

Use of Non Cigarette Tobacco Products (NCTP) Smokeless Tobacco Waterpipes Cigars Pipes

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Goals & Objectives

- Review NCTP definitions & products
- Discuss prevalence/trends of NCTP
- Describe NCTP pharmacology
- Discuss NCTP dependence measures/withdrawal

Review recommended treatments for NCTP







NCTP Definitions & Products





Pipes









Cigars









Images from www.trinketsandtrash.org



Cigar Definition U.S. Department of Treasury (1996): Cigar "Any roll of tobacco wrapped in leaf tobacco or any substance containing tobacco." VS.

<u>Cigarette</u>

"Any roll of tobacco wrapped in paper or in any substance not containing tobacco."



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Types of cigars on the U.S. Market in 1996: (1) bidi (imported from India), (2) little cigar with filter tip, (3) small cigar with plastic mouth piece, (4) regular cigar, (5) and (6) premium cigar.



NCI Monograph 9. Cigars: Health Effects and Trends.









Smokeless Tobacco Chewing tobacco

- Loose leaf (i.e., Redman)
- Plugs 0
- Twists

Snuff

- Moist (i.e., Copenhagen, Skoal)
- Dry (i.e., Honest, Honey bee, Navy, Square)







"Chewing Tobacco" = Cut tobacco leaves





"Snuff" = Moist ground tobacco





Type of ST Used in U.S.



Chewing TobaccoSnuff



National Survey on Drug Use and Health (NSDUH)

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"Spitless Tobacco" – Star Scientific







RJ Reynold's











Phillip Morris (Altria)





New Product: "Fully Dissolvables"





Waterpipe

- Use dates back 4 centuries in Asia & Africa
- Typically consumed socially with friends and family
- Becoming trendy in US among youth
- Hookah "cafes" gaining popularity
- Smoke described as smoother and more flavorful
- Often (mis)perceived as healthier alternative due to water filtration, cooler mouth feel, and reduced irritation





Anatomy of a Waterpipe





mouthpiece

tobacco

hose

Types of Waterpipe Tobacco

- Maasel/Mu'essel Combination of tobacco and molasses, honey or fruit
- Tumbak/Ajami Dark tobacco paste
- Jurak

Combination of tobacco and fruits, oils, honey or molasses. May be flavored or flavorless

 Moist tobacco → requires charcoal to keep burning



Hookah tobacco

Charcoal





Source: Knishkowy & Amitai. (2005). Pediatrics, 116, e113-e119.





NCTP: Trends & Prevalence





🖾 Cigarettes 📓 Cigars 💷 Pipe/roll your own 📟 Chewing 🔳 Snuff Pounds of Tobacco Per-Capita Chewing Cigarettes Pipe/roll your own Cigars Year

Per-capita consumption of different forms of tobacco in the US 1880-1997

MAYO CLINIC

NCI Monograph 9. Cigars: Health Effects and Trends.

Past Month Tobacco Use among Persons Aged 12 or Older



estimate is statistically significant at the .05 level.



Results from the 2010 National Survey on Drug Use and Health



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Cigar Smoking







Total U.S. cigar consumption 1880-1997 and significant events in the use of cigars



NCI Monograph 9. Cigars: Health Effects and Trends.

Figure 6.4 Annual Numbers of New Users of Tobacco: 1965–2001



< 18 years of age group constituted an increasingly greater proportion of the number of new cigar smokers:

SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 2002. The Monitoring the Future Study, University of Michigan, 2001 and 2002.



Prevalence of current cigarette and cigar smoking among California males of different incomes, 1996



NCI Monograph 9. Cigars: Health Effects and Trends.





