854	Reference	3128	Reference
Snus	198	1.06 (0.91,1.24)	60	1.30 (1.00, 1.70)
Cigarettes				
1-9/day	741	0.65 (0.60,0.71)	213	0.70 (0.61,0.82)
10+/day	203	0.46 (0.39,0.43)	81	0.72 (0.65,0.91)

*Adjusted for maternal age, BMI, parity, years of education

Wikström AK, Stephansson O, Chattingius S. Tobacco use during pregnancy and preeclampsia risk: effects of cigarette smoking and snuff. Hypertension. 2010 May;55(5):1254-9.

Sweden: Birth Weight

Live, singleton births from the Swedish Birth Register, 2002-2010

- 8,861 siblings from 4,104 mothers whose snus use was discordant across pregnancies
- **Conventional analysis* of continuing users:**
 - **47 g** reduction in birth weight (significant)
- **Sibling analysis:**
 - **20 g** reduction in birth weight (not significant)
- **Comparison to cigarette smoking: - 162 grams (1 to 9 CPD,) and - 226 g (10+CPD)**

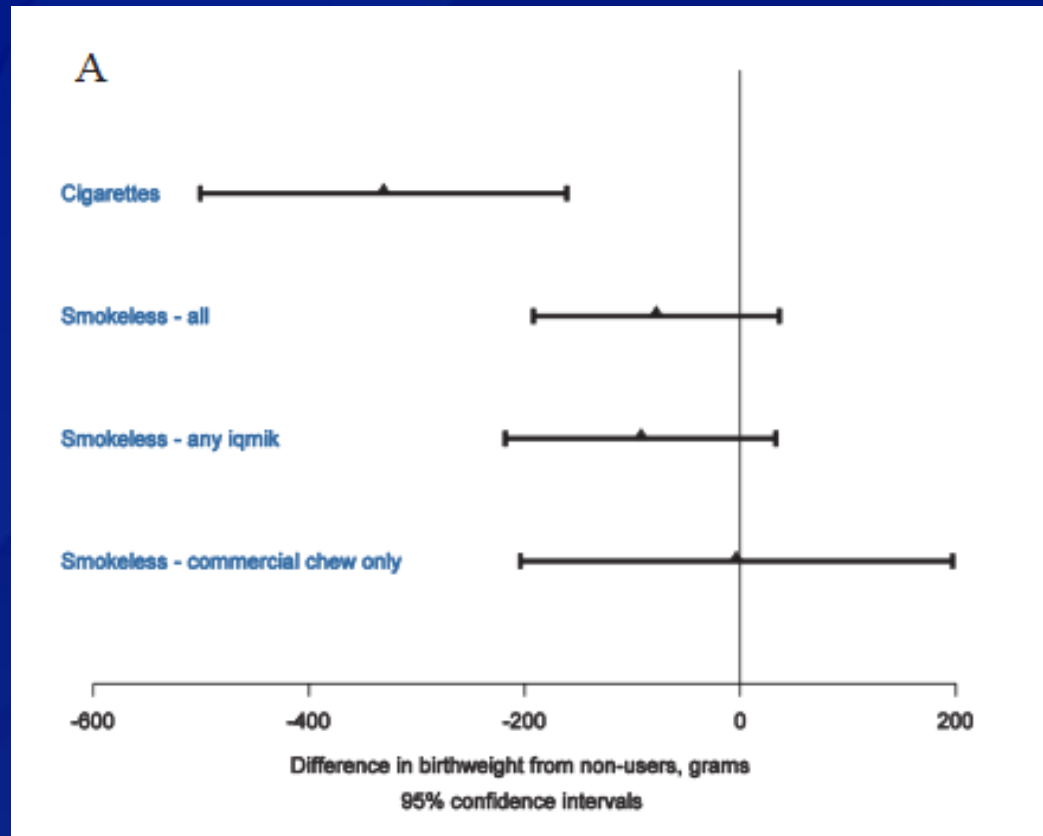
*All models adjusted for gestational age, marital status, maternal age, and infant sex.

Jua´rez SP, Merlo J (2013) The Effect of Swedish Snuff (Snus) on Offspring Birthweight: A Sibling Analysis. PLoS ONE 8(6): e65611.

Jua´rez SP, Merlo J (2013) Revisiting the Effect of Maternal Smoking during Pregnancy on Offspring Birthweight: A Quasi-Experimental Sibling Analysis in Sweden. PLoS ONE 8(4): e61734

Alaska: Birth Weight*

Controls n=497



***Adjusted for gestational age, parity, BMI, height, age, infant sex.**

England LJ, Kim SY, Shapiro-Mendoza CK, et al. Maternal smokeless tobacco use in Alaska Native women and singleton infant birth size. *Acta Obstet Gynecol Scand* 2012;91:93–103.

Studies Synthesizing Data from Animal Models of Nicotine and Human Studies of Cigarette Smoking

□ Support that nicotine...

- Increases the risk of SIDS
- Contributes to impaired lung development and adverse respiratory outcomes in childhood
- Causes structural brain changes and alterations in cognition, attention in human offspring
- Causes deficits in auditory processing
- Increases vulnerability to nicotine dependence in later life

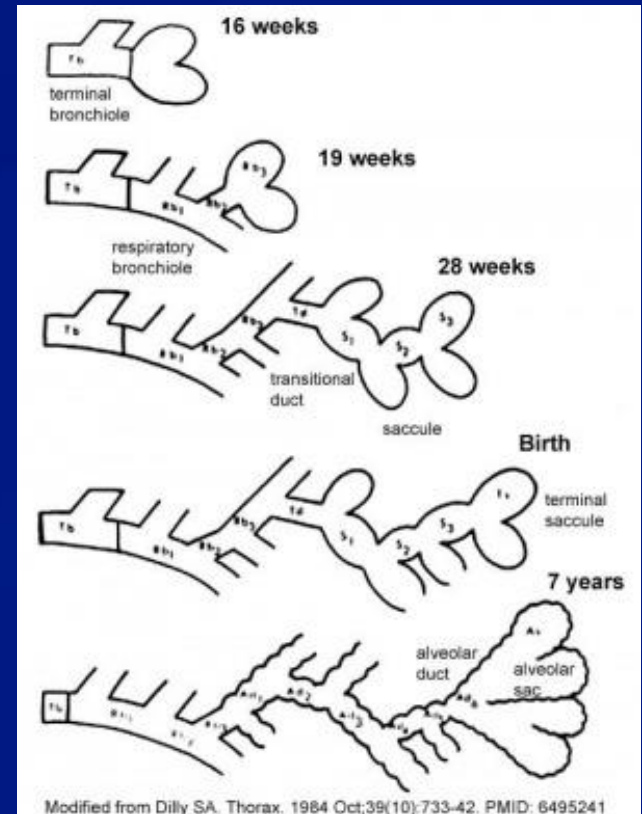
USDHHS. The Health Consequences of smoking—50 Years of progress: A Report of the Surgeon General. Atlanta, GA: USDHHS, CDC, NCCDPHP, Office on Smoking and Health; 2014.

U.S. Department of Health and Human Services. E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, CDC, NCCDPHP, Office on Smoking and Health, 2016.

McEvoy and Spindel. Pulmonary effects of maternal smoking on the fetus and child. *Paediatr Respir Rev.* 2017;21:27-33.

Lung Development

- ❑ nAChR present in the fetal lung (airway epithelium and fibro-blasts)
- ❑ Fetal lungs are susceptible to damage from environmental exposures
- ❑ Failure to reach maximum lung function potential in childhood can result in lifelong impairment
- ❑ Offspring of women who smoke have persistent adverse effects on lung function across childhood



USDHHS. The Health Consequences of smoking—50 Years of progress: A Report of the Surgeon General. Atlanta, GA: USDHHS, CDC, NCCDPHP, Office on Smoking and Health; 2014.

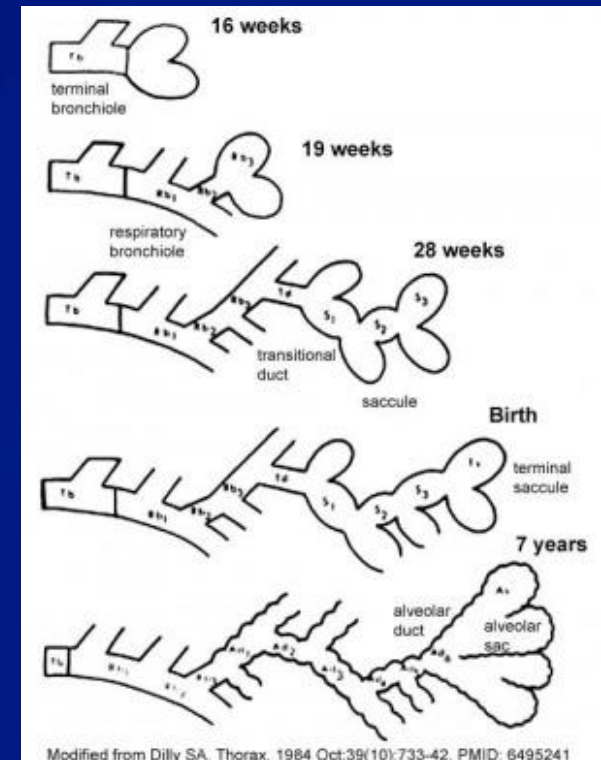
McEvoy and Spindel. Pulmonary effects of maternal smoking on the fetus and child. Paediatr Respir Rev. 2017;21:27-33.

Abbott and Winzer-Serhan, Critical Reviews in Toxicology, 2012.

Lung Development

□ Animal models of nicotine have consistent results across species:

- Decreased FEF
- Decreased lung volume
- Decreased alveolar surface area
- Decreased lung elastin
- Increased pulmonary resistance
- Increased lung collagen
- Increased airway wall thickening
- Increased narrow, smaller airways
- Increased airway reactivity



Spindel and McEvoy, Am J Respir Crit Care Med 2016;Vol 193(5) 486-94.

McEvoy and Spindel . Pulmonary effects of maternal smoking on the fetus and child. Paediatr Respir Rev. 2017;21:27-33.

Abbott and Winzer-Serhan, Critical Reviews in Toxicology, 2012.

Lung Development

Comparison of effects of prenatal nicotine (animal studies) to effects of in-utero smoke exposure (clinical studies) on lung development

Finding	Prenatal Nicotine	In-utero smoke exposure
↓ Pulmonary Function	Yes	Yes
↑ Airway thickening	Yes	Yes
↑ Airway tortuosity	Yes	?
↑ Airway reactivity	Yes	?
↑ Asthma and wheeze	?	Yes
Oxidative mechanism	Yes	Yes
Affected by nAChR SNPs	?	Yes

E-cigarette Use and Health Outcomes

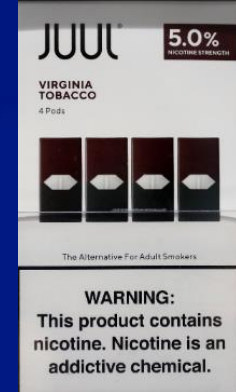
- Data on the potential impact of e-cigarette exposure on **reproductive health outcomes** are limited
- **PRAMS 2016-2018, N=79,176 (37 states and NYC)**
E-cigarette use in the last 3 months of pregnancy compared with no combustible cigarette use
 - **Preterm birth AOR 1.69 (1.20-2.39)**
 - **LBW AOR 1.88 (1.38, 2.57)**
 - **SGA AOR 1.10 (0.65-1.86)**

***All models adjusted for maternal age, race-ethnicity, education, marital status, prenatal care, WIC enrollment, vitamin use**

Montjean D, Godin Pagé MH, Bélanger MC, Benkhalifa M, Miron P. An Overview of E-Cigarette Impact on Reproductive Health. *Life (Basel)*. 2023 Mar 18;13(3):827.

Regan AK, Bombard JM, O'Hegarty MM, et al. Adverse birth outcomes associated with prepregnancy and prenatal electronic cigarette use. *Obstet Gynecol* 2021;138(1)85-94.

Warning Labels E-cigarettes, Oral Products



Includes one static warning label

"WARNING: This product contains nicotine derived from tobacco. Nicotine is an addictive chemical."

"WARNING: This product contains nicotine. Nicotine is an addictive chemical."

California Proposition 65

"This product contains nicotine, a chemical known to the State of California to cause birth defects or other reproductive harm."



Pregnant Women's Perceptions of E-cigarettes and NRT

- **Women are highly motivated to protect the health of their babies**
- **E-cigarettes are safer than smoking but...**
- **E-cigarettes can deliver an unsafe amount of nicotine**
- **Views on e-cigarettes for smoking cessation were mixed**
- **NRT is safer than smoking, but...**
- **NRT can deliver an unsafe amount of nicotine to a fetus**
- **NRT can be addictive like smoking; can be a barrier to NRT use**

Campbell K, Coleman-Haynes T, Bowker K, Cooper SE, Connelly S, Coleman T. Factors influencing the uptake and use of nicotine replacement therapy and e-cigarettes in pregnant women who smoke: a qualitative evidence synthesis. Cochrane Database of Systematic Reviews 2020, Issue 5. Art. No.: CD013629.

Women's Perceptions of Emerging Products and NRT

- **15 focus groups conducted in 4 cities in 2013**
 - Memphis, Tennessee; Philadelphia, Pennsylvania; Oklahoma City, Oklahoma; and Billings, Montana
- **Pregnant women who smoke, pregnant women who quit, and women who smoke and are planning a pregnancy**
- **Women discussed snus, dissolvables, e-cigarettes, NRT**



England L, Tong V, Koblitz A, et al. Perceptions of emerging tobacco products and NRT among pregnant women and women planning a pregnancy. Preventive Medicine Reports. 4(2016) 481-5.