Prevalence of ST Use

In 2010, 8.9 million (3.5%) used smokeless tobacco



MAYO CLINIC Results from the 2010 National Survey on Drug Use and Health: National Findings

SAMSHA

Percentages of Persons Aged 12 or Older Using Smokeless Tobacco in the Past Month, by Demographic and Geographic Characteristics: 2002 to 2007



Demographic and Geographic Characteristic	Past Month
Age Group in Years	
12 to 17	2.2%
18 to 25	5.0%
28 or Older	3.0%
Gender	
Male	6.2%
Female	0.4%
Race/Ethnicity	
White	4.1%
Black or African American	1.4%
American Indian or Alaska Native	7.1%
Native Hawaiian or Other Pacific Islander	2.9%
Asian	0.6%
Hispanic or Latino	0.9%
Two or More Races	2.9%
County Type	
Large Metropolitan	1.9%
Small Metropolitan	3.7%
250,000 to 1 Million Population	3.2%
<250,000 Population	4.7%
Non-Metropolitan	6.6%
Urbanized	5.5%
Less Urbanized	7.1%
Completely Rural	8.4%
Region	
Northeast	1.7%
Midwest	3.7%
South	4.2%
West	2.4%

Waterpipe

- After cigarettes, waterpipe use is the most common form of tobacco use among university students
- Predominantly young, males
- 30% ever use & 8.4% current use
- Used in a social context
 - More common in fraternities/sororities
- Most smoked < 2 years
 - 10% daily
- Most perceive less addictive and harmful
 - 67% said "cigarettes more harmful"





Ward KD, et al. Nicotine Tob Res. 2007 Dec;9(12):1339-46.

Primack BA, et al. Nicotine Tob Res. 2012 May 28.

Odds of Trying Waterpipe, Snus, or ENDDs (n = 3158)

Predictors	Have tried one of these products adjusted OR (95% confidence interval)	
Smoking status		
Former smoker	2.71 (2.06, 3.56)	
Nondaily smoker	6.13 (4.02, 9.33)	
Daily smoker	5.53 (4.03, 7.58)	
Region		
Northeast	1.68 (1.16, 2.42)	
Midwest	1.65 (1.20, 2.28)	
West	1.80 (1.36, 2.39)	
Age		
18-24	2.18 (1.60, 2.97)	
Sex		
Males	3.51 (2.77, 4.45)	
Education		
High school	1.58 (.99, 2.51)	
Some college	2.67 (1.69, 4.22)	
College degree	2.04 (1.26, 3.30)	

Model also included race, not significant. Reference groups were as follows: never smokers, south region, 25 years of age and older, females, and no high school degree.

McMillen R, et al. Use of emerging tobacco products in the United States. J Environ Public Health. 2012;2012:989474.

*Lifetime Use





Health Impact of NCTP

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Adjusted relative risk* (95% CI) of death Sustainer = No switching



	'Sustainers'		
Deaths from	Never smoked	Pipe only	Cigarettes only
Men (n=16 932 aged 20-49 years)			
All causes	1.00	1.99 (1.73 to 2.27)	2.44 (2.27 to 2.62)
lschaemic heart disease	1.00	3.07 (2.35 to 4.00)	3.17 (2.69 to 3.73)
Stroke	1.00	1.54 (0.84 to 2.82)	2.30 (1.71 to 3.11)
Cardiovascular disease	1.00	2.49 (1.99 to 3.10)	2.81 (2.48 to 3.20)
Lung cancer	1.00	10.32 (5.55 to 19.18)	16.78 (10.31 to 27.33)
Other smoking related cancer	1.00	1.47 (0.99 to 2.18)	1.95 (1.59 to 2.38)

Tverdal et al. Tob Control 2011;20 123-130



Disease Risks



- Tar of cigar is more carcinogenic than cigarette smoke tar
- Morbidity and mortality correlates with:
 - +/- inhalation
 - depth of inhalation
 - number of cigars they smoke



Levels of Inhalation, CPS-1 Study





NCI Monograph 9. Cigars: Health Effects and Trends.



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Mortality Ratios for Cigar & Cigarette Smokers vs. Never Smokers







NCI Monograph 9. Cigars: Health Effects and Trends.

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Lung cancer death rates for cigar smokers with different patterns of inhalation and number of cigars per day compared with one pack per day cigarette smokers



NCI Monograph 9. Cigars: Health Effects and Trends.



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Cigar Smoking – Pancreatic Cancer Risk

- Compared with never tobacco users, cigar-only smokers have an increased risk for pancreatic cancer
 - OR 1.6 (95% CI: 1.2-2.3)

Comparable to that of cigarette-only smokers
OR 1.5 (95% CI 1.4-1.6)





Bertuccio P, et al Ann Oncol. 2011 Jan 18. PubMed PMID: 21245160.

ST – Health Consequences

Report on Carcinogens, 10th Edition, National Toxicology Program, USDHHS Smokeless tobacco

"Known to be a human carcinogen"







28 Known Carcinogens in ST

- Including.....
- β-Angelica lactone
- Coumarin
- Ethyl carbamate (urethane)
- Formaldehyde
- Acetaldehyde
- Crotonaldehyde

Smokeless Tobacco and Some Tobacco-specific N-Nitrosamines. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (2004)

- Tobacco-specific N-nitrosamines (TSNA)
 - N'-Nitrosonornicotine (NNN)
 - 4-(Methylnitrosamino)-1-(3pyridyl)-1-butanone (NNK)
 - 4-(Methylnitrosamino)-1-(3pyridyl)-1-butanol (NNAL)
 - N'-Nitrosoanabasine (NAB)
- Arsenic
- Nickel compounds
- Polonium-210
- Uranium-235
- Uranium-238



Health Effects: Cancers – U.S. Data

Location

Cancer, Mouth and Gum Gum & Buccal Mucosa Larynx Salivary gland Kidney Pancreatic OR (95% Cl) 11.2 (4.1-30.7)^A 4.2 (2.6-6.7)^B 7.3 (2.9-18.3)^A 5.3 (1.2-23.4)^A 4.0 (1.2-12.9)^C 3.6 (1.0-12.8)^D

A - Stockwell HG, et al. Head Neck Surg. 1986 Nov-Dec;9(2):104-10.

- B Winn DM, et al. N Engl J Med. 1981 Mar 26;304(13):745-9.
- C Goodman MT, et al. Am J Epidemiol. 1986 Dec;124(6):926-41.
- D Muscat JE, et al. Cancer Epidemiol Biomarkers Prev. 1997 Jan; 6(1):15-9.



ST Health Effects: CV Disease



- *Current ST use vs. never associated with <u>death</u> from:
 - <u>All causes</u>: HR 1.18 (95% CI: 1.08-1.29)
 - <u>CHD</u>: HR 1.26 (95% CI: 1.08-1.47)
 - <u>Cerebrovascular dz</u>: HR 1.40 (95% CI: 1.10-1.79)
- No difference between snuff and chewing tobacco
- Former use did increase the risk of death in any category

*Multivariate-adjusted



Henley et al., Canc Cause Control. 2005; 16: 347-358.

ST – Oral Lesions

- Leukoplakia
- Oral cancer
- Dental disease
 - erosion of enamel
 - dental caries
- Periodontal Disease
 - gingival recession
 - soft tissue/hard tissue loss
 - gingivitis





Waterpipe – Health Effects

- 1-hour session involves inhaling 100-200 times volume of smoke from a single cigarette
- Smoke contains CO, heavy metals, and carcinogens
- Charcoal added to keep tobacco burning increases health risks
- Sharing = tuberculosis & hepatitis
 WHO. TobReg Advisory Note. Waterpipe Tobacco Smoking

Google: " who tobreg water pipe"





Waterpipe Analysis





Eissenberg T, et al. American journal of preventive medicine. 2009 Dec;37(6):518-23.