Women's Perceptions Cont'd

Themes:

E-cigarettes are easy to use in excess

"What threw me off with them was that there's no end point. Like if I'm smoking a regular cigarette, I know I got five and a half, six minutes, then I'm out. But I could smoke [e-cigs] all day long, and next thing I know, I been outside 30 minutes and I'm like oh God, I got to go back to work or whatever." -[Pregnant Quitter]

Dissolvable products reviews were mixed

Oral products are discreet and can lessen stigma

"Maybe you wouldn't get judged by people because you could hide it better than smoking. I don't like being judged by people. I hate that." -[Pregnant smoker]

Oral products go directly to the baby

"It's kind of like feeding it to your baby directly. You're feeding it cigarettes. It's crazy." -[Pregnant smoker]

England L, Tong V, Koblitz, A et al. Perceptions of emerging tobacco products and NRT among pregnant women and women planning a pregnancy. Preventive Medicine Reports. 4(2016) 481-5.

Future Directions

Continuum of Risk Framework

More toxic

**Combusted products/
conventional cigarettes**

**Non-combusted tobacco
products**

Less toxic

Nicotine only products

No nicotine use

Adapted from Zeller M, Hatsukami D; Strategic Dialogue on Tobacco Harm Reduction Group.
Tob Control. 2009 Aug;18(4):324-32.

Future Directions



- ❑ **Precautionary principle (multidisciplinary, transparent)**
- ❑ **Unintended consequences of growth in emerging tobacco product markets: high e-cigarette use in female youth and in women < 20 with a live birth (quit rates are high)**
- ❑ **Potential unintended consequences include**
 - Increased prevalence of nicotine exposure during pregnancy through higher prevalence of tobacco product use in general
 - Increased nicotine exposure in individuals through dual use, increased frequency/intensity of use of newer products, advances in technology (nicotine delivery)
- ❑ **Vulnerabilities include desire to reduce stigma, misconceptions about nicotine exposure, attraction to reduced risk and “cleaner” product claims/marketing**

Future Directions

- ❑ **Continue to monitor product development and tobacco industry tactics, public perceptions/attitudes**
- ❑ **Adapt surveillance of emerging product use (during pregnancy) to better meet public health needs**
- ❑ **Continue to research the health effects of emerging products and nicotine exposure on health outcomes for vulnerable populations**
- ❑ **Promote provider awareness, provide educational materials**
- ❑ **Counter industry efforts to normalize recreational nicotine, especially in vulnerable populations**

Contact Information

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Nicotine Exposure in Adolescence

- Adolescence is marked by major plasticity of brain systems regulating motivated behavior and cognition
- Synaptic formation and learning highly strengthened by stimulation from environmental experience; addictive drugs can activate and strengthen reward circuits to create an addicted state
- Nicotine appears to increase rewarding effects of other drugs
- Nicotine disrupts adolescent brain development
 - Decreases attention
 - Alters mood
 - Increases impulsivity

England LJ, Aagaard K, Bloch M, et al. Developmental toxicity of nicotine: A transdisciplinary synthesis and implications for emerging tobacco products. *Neurosci Biobehav Rev.* 2017 Jan;72:176-189.

Summary and Conclusions

- ❑ Tobacco use continues to pose a major global public health burden
- ❑ The tobacco industry offers a full spectrum of rapidly evolving “recreational” nicotine-containing products and NRT, giving them flexibility to adapt to FDA regulations and consumer preferences
- ❑ Industry investments in NRT/other pharmaceuticals are of special concern; conflicts of interest are hidden
- ❑ Pregnant women and women of reproductive age may be especially vulnerable to reduced risk and “cleaner” product claims

Summary and Conclusions

- ❑ Health risks of tobacco products such as e-cigarettes and heat-not-burn may take decades to fully manifest
- ❑ Human and animal research supports that nicotine adversely affects pregnancy outcomes, fetal and adolescent brain development, fetal lung development, and infant cardio-respiratory function
- ❑ Increasing use in young women with a live birth and during pregnancy/dual are of concern—more data are needed

Warning Labels Cigarettes



•**SURGEON GENERAL'S WARNING:**
Smoking By Pregnant Women May
Result in Fetal Injury, Premature
Birth, And Low Birth Weight.



Warning - Cigarette smoke harms
babies before and after they are
born. It causes low birth weight and
lung problems in babies.

Health Canada

You can quit. We can help.

gosmokefree.gc.ca/quit

1-866-366-3667

<https://www.fda.gov/tobacco-products/retail-sales-tobacco-products/retailers-chart-required-warning-statements-tobacco-product-packaging-and-advertising>

<https://www.canada.ca/en/health-canada/services/health-concerns/tobacco/legislation/tobacco-product-labelling.html>

Co-opting Harm Reduction

The screenshot shows the top navigation bar of the Philip Morris International website. The logo is on the left, followed by the tagline "Delivering a Smoke-Free Future" and a menu with items: ABOUT US, OUR BUSINESS, OUR TRANSFORMATION, OUR SCIENCE, INVESTOR RELATIONS, SUSTAINABILITY, and CAREERS. Below the navigation, there's a breadcrumb trail: HOME > Our science > Tobacco harm reduction. The main heading is "Tobacco harm reduction" with a sub-headline: "The best choice for any smoker is to quit products containing nicotine and tobacco altogether. However, many don't. Better alternatives exist for those adult smokers who would otherwise continue to smoke. This is tobacco harm reduction." Below this, there's a paragraph: "Innovations to reduce the harm caused by certain behaviors and activities are woven into our everyday lives. PMI is calling for a similar approach to be applied to the known risks of smoking." A link says "Find out how tobacco harm reduction could have a positive impact on the lives of adult smokers who don't quit." The bottom section features three cards: 1. "Smoke-free alternatives could deliver a 10-fold reduction in smoking-attributable deaths" with a sub-headline "Using data, estimates, and methods from the WHO and other third parties, we have calculated the potential positive impact to public health if the world's smokers switched from cigarettes to smoke-free products." and a "READ MORE" link. 2. "What is tobacco harm reduction?" with a "READ MORE" link. 3. "The facts about nicotine" with a "READ MORE" link. On the left side of the screenshot, there is a quote in a white box.

PHILIP MORRIS INTERNATIONAL

Delivering a Smoke-Free Future
ABOUT US OUR BUSINESS OUR TRANSFORMATION OUR SCIENCE INVESTOR RELATIONS SUSTAINABILITY CAREERS

HOME > Our science > Tobacco harm reduction

Tobacco harm reduction

The best choice for any smoker is to quit products containing nicotine and tobacco altogether. However, many don't. Better alternatives exist for those adult smokers who would otherwise continue to smoke. This is tobacco harm reduction.

Innovations to reduce the harm caused by certain behaviors and activities are woven into our everyday lives. PMI is calling for a similar approach to be applied to the known risks of smoking.

Find out how tobacco harm reduction could have a positive impact on the lives of adult smokers who don't quit.

“Existing efforts to discourage people from smoking and encouraging those who do to quit must continue. But supplementing these measures with a tobacco harm reduction approach can accelerate a decline in smoking. If better alternatives to smoking are also made available, and enough smokers switch to them, we can more rapidly achieve a significant milestone in global health—a world without cigarettes. Who would deny society a harm-reduction opportunity like that?”

Smoke-free alternatives could deliver a 10-fold reduction in smoking-attributable deaths

Using data, estimates, and methods from the WHO and other third parties, we have calculated the potential positive impact to public health if the world's smokers switched from cigarettes to smoke-free products.

READ MORE →

What is tobacco harm reduction?

READ MORE →

The facts about nicotine

READ MORE →

<https://www.pmi.com/our-science/tobacco-harm-reduction/what-is-tobacco-harm-reduction>

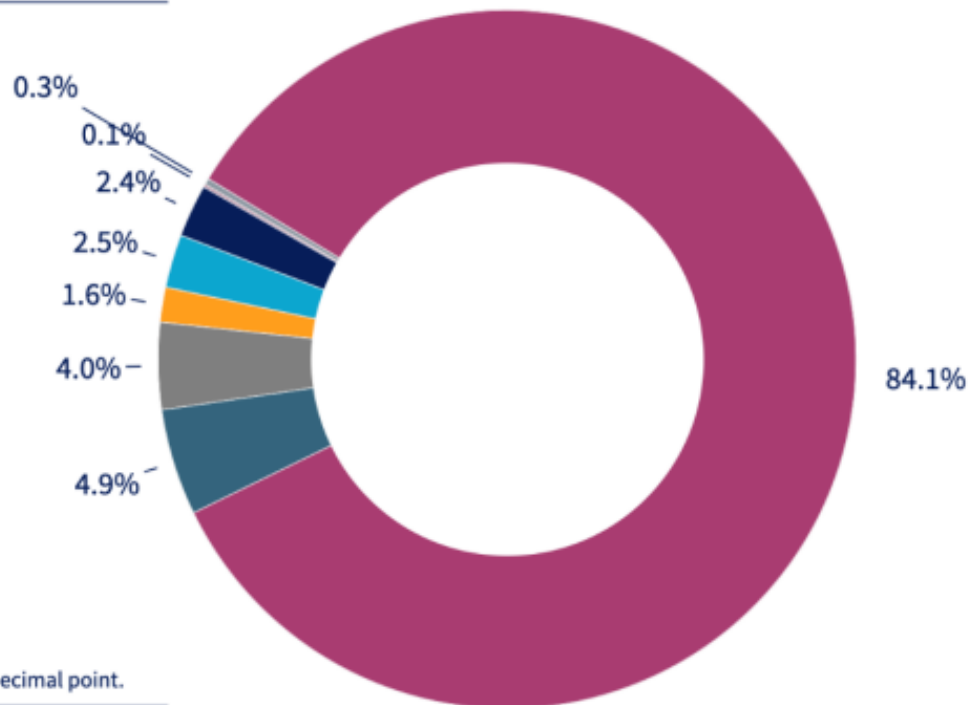
Global Nicotine Products Retail Value

Global category market size

Global Nicotine Ecosystem by Product Category

Retail Value Sales, 2020

- Cigarettes
- Cigars and Cigarillos
- Smoking Tobacco
- Smokeless Tobacco
- Vaping Products
- Heated Tobacco
- Tobacco-Free Oral Nicotine
- NRT Smoking Cessation Aids

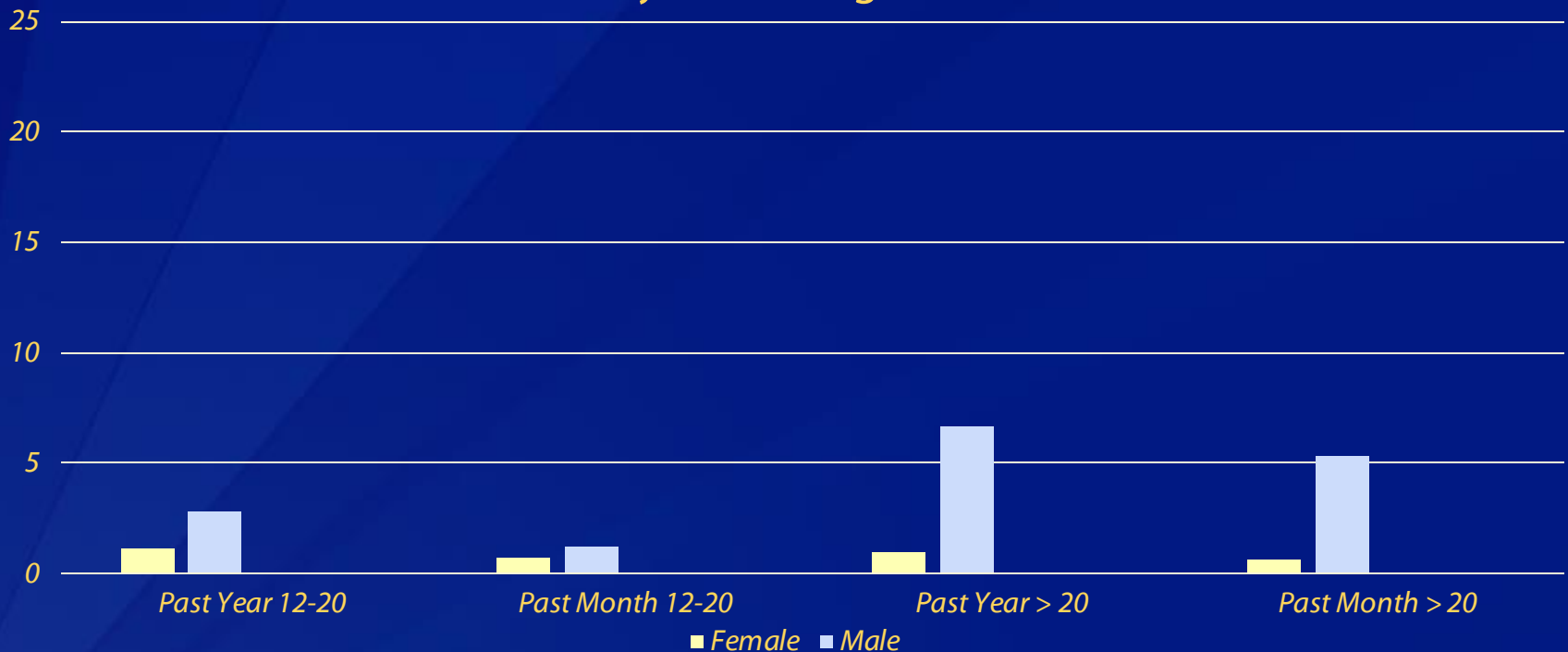


Source: Euromonitor Passport. Figures rounded to the nearest decimal point.

Note: Retail value in current (nominal) terms, fixed 2020 exchange rate.

US Prevalence of Smokeless Tobacco Use 2021

Percentage past and current smokeless tobacco use
by sex and age, NSDUH 2021



NSDUH—<https://www.samhsa.gov/data/report/2021-nsduh-detailed-tables>

E-cigarette Ads Targeting Women



1976: Lorillard
Considering all I'd heard,
I decided to either quit
or smoke True.
I smoke True.

The low tar, low nicotine cigarette
Think about it.

Warning: The Surgeon General Has Determined
That Cigarette Smoking is Dangerous to Your Health.

King: Tar: 11 mg. "tar", 0.8 mg. nicotine av. per cigarette by FTC method. Soft: Tar: 0.7 mg. nicotine av. per cigarette, FTC Method. Non-TOB.



GIVE THE GIFT
of fresh air!

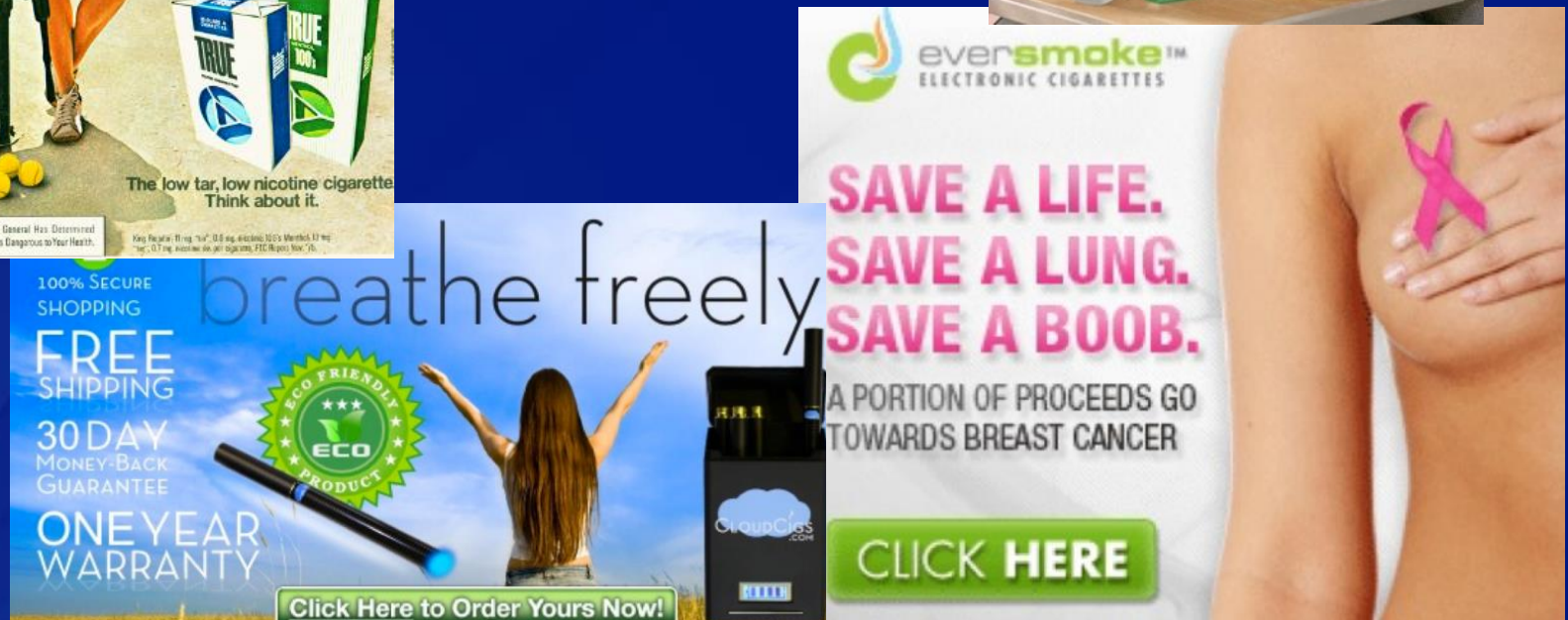
- Eliminate the tar, ash and unwanted chemical additives from your cigarettes

>> Shop WhiteCloud

White Cloud
CIGARETTES



No lighters. No ashtrays. Just real tobacco with less lingering odor.



ever**smoke**™
ELECTRONIC CIGARETTES

**SAVE A LIFE.
SAVE A LUNG.
SAVE A BOOB.**

A PORTION OF PROCEEDS GO
TOWARDS BREAST CANCER

CLICK HERE

100% SECURE SHOPPING
FREE SHIPPING
30 DAY MONEY-BACK GUARANTEE
ONE YEAR WARRANTY

breath**re** freely

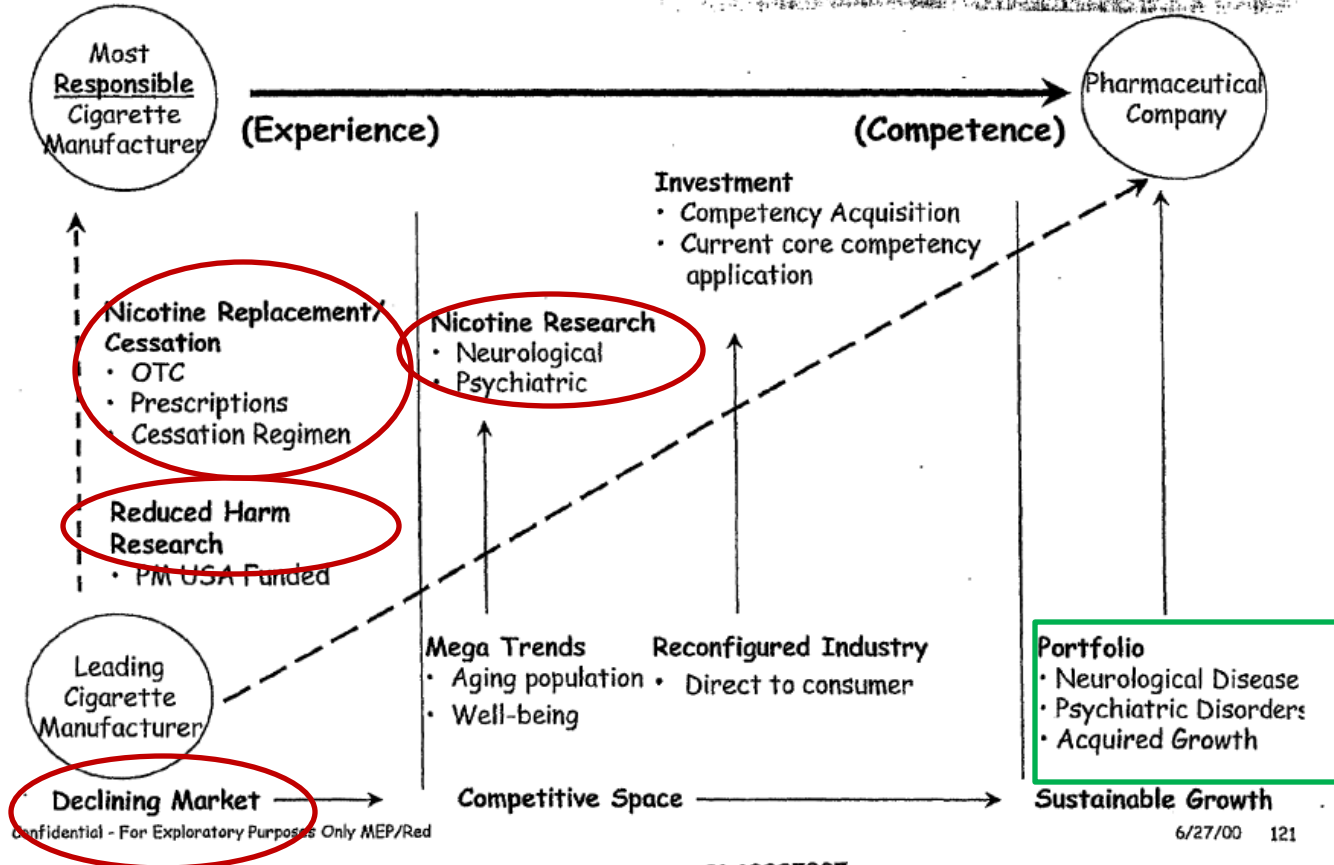
ECO FRIENDLY
ECO PRODUCT

Click Here to Order Yours Now!

CloudCiss.com

<https://truthinitiative.org/research-resources/targeted-communities/old-tactics-new-products-how-big-tobacco-targets-women#>

Pharmaceutical Exploration

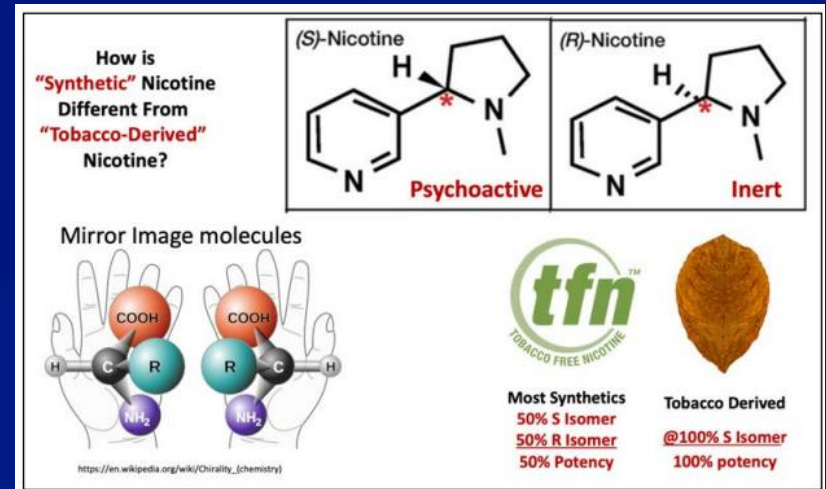


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Changing Products

Synthetic Nicotine

- Regulation loophole now closed
- Marketed as “tobacco-free” and “pure” and “addiction-free”
- The cost of producing synthetic nicotine has plummeted



A POUCH DESIGNED WITH YOU IN MIND

This small, white pouch allows for a neat and manageable experience.



<https://tobacco-img.stanford.edu/wp-content/uploads/2022/03/13161808/Synthetic-Nicotine-White-Paper-3-8-2022F.pdf>

Sweden: SIDS, SUID, Post-neonatal Mortality

Table 4. Maternal tobacco use in early pregnancy and cessation of tobacco use before the antenatal booking and risk of post neonatal mortality, SUID, and SIDS, $N = 1,996,980$.

	<i>n</i> (%)	Crude ^a OR (95% CI)	Adjusted ^b OR (95% CI)	Adjusted ^c OR (95% CI)
Post neonatal mortality ^d , $N = 1514$				
Nonuser	1072 (0.07)	Reference	Reference	Reference
Snuff user	22 (0.13)	1.95 (1.27–3.01)	1.81 (1.17–2.80)	1.75 (1.13–2.71)
Stopped using snuff	27 (0.07)	1.08 (0.73–1.59)	1.21 (0.82–1.79)	1.24 (0.84–1.84)
Smoker	263 (0.19)	2.94 (2.56–3.39)	2.09 (1.79–2.44)	1.73 (1.48–2.02)
Stopped smoking	130 (0.07)	1.13 (0.94–1.37)	1.03 (0.85–1.24)	1.02 (0.84–1.23)
SIDS, $N = 354$				
Nonuser	160 (0.01)	Reference	Reference	Reference
Snuff user	11 (0.06)	6.16 (3.25–11.7)	4.36 (2.29–8.31)	4.33 (2.27–8.26)
Stopped using snuff	8 (0.02)	2.20 (1.08–4.49)	2.13 (1.04–4.34)	2.15 (1.05–4.40)
Smoker	141 (0.10)	10.3 (8.16–13.1)	5.46 (4.15–7.18)	4.96 (3.77–6.54)
Stopped smoking	34 (0.02)	1.71 (1.14–2.56)	1.35 (0.89–2.05)	1.35 (0.89–2.04)
SUID, $N = 579$				
Nonuser	324 (0.02)	Reference	Reference	Reference
Snuff user	14 (0.08)	3.97 (2.28–6.91)	3.20 (1.83–5.60)	3.16 (1.81–5.53)
Stopped using snuff	10 (0.02)	1.36 (0.73–2.56)	1.37 (0.73–2.58)	1.40 (0.74–2.63)
Smoker	174 (0.13)	6.35 (5.24–7.70)	3.95 (3.17–4.91)	3.46 (2.78–4.32)
Stopped smoking	57 (0.03)	1.54 (1.14–2.07)	1.29 (0.95–1.74)	1.27 (0.93–1.72)

CI confidence interval, OR odds ratio.

^aCrude odds ratios calculated with the same population as adjusted models.

^bAdjusted for maternal age, parity, maternal education, cohabitant with father-to-be, mother's country of birth.

^cAdjusted for maternal age, parity, maternal education, cohabitant with father-to-be, mother's country of birth, gestational age, birth weight according to gestational age.

^dPopulation for neonatal mortality was $n = 1,994,209$. Infants who died in the neonatal period were excluded, $n = 2771$.

Gunnerbeck, A., Lundholm, C., Rhedin, S. *et al.* Association of maternal snuff use and smoking with Sudden Infant Death Syndrome: a national register study. *Pediatr Res* **94**, 811–819 (2023).

Sweden: Apnea

- Live singleton births 1999-2006 N=610,000
- ICD 10 codes included **cyanotic attacks, primary and secondary apnea**

Tobacco Use in Early Pregnancy	Cases	Adjusted OR, 95% CI Model 1*	Adjusted OR, 95% CI Model 2**
No tobacco use	771	Reference	Reference
Snus	26	2.15 (1.44, 3.20)	1.96 (1.30, 2.96)
Cigarettes			
1-9/day	94	1.31 (1.04, 1.65)	1.08 (0.85, 1.37)
10+/day	40	1.49 (1.07, 2.08)	1.08 (0.76, 1.52)

*Adjusted for age, height, education,

Also adjusted for **mode of delivery, gender, gestational age, SGA

Gunnerbeck A, Wikstrom AK, Bonamy et al. Relationship of maternal snuff use and cigarette smoking with neonatal apnea. Pediatrics. 2011 Sep;128(3):503-9.