Waterpipe vs. Cigarette

 Directly compare waterpipe use & cigarette smoking



- 31 participants reporting monthly waterpipe use & weekly cigarette smoking
- Cross-over: 45 minutes with waterpipe (WP) and 1 cigarette
- CO (carbon monoxide): 23.9 ppm WP vs. 2.7 C
- COHb (carboxyhemoglobin): 3.9% WP vs. 1.3% C
- Puff volume: 48.6 L WP vs. 1.0 L C
- Peak nicotine levels were comparable
 - 1.7 times the nicotine exposure



Disease Risks

- Burning charcoal is normally placed atop the tobacco to smoke the narghile waterpipe
- Waterpipe smokers thus also inhale large quantities of combustion-generated toxicants





Monzer B, et al. Food Chem Toxicol. 2008 Jun 4

Waterpipe – Health Effects



Single narghile smoking session:

- 50 times the quantities of carcinogens as one cigarette^A
- Many times the formaldehyde, acetaldehyde and acrolein typically found in a cigarette^B
- 2.25 mg nicotine^C
- 242 mg nicotine-free dry particulate matter (NFDPM)^C
- Higher levels of arsenic, chromium and lead than a cigarette^C
 - A Sepetdjian E, et al. Food Chem Toxicol. 2008 May;46(5):1582-90.
 - B Al Rashidi et al. Volatile aldehydes in the mainstream smoke of the narghile waterpipe. Food Chem Toxicol. 2008 Nov;46(11):3546-9.
 - C Shihadeh A. Investigation of mainstream smoke aerosol of the argileh water pipe. Food Chem Toxicol. 2003 Jan;41(1):143-52.



Waterpipe

- Waterpipe tobacco smoking negatively affects lung function
 - Significant reduction in FEV1 compared to no smoking (4% lower FEV1)
 - Trend toward lower FVC (1.38% lower FVC) compared to no smoking
 - No statistically significant difference in FEV(1), FVC, and FEV(1)/FVC compared to cigarette smoking
- May be as harmful as cigarette smoking
- Likely to be a cause of COPD





Waterpipe

- Literature review
 - Cohort, case-control and cross-sectional studies
- Increased risk for
 - Lung cancer
 - Respiratory illness
 - Low birth-weight
 - Periodontal disease





Warnakulasuriya S. Evid Based Dent. 2011;12(2):44-5. PubMed PMID: 21701545.



Pharmacology



NCTP Bioavailability of Nicotine (aka "Smoke Yields")

Nicotine (mg) <u>Type</u> Cigarette (filter) 1.1 Pipe 5.2 Smokeless tobacco Chewing tobacco 4.5 Moist snuff 3.6 Cigars Little cigars, Swishers 3.8 Premium, Macanudo 13.3 4 mg nicotine gum 1.9





Smokeless Tobacco Nicotine "Content"

- 4.8 mg nicotine/gm of moist snuff x 30 gm/can = 144 mg
- 144 mg nicotine/(1.8 mg nicotine/cigarette) = 80 cigarettes
- 80 cigarettes/(20 cigarettes/pack) = 4 packs
- 1 can snuff = 4 packs of cigarettes
- ST Users are exposed to as much, and possibly more, daily nicotine than cigarette smokers