Neonatal Apnea

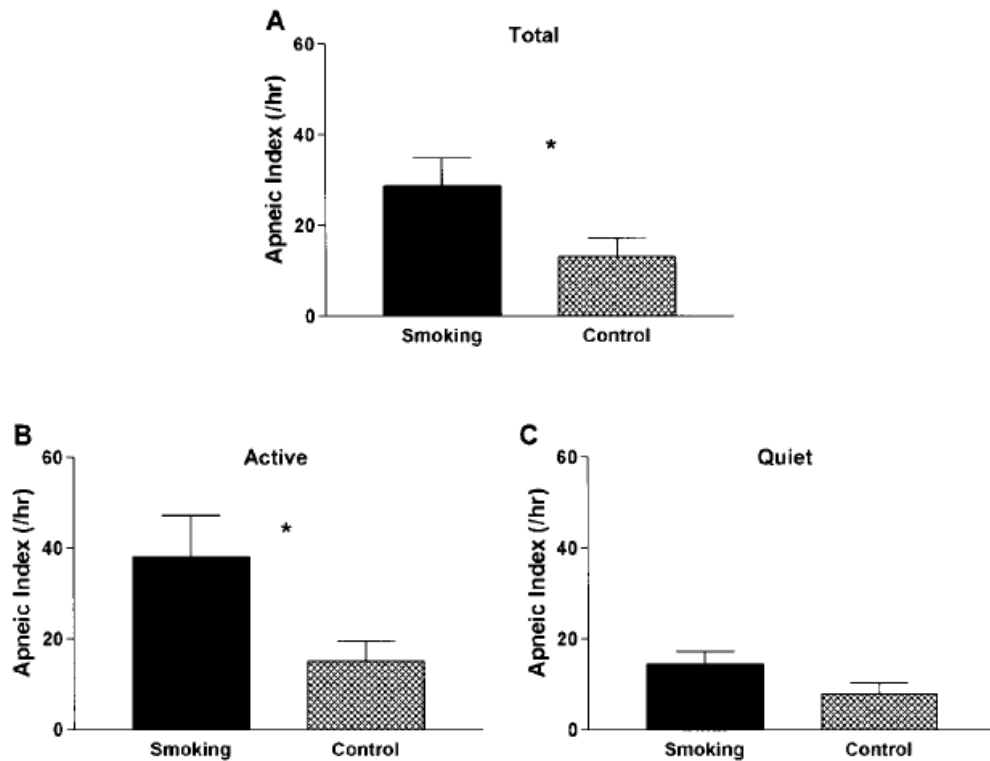


Figure 1. The effect of maternal smoking during pregnancy on apneic index (AI) in preterm infants. The overall AI (A) was increased in preterm infants born to smoking mothers, and this effect was more prominent during active sleep (B). Data represent means \pm SE; *p values less than 0.05 compared with the control group.

Neonatal Arousal

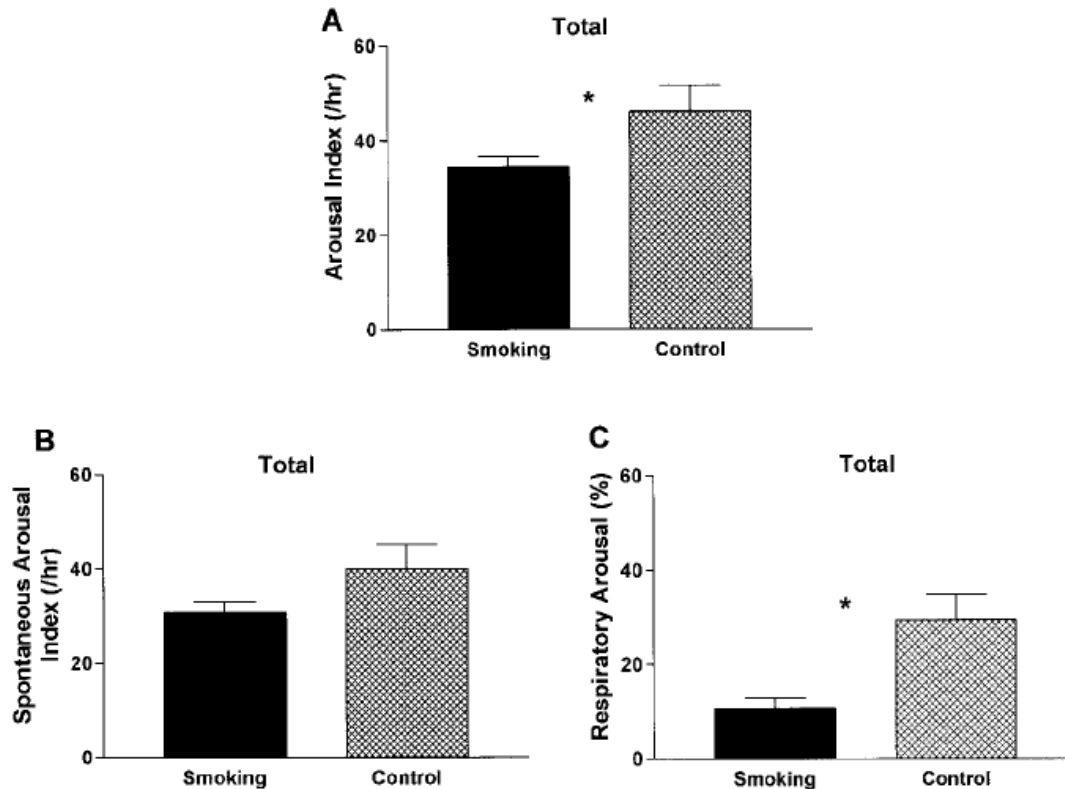


Figure 3. The effect of maternal smoking during pregnancy on total arousal index, spontaneous arousal index, and respiratory arousals (percentage of arousals after apneic events) in preterm infants. Prenatal exposure to cigarette smoke was associated with significant decrease in the total arousal index (A) and specific decrease in respiratory arousals (C). No significant difference in spontaneous arousals (B) was noted. Data represent means \pm SE; *p values less than 0.05 compared with the control group.

Smokeless Tobacco in Pregnancy (STiP)

- Western Alaska
- Large population of indigenous peoples
- Many still practice subsistence living
- Single health care system
- Local providers reported high rates of abruption and preeclampsia in iqmik users

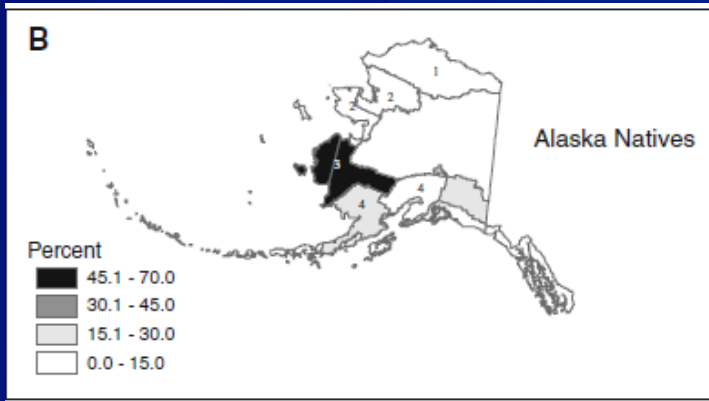


Iqmik

- A mixture of fire-cured tobacco leaves with the ash generated from burning punk fungus, high pH.



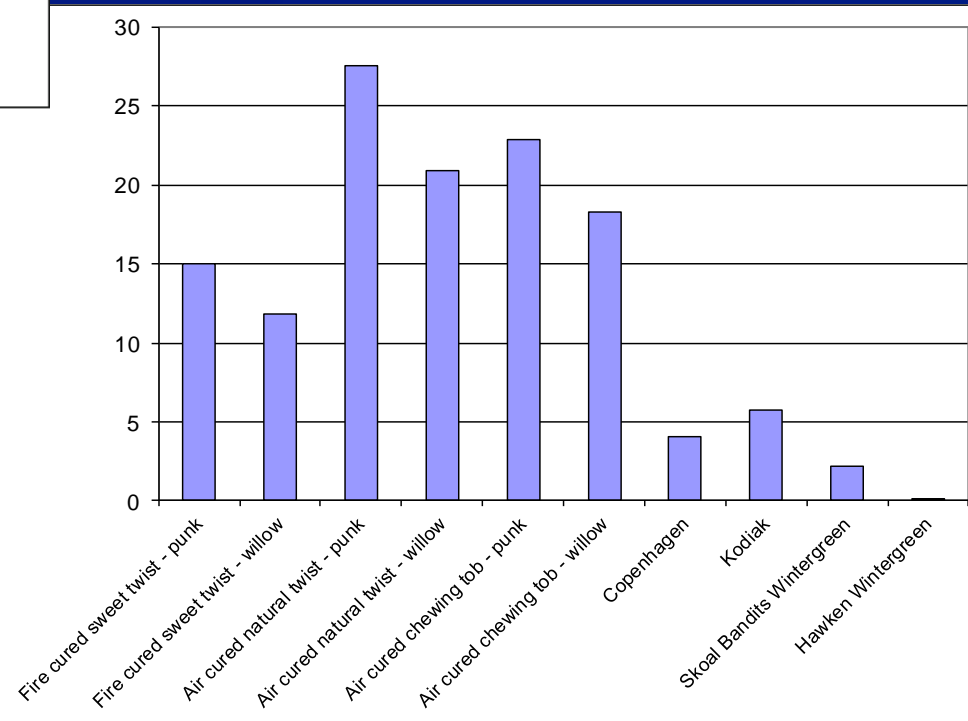
Case study: Birthweight and Iqmik



Free nicotine values for Iqmik and selected commercial smokeless products



Free nicotine mg/g tobacco



Alaska: Birth Weight (Controls)

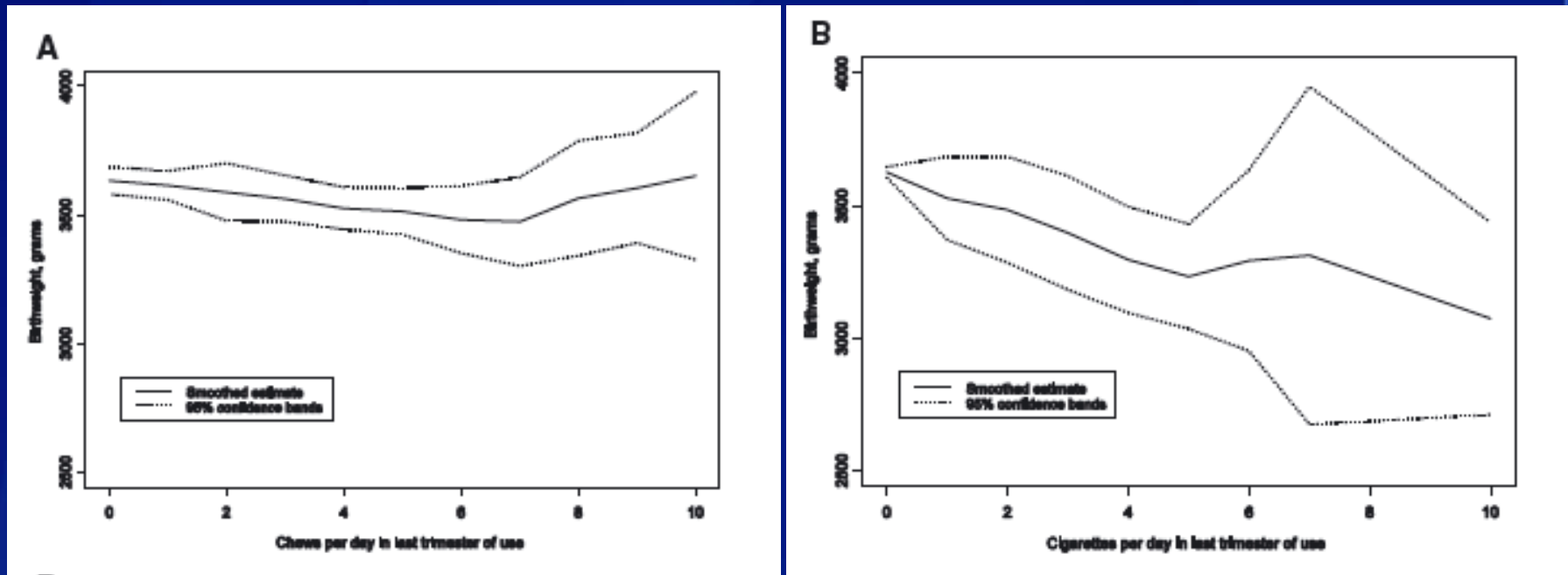


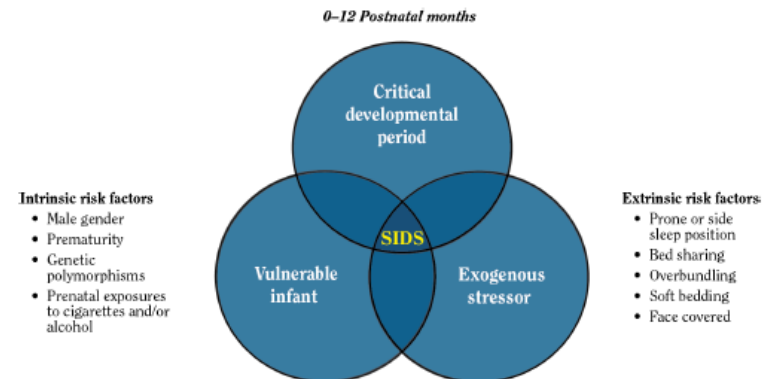
Figure 2. A, dose-response relation between chews per day and infant birth weight. B, dose-response relation between cigarettes per day and infant birthweight.

England LJ, Kim SY, Shapiro-Mendoza CK, et al. Maternal smokeless tobacco use in Alaska Native women and singleton infant birth size. *Acta Obstet Gynecol Scand* 2012;91:93-103.

Case Study: SIDS

- **Leading cause of death in infants 1 - 12 mths**
- **Possible mechanisms:**
 - Newborn's autonomic control of respiratory and cardiovascular systems are immature
 - Sleep "architecture" still developing as well; sleep influences respiratory and cardiovascular control
 - Apnea and hypoxia are common problems in infants (preterm)
 - Survival of hypoxic challenges depends on responses mediated by catecholamines

Figure 9.2 Triple-risk model for sudden infant death syndrome (SIDS)



Source: Trachtenberg et al. 2012. Reprinted with permission from American Academy of Pediatrics, © 2012.

Prenatal Nicotine Exposure Affects Autonomic Control of Respiratory and Cardiovascular Systems

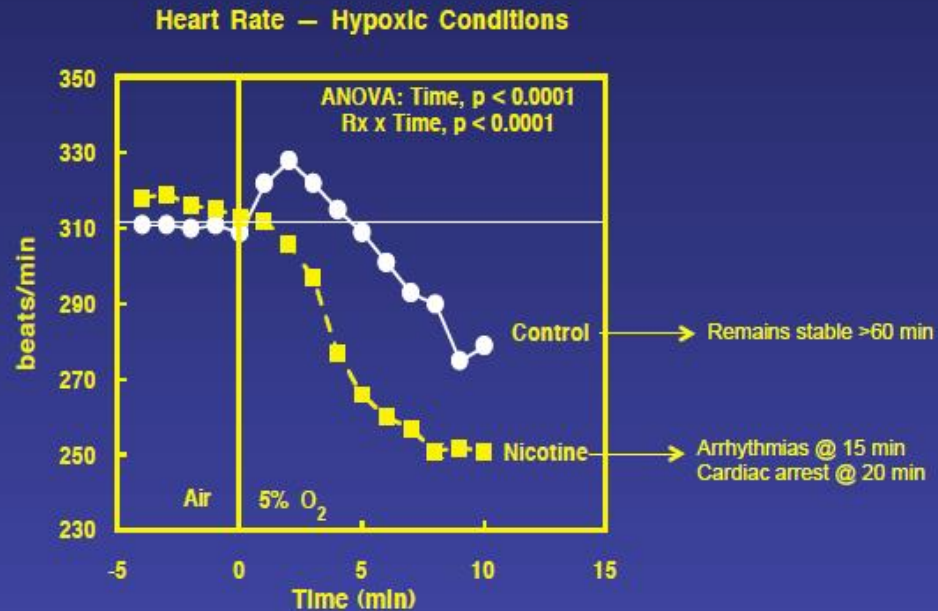
□ Normal neonates

- nAChRs regulate brainstem neuron activity
- During hypoxia, breathing and heart rate first increase, then decrease to prolong survival by reducing metabolic demands

□ Response to hypoxia in infants of smokers

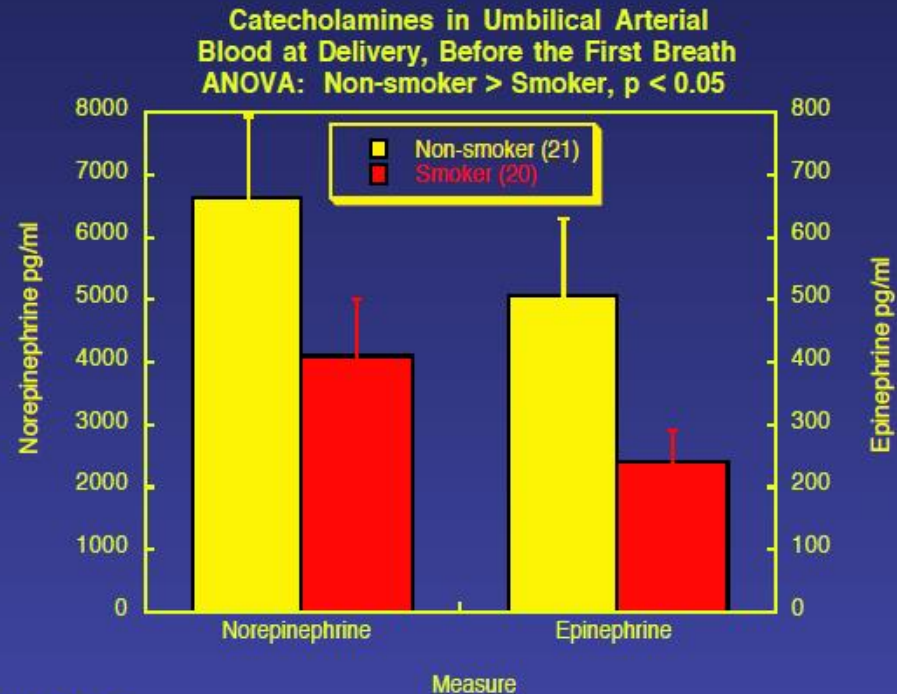
- Steeper ventilatory deceleration
- Shorter time to reach lowest oxygen saturation
- Response to hypoxia particularly impaired when prone

Maternal Smoking and SIDS: Proposed Mechanism



Slide courtesy of Theodore Slotkin. Fetal nicotine or cocaine exposure: which one is worse? *The Journal of Pharmacology and Experimental Therapeutics*, 1998.

Maternal Smoking and SIDS: Proposed Mechanism



Subjects matched for:

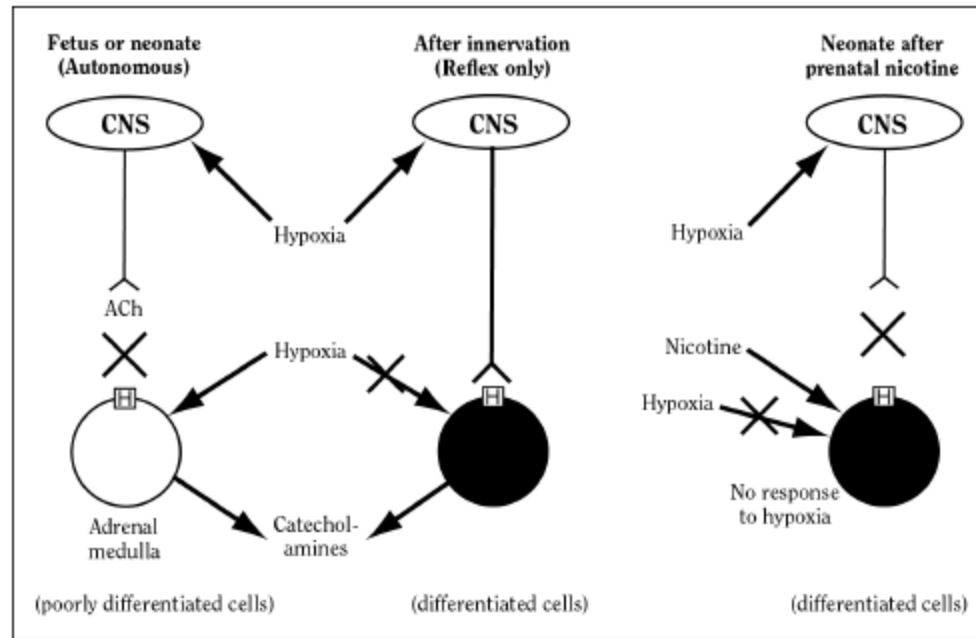
age, parity, SES, P_aO_2 , P_aCO_2 , pH_a

Slide courtesy of Theodore Slotkin

Oncken CA, Henry KM, Campbell WA, Kuhn CM, Slotkin TA, Kranzler HR. Effect of maternal smoking on fetal catecholamine concentrations at birth. *Pediatr Res.*

Maternal Smoking and SIDS: Proposed Mechanism

Figure 9.1 Catecholamine response to hypoxia by nicotine-exposed and unexposed rats

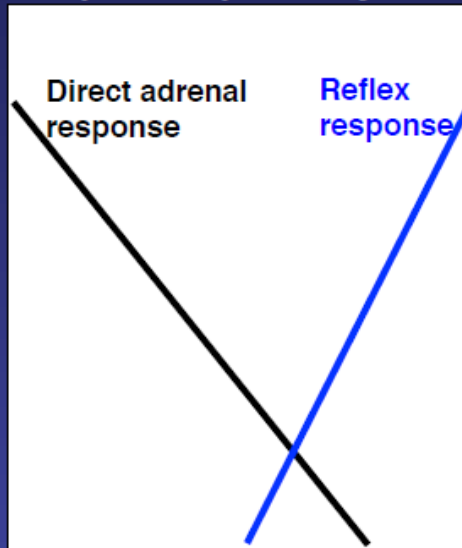


Source: Slotkin 1998. Reprinted with permission from American Society for Pharmacology & Experimental Therapeutics, © 1998.

Note: CNS = central nervous system.

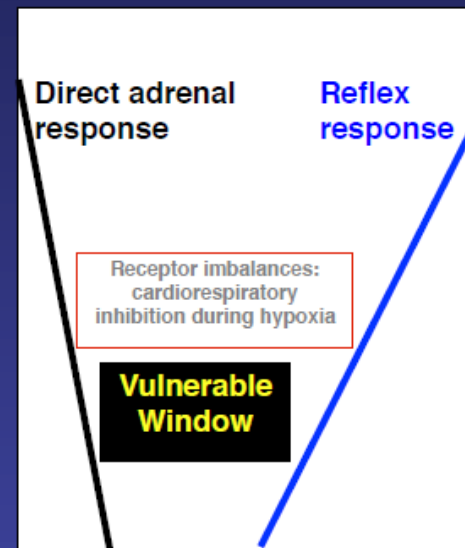
Maternal Smoking and SIDS: Proposed Mechanism

Normal Development: Direct response replaced by reflex



Increasing Age →

Nicotine Treatment: accelerated adrenomedullary development



Increasing Age →

- Vulnerable window at birth: perinatal morbidity/mortality
- Vulnerable window after birth: increased SIDS risk

Global Prevalence of Smoked Tobacco Use



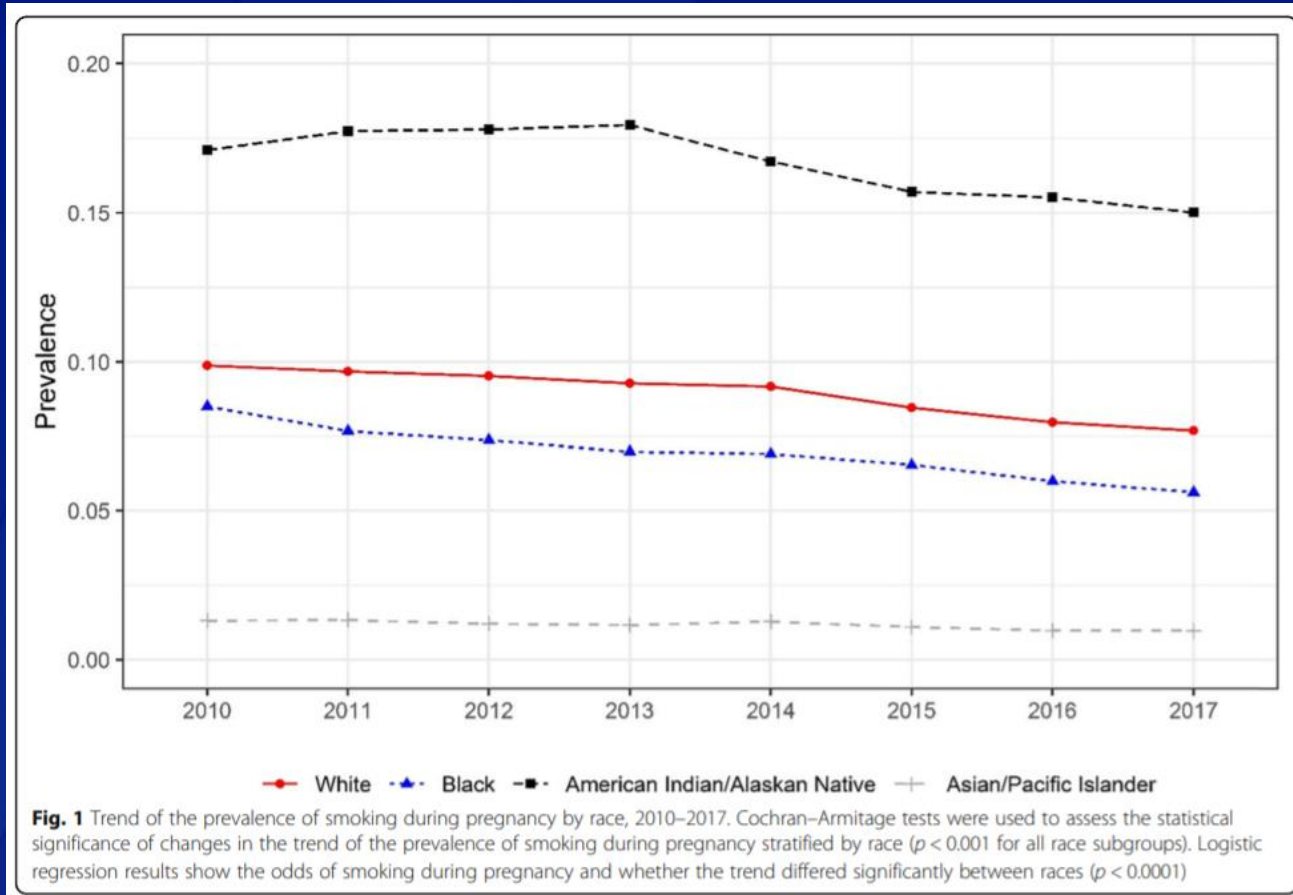
Pooled prevalence estimates*

- Cigarette smoking in women:
 - Ever smoked: 28% (95% CI: 24-32%)
 - Currently smokes: 17% (95% CI: 14-19%)
- Ever smoked cigarettes in subgroups:
 - Adolescent girls/students: 23% (95% CI: 20-27%)
 - Adult women: 27% (95% CI: 19-35%)
 - Pregnant women: 32% (95% CI: 22-42%)

***The study includes 36 studies from the Americas, 34 studies from Asia, 27 studies from Europe, 8 studies from Africa, and 4 studies from the Oceania region.**

Jafari A, Rajabi A, Gholian-Aval M, Peyman N, Mahdizadeh M, Tehrani H. National, regional, and global prevalence of cigarette smoking among women/females in the general population: a systematic review and meta-analysis. Environ Health Prev Med. 2021 Jan 8;26(1):5.