Alkaloids, mg/g dry weight TSNAs^a, µg/g dry weight Nicotine **NNN^a NNK^a** NATa NABa Total Product Total Free Nornicotine Anatabine Anabasine pН New products Taboka ND^b Original 1.05 0.077 0.370 1.50 6.64 21.1 0.844 1.04 3.78 0.149 Green 0.948 0.092 0.292 0.002 1.33 6.85 19.9 1.26 1.02 4.03 0.197 Marlboro Snus Rich 1.27 0.259 0.455 ND 1.98 17.8 1.08 0.438 2.60 0.111 6.83 1.52 0.229 0.234 ND 1.98 6.47 12.8 0.350 0.484 1.82 0.072 Mild Spice 1.56 0.257 0.246 ND 2.06 6.85 17.9 1.13 0.411 2.17 0.097 Mint 3.28 0.215 0.221 ND 3.72 6.58 20.0 0.701 0.454 1.97 0.063 Camel Snus 0.164 Original 1.15 0.270 0.297 0.012 1.73 7.46 28.2 6.09 0.353 1.39 Spice 1.27 0.157 0.305 0.015 1.75 7.75 25.4 9.16 0.314 1.09 0.183 1.20 Frost 0.267 0.204 0.009 1.68 7.59 23.7 6.40 0.313 0.741 0.103 Skoal Drv ND Regular 3.57 0.360 0.478 7.23 11.3 1.57 0.345 1.41 0.117 4.41 5.30 6.85 11.9 0.751 0.324 1.02 Cinnamon 0.313 0.572 0.002 6.19 0.130 Menthol 2.53 0.279 0.203 ND 7.18 11.9 1.51 1.37 0.127 3.01 0.386 Mean for new products 2.05 0.231 0.323 0.008 2.61 18.5 2.57 0.490 1.95 0.126 Traditional products General Snus 1.66 0.464 0.969 7.69 0.223 0.072 0.008 3.10 7.95 16.7 0.367 Copenhagen Snuff 5.12 1.40 1.12 0.152 7.79 7.45 23.0 4.88 0.248 1.43 0.150 Copenhagen Long Cut 3.76 1.10 1.35 0.062 6.27 7.53 26.7 7.14 0.157 0.770 0.037 Skoal Long Cut 4.66 1.64 1.59 0.074 7.96 7.51 25.6 6.03 0.233 1.02 0.049 Kodiak Wintergreen 6.86 1.41 3.58 0.179 12.0 8.23 19.6 12.1 0.164 0.438 0.055 1.20 1.72 Mean for traditional products 4.41 0.095 7.42 22.3 7.57 0.205 0.805 0.073

Table 1. Tobacco-specific nitrosamines, pH, total and unprotonated nicotine, and minor tobacco alkaloids in smokeless tobacco products.

Note. ^aAbbreviations: TSNAs, tobacco-specific *N*-nitrosamines; NNN, *N'*-nitrosonornicotine; NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NAT, *N'*-nitrosoanatabine; NAB, *N'*-nitrosoanabasine. ^bND, not detected.



Stepanov I et al. Nicotine & Tobacco Research Volume 10, Number 12 (December 2008) 1773–1782.

ST Characteristics Affecting Nicotine Blood Concentrations

- Concentration of nicotine in ST product
- Size of the tobacco cuttings
 - Long cut
 - Fine cut (higher)



- Ammonium bicarbonate (additive)
 - Lower acid level of product = higher free nicotine
- Acetic acid (additive)
 - Increases salivation enhances absorption



pH Manipulation by Industry

- October 1994, Wall Street Journal:
- "US Tobacco routinely adds chemicals to its snuff to deliver the free nicotine faster and to make the product stronger."
 - Larry Story, former UST chemist
- "It (Copenhagen) was brought up to a pH of 7.8 by adding more sodium bicarbonate and ammonium carbonate."
 - Larry Story, former UST chemist26





Connolly, G. N. Tob Control 4: 73-79.

Impact of pH Manipulation: Long-Term

- Likelihood of choosing a brand with higher nicotine content is related to:
 - Increasing duration of use
 - Increasing intensity of use
 - Frequency of ST use



- ST users who have used higher nicotine-containing products are more likely to report:
 - More nicotine withdrawal symptoms
 - Continued use because of <u>difficulty quitting</u>





Waterpipe

- Data indicates that daily waterpipe use of the produced a 24-hr urinary cotinine level of: 0.785 microg/ml (95% CI = 0.578-0.991 microg/ml)
- Daily waterpipe smoking is equivalent to smoking 10 cigarettes (95% CI: 7-13)





Neergaard J, et al. *Nicotine Tob Res.* 2007 Oct;9(10):987-94. Review.