Pregnancy and Smoking



Azagba, S., Manzione, L., Shan, L. *et al.* Trends in smoking during pregnancy by socioeconomic characteristics in the United States, 2010–2017. *BMC Pregnancy Childbirth* 20, 52 (2020).

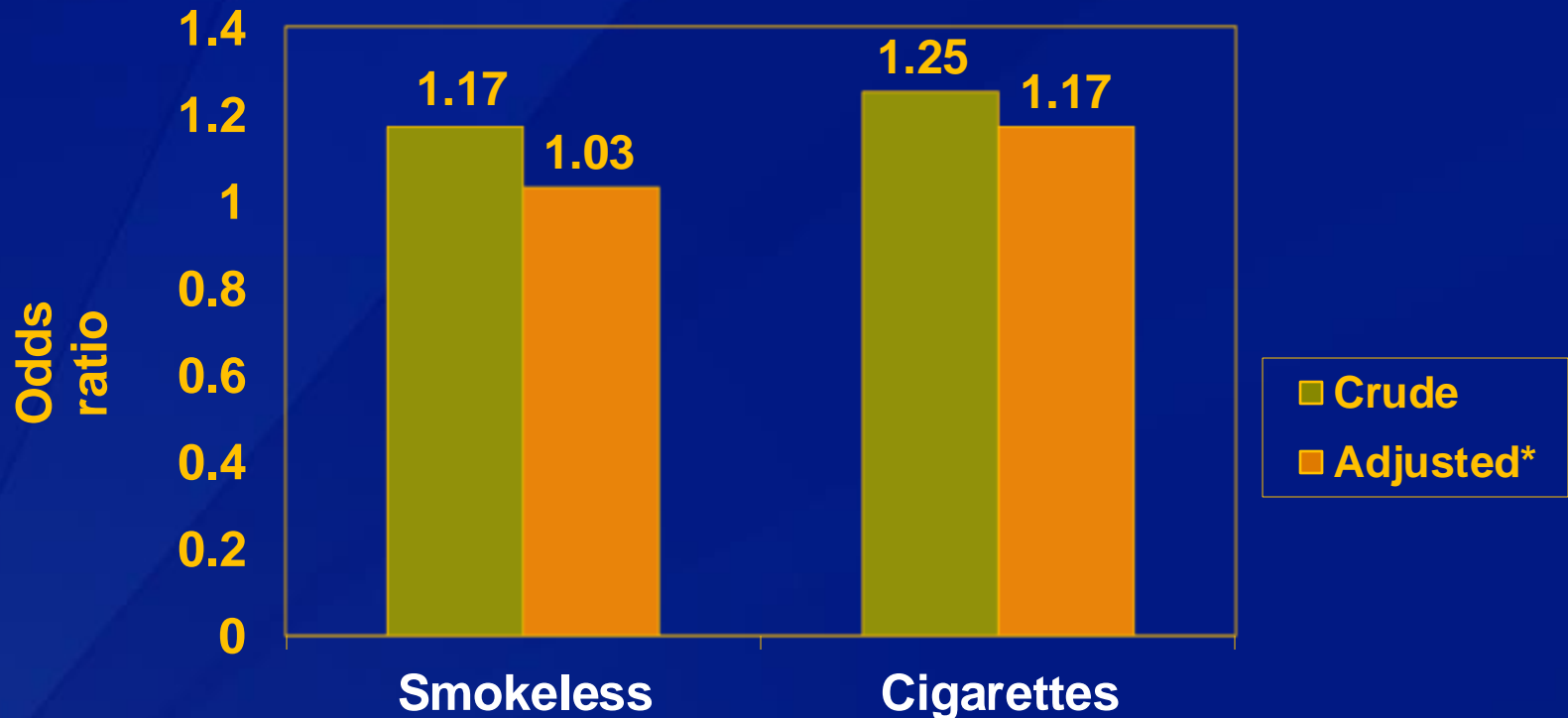
Gaps in Regulation

- Warning labels
- Nicotine conc/amount
- Internet sales to underaged individuals
- Flavored products (sale ban in 2020, but doesn't cover disposables and tanks, menthol or tobacco flavors)
- NRT as a recreational product
- Counterfeit products produced in unregulated facilities

<https://www.fda.gov/tobacco-products/ctp-newsroom/looking-back-looking-ahead-fdas-progress-tobacco-product-regulation-2022#>

<https://www.publichealthlawcenter.org/commentary/230208/2/8/2023-report-highlights-holes-fdas-enforcement-online-sales-e-cigarettes>

Placental Abruption

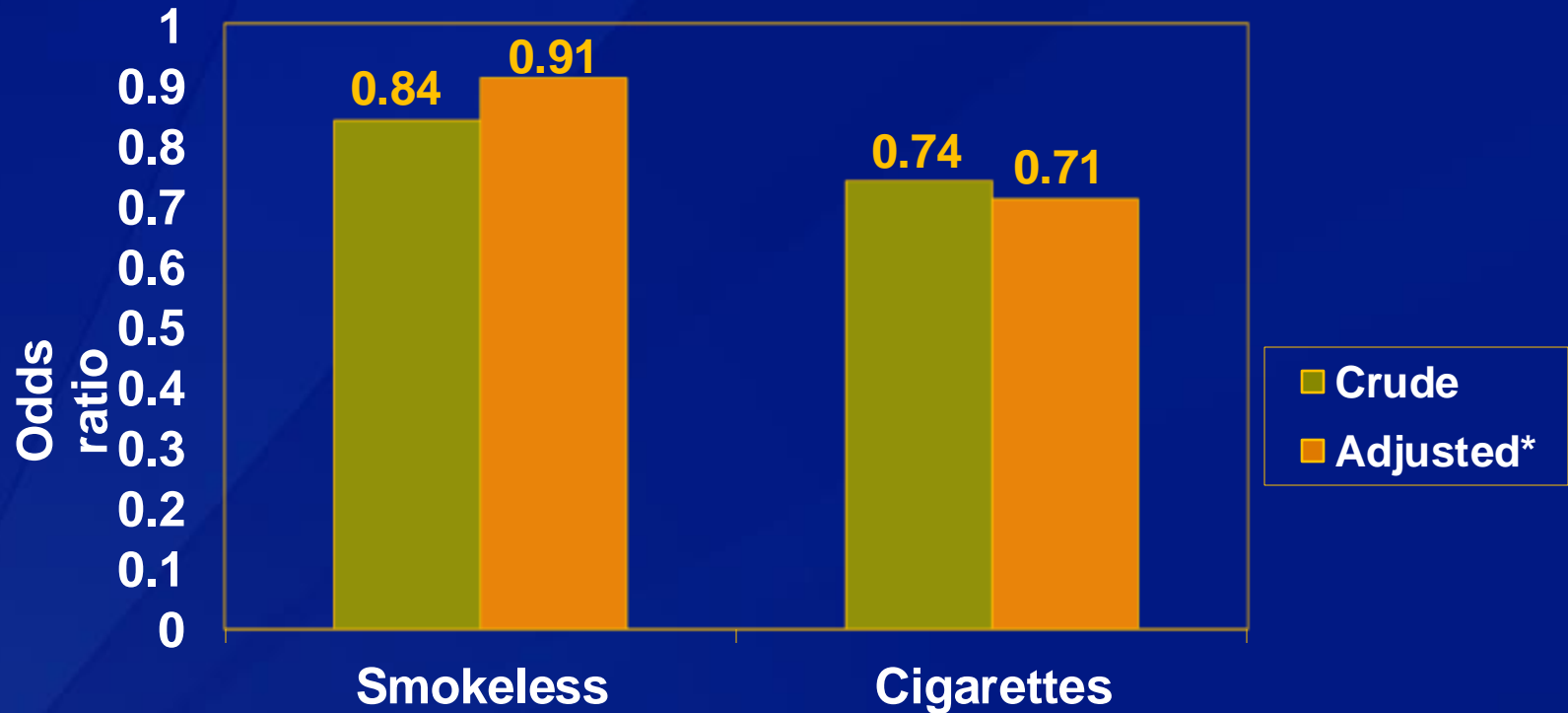


No comparisons were significant

*Adjusted for parity, pre-pregnancy BMI, age

England LJ, Kim SY, Shapiro-Mendoza CK, et al. Effects of maternal smokeless tobacco use on selected pregnancy outcomes in Alaska Native women: a case-control study. Acta Obstet Gynecol Scand 2013

Alaska: Preeclampsia



No comparisons were significant

*Adjusted for parity, pre-pregnancy BMI, age

England LJ, Kim SY, Shapiro-Mendoza CK, et al. Effects of maternal smokeless tobacco use on selected pregnancy outcomes in Alaska Native women: a case-control study. Acta Obstet Gynecol Scand 2013

Tobacco Industry and MCH

RESEARCH PROJECT 1993

ETS AND PREGNANCY

To be identified

Head of Obstetrics

Private Practice

Regional Hospital - Pediatric Polyclinic

SWITZERLAND ?

1. - INTERNAL

2. - 30KCHF

(PENDING OF SA. REP.)

The issues of maternal, spousal and work-place smoking all come together when considering pregnancy. In addition, women of child-bearing age constitute a significant part of our market, not to mention a powerful political force. Directly mobilizing such a significant segment of the adult population around such an emotional issue has the potential for providing tremendous impetus to all sorts of restrictive legislation in the home, in public areas as well as in the workplace. There is perhaps no other issue as powerful facing the industry.

-Philip Morris International 1993

Author unknown

<https://www.industrydocuments.ucsf.edu/tobacco/docs/#id=ptfg0111>

Tobacco Industry and MCH

REVIEW OF RISK FACTORS FOR SUDDEN INFANT DEATH SYNDROME

F M Sullivan & S M Barlow

Prepared for Philip Morris

stressful conditions. Further refinement of the relative contributions of different risk factors will be achieved by better control of confounding factors in epidemiological studies.

4201 Commerce Rd
Richmond Va
23234
Gate ~~A~~ Door 17?

- Overall - excellent job -
- Complete data capture
 - I would have like some more creativity - bottle / breast - age - immune infection
 - role of diagnosis vs study
 - Clearly a move in depth maternal smoking / Fetal development / newborn beyond scope of this analysis: but needs to be done
- but needs to be done

2505644921

Health Effects of Vaping in Adolescents

- Pulmonary effects
 - Exposure before maturity could result in the failure to reach full adult lung function potential and earlier onset of asthma, COPD, ILD if additional insults (as with adolescent onset smoking, SHS exposure). Supported by animal studies.
- Cardiovascular Effects
 - Systemic inflammation and endothelial dysfunction similar to that seen in smokers raises concerns about increased CVD risk
 - Animal studies with long-term e-cig exposure: cardiac fibrosis, decreased ejection fraction, atherosclerosis

Wold LE, Tarran R, Crotty Alexander LE, et al.; on behalf of the American Heart Association Council on Basic Cardiovascular Sciences; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Hypertension; and Stroke Council. Cardio-pulmonary consequences of vaping in adolescents: a scientific statement from the American Heart Association. *Circ Res.* 2022;130:e70–e82.

Adolescent Smoking

- Earlier initiation of smoking is associated with difficulty quitting
- Chronic impairments in verbal and working memory, worsen with withdrawal (associated with reduced efficiency in the hippocampus and parahippocampal gyrus—regions that support mnemonic processing)
- Aberrant development of white matter microstructure (anterior cortical and internal capsule fibers), which may lead to impairments in auditory processing
- Indices of smoking behavior negatively associated with neural function of the prefrontal cortex.

Jacobsen, Krystal, Mendel et al. *Biol Psychiatry* 2005 57:56-6.

Jacobsen, Picciotto, Heath, et al. *Biol Psychiatry* 2007 27(49):13491-8.

Galvan, Poldrack, Baker, et al. *Neuropharmacology* 2011 36:970-8.

Jacobsen, Picciotto, Heath, et al. *Biol Psychiatry* 2009 65(8):671-9.

Nicotine as a Gateway to Other Drugs

- Adolescent cigarette use tends to precede initiation of other drugs
- Nicotine primes animals to self-administer other substances (cocaine) but not the reverse
 - Nicotine encourages expression in the reward circuit of FOSB, a gene involved in learning processes. This makes it easier for other drugs to teach users' brains to repeat use
- Smoking seems to both enhance and prolong the pleasure of other non-drug related activities.

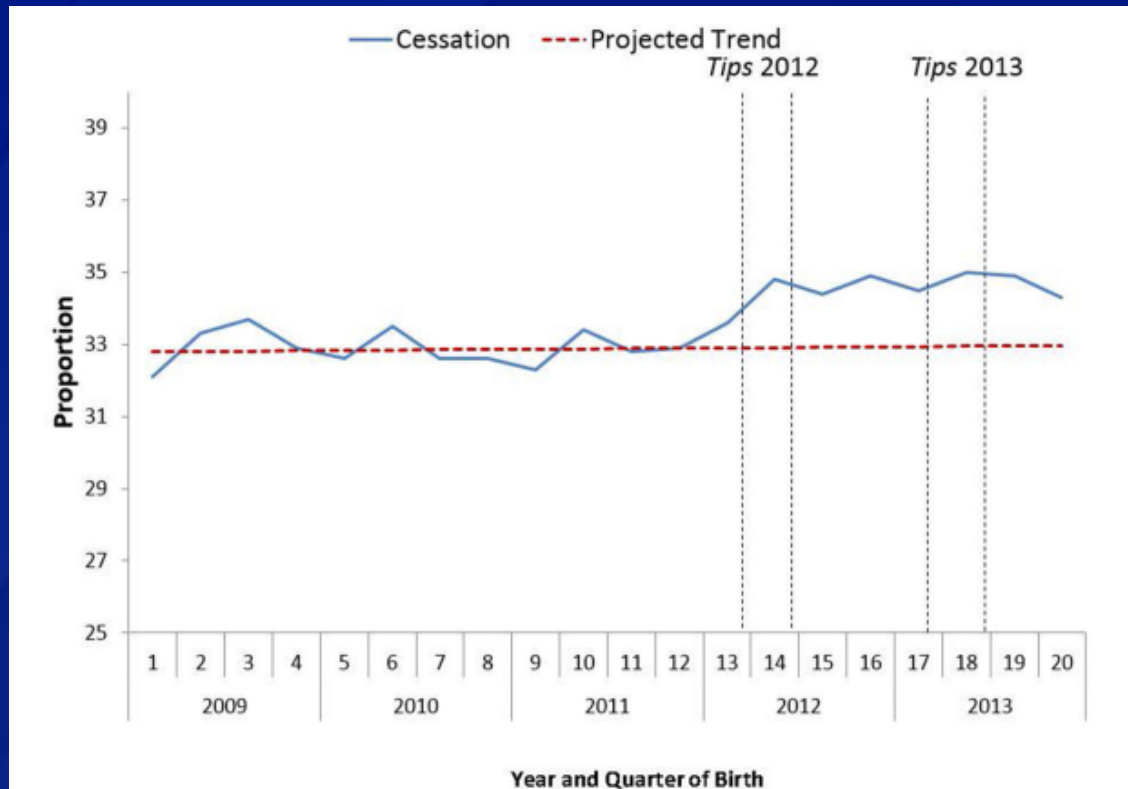
Kandel ER, Kandel DB. Shattuck Lecture. A molecular basis for nicotine as a gateway drug. N Engl J Med. 2014 Sep 4;371(10):932-43.

<https://blogs.scientificamerican.com/observations/recent-research-sheds-new-light-on-why-nicotine-is-so-addictive/>

Tobacco Cessation: Sex/Gender Differences

- Smoking a cigarette with nicotine, as compared to a de-nicotinized cigarette, alleviated the symptoms of withdrawal and negative mood to a greater extent in men than women.
- Women obtained equal relief from cigarettes with and without nicotine, suggesting that they found the drug less rewarding than men.
- Women may have difficulty quitting is post-cessation weight gain.
- The overall lower cessation rate for women may reflect sex differences in response to particular medications
 - Varenicline has greater short- and immediate-term efficacy (at 3 and 6 months) among women smokers. However, women and men show similar 1-year quit rates when using varenicline. In contrast, a combination of varenicline plus bupropion was less effective for cessation among women compared with men.
 - <https://nida.nih.gov/publications/research-reports/tobacco-nicotine-e-cigarettes/are-there-gender-differences-in-tobacco-smoking>

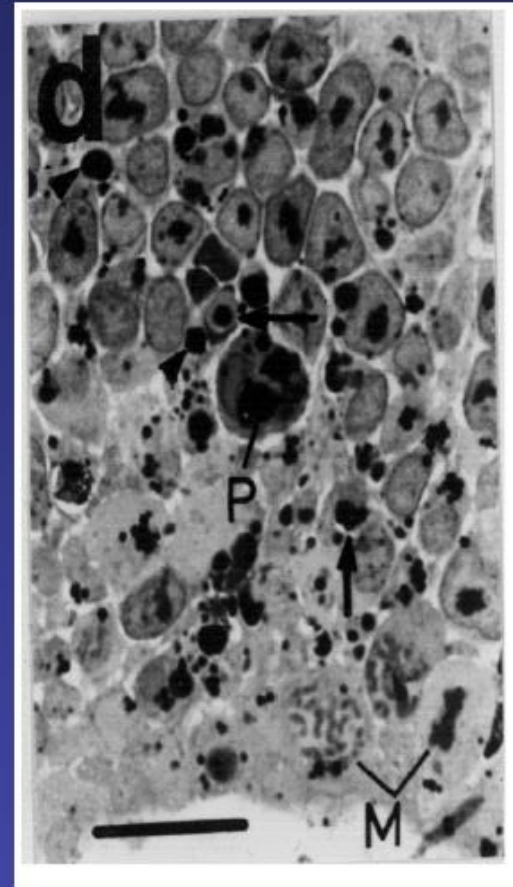
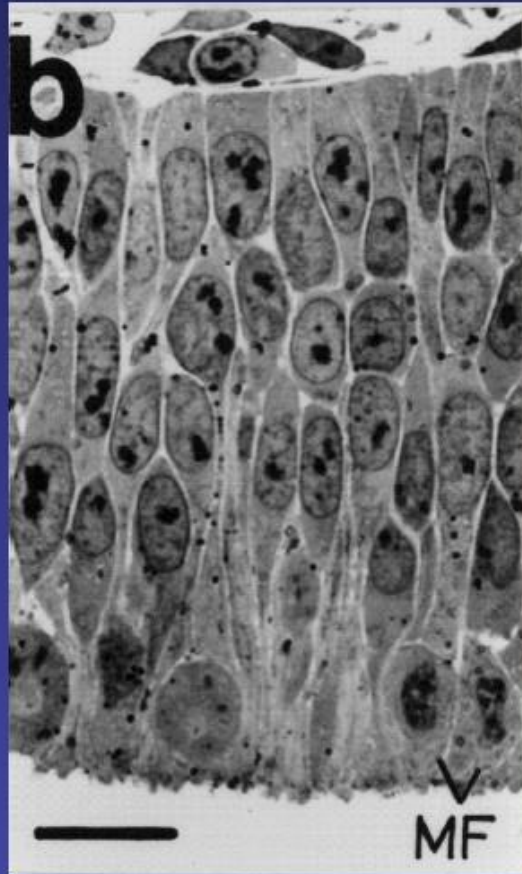
Tobacco Cessation: Public Health Campaigns



^a The percentage of women **who reported smoking >0 cigarettes per day for the three months before pregnancy** and then reported smoking 0 cigarettes per day during the third trimester of pregnancy.

^b Projected cessation trend using general linear models and pre-campaign data from January 1, 2009 through March 18, 2012, and extrapolated for 2012-2013 (intercept= 32.8; slope = 0.009). The *Tips 2012* campaign ran from March 19-June 10, 2012, and *Tips 2013* ran from March 4-June 24, 2013.

Effects During Neural Tube Stage



Slide courtesy of Theodore Slotkin

Harm Reduction

Harm reduction is a set of practical strategies and ideas aimed at reducing negative consequences associated with drug use. Harm Reduction is also a movement for social justice built on a belief in, and respect for, the rights of people who use drugs.

Harm Reduction Coalition

<http://harmreduction.org/about-us/principles-of-harm-reduction/>

Harm reduction refers to policies, programmes and practices that aim to reduce the harms associated with the use of psychoactive drugs in people unable or unwilling to stop. The defining features are the focus on the prevention of harm, rather than on the prevention of drug use itself, and the focus on people who continue to use drugs.

Harm Reduction International

<http://www.ihra.net/what-is-harm-reduction>

Harm reduction is a public health philosophy and intervention that seeks to reduce the harms associated with drug use and ineffective drug policies. A basic tenet of harm reduction is that there has never been, and will never be, a drug-free society.

The Drug Policy Alliance

<http://www.drugpolicy.org/about-drug-policy-alliance>

Harm Reduction

- ❑ **A harm reduction strategy needs to target addicted users, be conducted under rules established by health/governmental agencies whose only interest is to reduce harm, and includes the following critical elements:**
 - ***Scientific review concluding that that a product will/is highly likely to reduce a tobacco user's health risk and result in an overall public health benefit under the conditions that the products will be marketed, distributed and used.***
 - ***Measures in place to provide smokers with accurate information about what products/treatments have been determined to be effective at helping smokers quit and/or reduce the health risks for those smokers who can't or won't quit smoking tobacco products.***

Harm Reduction

- ***Regulation of product packaging, marketing and health claims to prevent misleading claims.***
- ***Distribution of the less harmful product is part of an intervention designed by health professionals.***
- ***Distribution and surveillance are monitored by appropriate health authorities.***
- ***A recognition that government-approved nicotine replacement therapies such as patches and gum can safely help smokers quit***
- ***Instructions for use so the product is used in ways that reduce harm and/or increase the ability of a smoker to successfully quit smoking and does not increase nicotine dependence.***

Harm Reduction

❑ **Genuine harm reduction does NOT:**

- Allow for the addictive product to be sold in settings accessible to the general public and without instructions for how to use the product most effectively.
- Include marketing that makes the product appealing to individuals not already addicted.
- Lead youth or other non-tobacco users to initiate use of the addictive product.
- Permit the industries that profits from causing the problem and sustaining the use of the more harmful product to drive the solution or control distribution of the alternative product.

TFK fact sheet https://www.tobaccofreekids.org/what-we-do/industry-watch/e-cigarettes/?utm_medium=ads&utm_source=GoogleSearch&utm_content=E-CigaretteKeywords&utm_campaign=AlwaysOnSearch-2022&gclid=Cj0KCQiAi8KfBhCuARIsADp-A576gtOm2mdKPOog4LkcScbIL-FUCctwT_qoxP2SpwOFFHlvDjEzUXAaAnkiEALw_wcB

Health Effects of Vaping

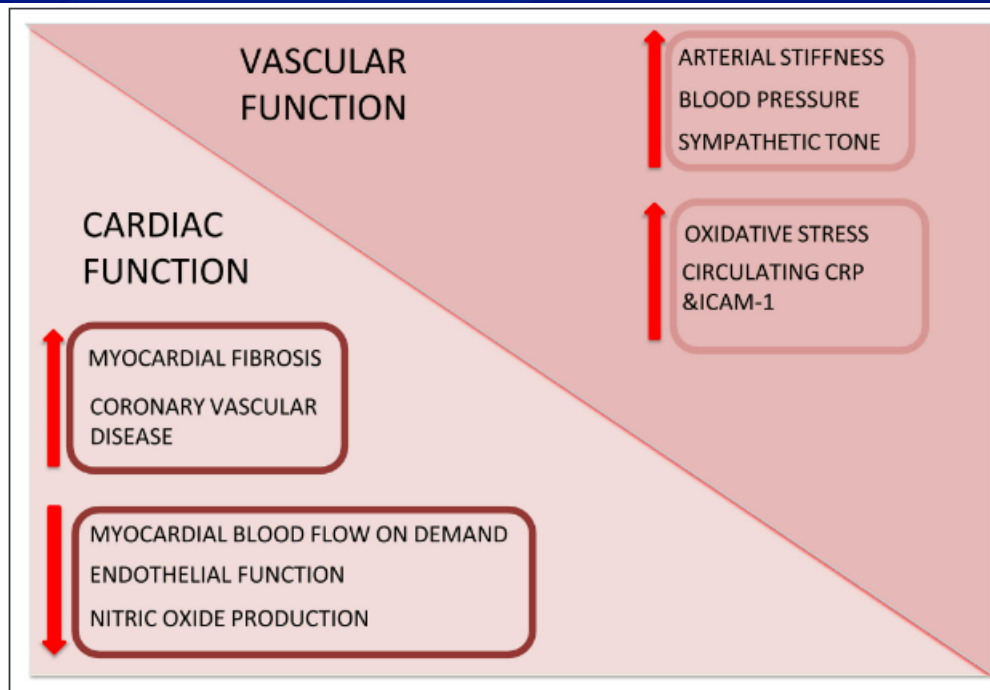


Figure 2. Schematic representation of known cardiac and vascular effects of vaping on heart and vascular function. Cardiac effects include increased myocardial fibrosis and coronary vascular disease, coupled with decreased myocardial blood flow, endothelial function, and nitric oxide production. Vascular effects include increased arterial stiffness, blood pressure, and sympathetic tone, along with elevated oxidative stress and inflammation. CRP indicates C-reactive protein; and ICAM-1, intracellular adhesion molecular-1.

[Cardiopulmonary Consequences of Vaping in Adolescents: A Scientific Statement From the American Heart Association](#)
Loren E. Wold, Robert Tarran, Laura E. Crotty Alexander, et al. on behalf of the American Heart Association Council on Basic Cardiovascular Sciences; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Hypertension; and Stroke Council

Why Girls and Women?

□ **Addiction characteristics differ**

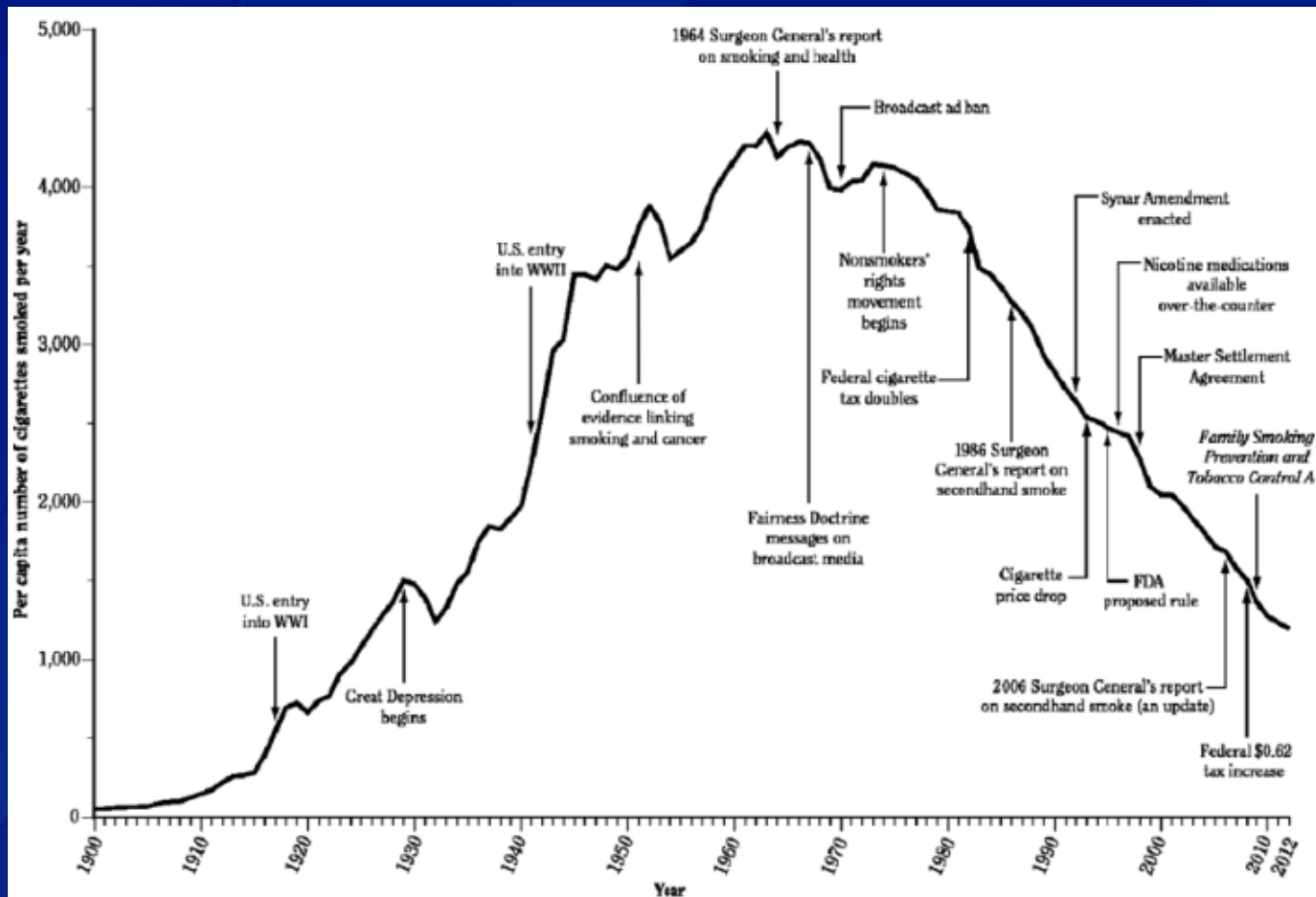
- Neuroimaging studies suggest that smoking activates men's reward pathways more than women's
- Men may smoke for the reinforcing effects of nicotine, women smoke to regulate mood
- Women experience stronger craving in response to stress, but men may be more responsive to environmental cues

□ **Barriers to quitting differ**

- Men and women appear to be similar in quit attempts
- Women less likely to quit
 - Might be due in part to concerns about weight gain

□ **E-cigarette use in female youth now exceeds that in male youth**

How Did We Get Here?



Sources: Adapted from Warner 1985 with permission from Massachusetts Medical Society, ©1985; U.S. Department of Health and Human Services 1989; Creek et al. 1994; U.S. Department of Agriculture 2000; U.S. Census Bureau 2013; U.S. Department of the Treasury 2013.

Adults ≥18 years of age as reported annually by the Census Bureau.

Industry Messages Haven't Changed...

Is nicotine harmful?

Because nicotine is so closely associated with smoking we understand why some people may think it is responsible for many of the harmful effects of smoking. Consuming nicotine is not completely risk free. Rapid absorption of a large dose through skin contact or oral ingestion can cause severe reactions requiring medical attention and poses risk of fatality in children, animals or highly vulnerable persons. However, at typical recreational doses it is usually safe for healthy adults. It is now widely acknowledged that the cause of most of the serious health risks associated with conventional cigarettes is the toxicants in the smoke produced when tobacco is burned – and not the nicotine.

Is nicotine addictive?

any nicotine product

What are the effects of using nicotine?

First-time users of nicotine often experience dizziness and/or nausea. After becoming accustomed to using nicotine, effects have been reported to range from helping adults to relax to acting as a stimulant. Other reported effects include improvements in mood and concentration. Nicotine can cause acute increases in heart rate and blood pressure. As a result, reduced-risk nicotine **† products are not suitable people with heart conditions, severe hypertension or diabetes. Also, nicotine use has been linked with adverse outcomes in pregnancy, so women should consult with their doctor before using any nicotine product during pregnancy.

<https://www.bat.com/nicotine#> (accessed 9/10/23).

Safer, Acceptable Cigarettes Ads Targeting Women



Considering all I'd heard, I decided to either quit or smoke True.


I smoke True.




The low tar, low nicotine cigaret
Think about it.

Warning: The Surgeon General Has Determined That Cigarette Smoking is Dangerous to Your Health.

King Packet: 11 mg. "tar", 0.8 mg. nicotine av. per cigarette, FTC Report Nov. '88.
"tar", 0.7 mg. nicotine av. per cigarette, FTC Report Nov. '88.



INTRODUCING THE NEW CAPRI ULTRA LIGHTS 120's. ARRIVING IN STYLE.




Indulge in the fine taste of Capri with the new longer Ultra Lights 120's. Offered in Regular and Menthol flavors.


Capri Ultra Lights 120's are only available through the DWT Direct delivery system. Call 1-800-800-8740 and order your free copy today.*

BY THE WAY CIGARETTE HOME DELIVERY

Newport Lights



live with pleasure!
Newport pleasure comes to low-tar menthols



The Surgeon General Has Determined that Smoking is Dangerous to Your Health.

King & Box: 9 mg. "tar", 0.7 mg. nicotine av. per cigarette, FTC Report March 1988.
100's: 10 mg. "tar", 0.8 mg. nicotine av. per cigarette, FTC Report March 1988.

SCRATCH 'N' STUFF HERE
SMOKE THAT SMELLS GOOD

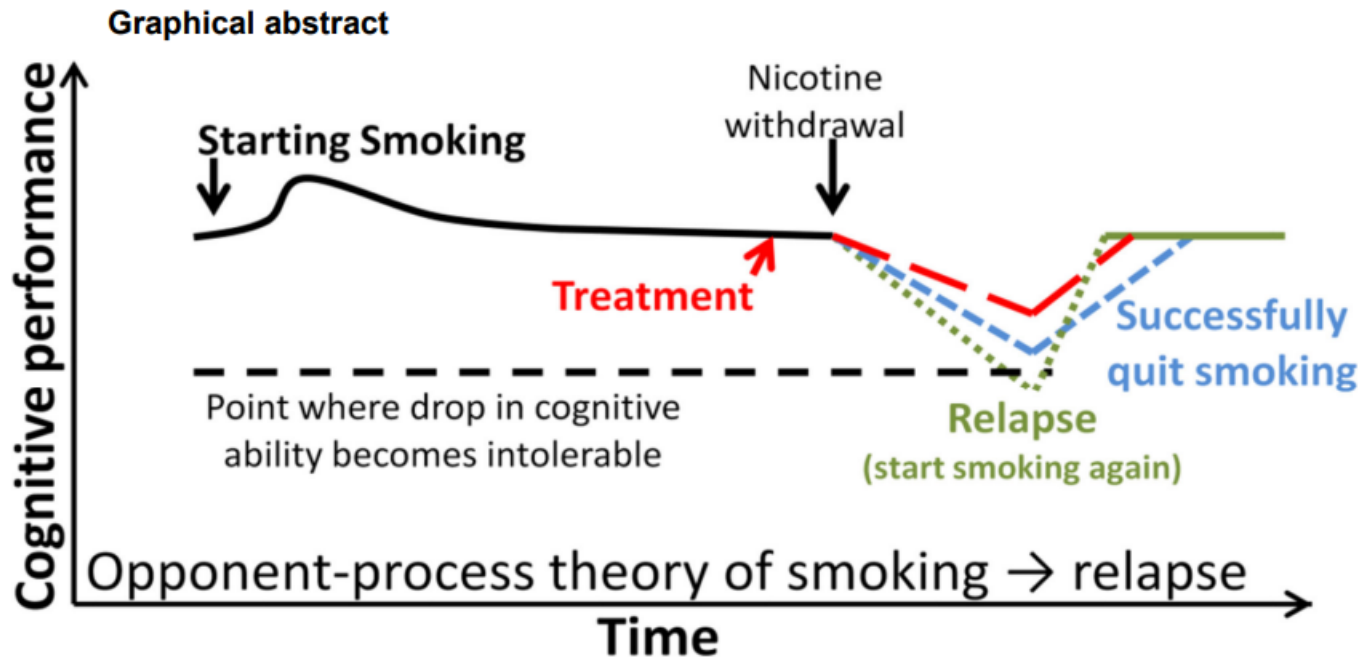
New Chelsea

It's true. New Chelsea is the first cigarette that actually smells good. Its light, pleasant aroma makes smoking more enjoyable for you and those around you. You're going to like Chelsea.

Introducing The First Cigarette That Smells Good.

100-486 PHOTO BY GUY

Nicotine Withdrawal



Affective and Cognitive impairments, either premorbid in origin, or associated with nicotine withdrawal (as described above) contribute to nicotine dependence. Greater consideration of these processes, and the potential role of negative reinforcement, needs to be incorporated into animal models of nicotine dependence.

Hall FS, Der-Avakian A, Gould TJ, Markou A, Shoab M, Young JW. Negative affective states and cognitive impairments in nicotine dependence. *Neurosci Biobehav Rev.* 2015 Nov;58:168-85.

Health Effects from E-cigarettes

- Cigarette smoking and e-cigarette use both cause endothelial dysfunction, although through different mechanisms
- Dual product use may be worse for respiratory and vascular health than using either alone.
- Studies of health effects of e-cigarette use during pregnancy have generated mixed findings, animal studies raise additional concerns.

Nabavizadeh P, Liu J, Rao P, et al. Impairment of endothelial function by cigarette smoke is not caused by a specific smoke constituent but by vagal input from the airway. *Arterioscler Thromb Vasc Biol.* 2022; 42:1324–1332.

Mohammadi L, Han DD, Xu F, et al. Chronic e-cigarette use impairs endothelial function on the physiological and cellular levels. *Arterioscler Thromb Vasc Biol.* 2022; 42:1333–1350.

Pisinger C, Rasmussen SKB. The Health Effects of Real-World Dual Use of Electronic and Conventional Cigarettes versus the Health Effects of Exclusive Smoking of Conventional Cigarettes: A Systematic Review. *Int J Environ Res Public Health.* 2022 Oct 21;19(20):13687.

Burrage EN, Aboaziza E, Hare L, et al. Long-term cerebrovascular dysfunction in the offspring from maternal electronic cigarette use during pregnancy. *Am J Physiol Heart Circ Physiol.* 2021 Aug 1;321(2):H339-H352.

Pregnancy and E-cigarettes

Table 2 ENDS and cigarette use by timing related to pregnancy, PRAMS, 2016–2019

	2016 n = 35,994 N = 2,027,327 % (95% CI)	2017 n = 38,549 N = 1,950,071 % (95% CI)	2018 n = 44,638 N = 2,204,706 % (95% CI)	2019 n = 45,201 N = 2,332,161 % (95% CI)	<i>p</i> ^a
ENDS and cigarette use ^{b,c}					
Dual use of ENDS and cigarettes					
During the 3 months before pregnancy	2.8 (2.5–3.1)	2.6 (2.4–2.9)	2.6 (2.3–2.8)	2.6 (2.4–2.9)	0.284
During the last 3 months of pregnancy	0.7 (0.6–0.8)	0.7 (0.6–0.8)	0.7 (0.6–0.9)	0.7 (0.5–0.8)	0.995
ENDS only ^d					
During the 3 months before pregnancy	0.8 (0.7–1.0)	1.1 (0.9–1.3)	1.2 (1.1–1.4)	1.6 (1.5–1.9)	< 0.001
During the last 3 months of pregnancy	0.4 (0.3–0.5)	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.6 (0.5–0.7)	0.012
Cigarettes only ^d					
During the 3 months before pregnancy	14.2 (13.7–14.8)	15.0 (14.5–15.6)	14.1 (13.6–14.6)	12.5 (12.0–13.0)	< 0.001
During the last 3 months of pregnancy	7.0 (6.6–7.4)	7.5 (7.1–7.9)	7.2 (6.8–7.6)	6.2 (5.8–6.6)	0.002

Head SK, Zaganjor I, Kofie JN, Sawdey MD, Cullen KA. Patterns and Trends in Use of Electronic Nicotine Delivery Systems Before and During Pregnancy: Pregnancy Risk Assessment Monitoring System, United States, 2016–2019. *J Community Health*. 2022