Current Recommendations for Treatment



Pipes, Cigars, & Waterpipe





Treatment Options

Non-daily users

- Nicotine gum
- Nicotine lozenge
- Nicotine inhaler
- Nicotine nasal spray
 Daily users
- Nicotine patch
- Bupropion SR
- Varenicline







Smokeless Tobacco (ST)



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Assessing Dependence in ST Users Number of cans per week

- Strongest correlation with nicotine/cotinine blood concentrations
- Used for dosing guidelines





Nicotine Patch Dosing Algorithm for ST Users

	Peak serum nicotine concentrations (ng/mL)	Cans or pouches per week	Patch dose				
Low	0-10	< 2	14 mg/d				
Intermediate	11-20	2-3	21mg/d				
High	> 20	> 3	42 mg/d				





Bupropion SR: Dosing 150 mg daily for 3-4 days then 150 mg twice a day for 3-4 days THEN STOP CHEWING



3 to 12 months – No taper needed



Snuff Substitutes

- Smokey Mountain®
- Golden Eagle®
- Oregon Mint®
- KIK IT®
- Jerky®
- Bacc-Off®





Nicotine Lozenge

- 2 mg & 4 mg
- Dissolves in mouth over 20-30 minutes

 Delivers 25% more nicotine than the gum







Generic (large) lozenge



Nicorette "Mini" – 2 mg/4 mg



Nicotine Lozenge: Dosing

- Not to be chewed or swallowed whole
- Avoid eating or drinking food during and 15 minutes prior to use
- Monotherapy
 - 2 mg
 - First dip <u>></u> 30 min
 - < 3 cans/week</p>
 - 4 mg
 - First dip < 30 min
 - > 3 cans/week
- Combination may be optimal (patch)
- 1-2 lozenges every 1-2 hours
- Minimum of 9/day
- Taper over 12 weeks





Nicotine Gum

- Monotherapy
 - 2 mg
 - First dip <u>></u> 30 min
 - < 2 cans/week</p>
 - 4 mg
 - First dip < 30 min
 - > 2 cans/week
- "Chew and Park"
- Combination with nicotine patch may be optimal





Scandinavian Snus



32% of men aged 16-35 use snus daily

NORWEGIAN SA NORRBOTTEN

19% adult snus use prevalence





Varenicline (Chantix[™]) for Snus Users

- Norway (7 sites) & Sweden (9 sites)
- Male/female daily ST users
 - Use at least 8 times/day
- Randomized to:
 - Varenicline for 12 weeks
 - Placebo
- Biochemical confirmation of abstinence
 - Salivary cotinine > 15 ng/mL









Fagerström K, et al. BMJ. 2010 Dec 6;341.







Your brain and nicotine: The physical challenge of quitting

You use chew for many reasons. One main reason is because smokeless tobacco contains an addicting drug called nicotine. This is the substance that makes it so difficult to stop, even though you want to.



Nicotine from chewing tobacco is absorbed into your bloodstream mouth (blue arrows). Nicotine from swallowed tobacco juice is al small intestine and then passes through your liver before enterin arrows). Your heart pumps nicotine to your brain and the rest of

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Comments:



Varenicline Available doses: 0.5 mg 1 mg

Bupropion Available dose:

150 mg

Comments:

Blood nicotine levels of chewing tobacco vs. ni



Hisotine in chewing tobacco is absorbed very rapidly and peaks within placement. Even after the chew is removed, nicoline is absorbed through and small intestine. In comparison, the nicotine absorbed through the of the mouth iform gumi is absorbed much more slowly and often resi obtained with chewing tobacco.



Normal inside cheek





Snuff dipper pouch (where chew is placed)



Recommended ST Treatment Approach

- Bupropion SR
 - Weight gain prevention
 - Craving reduction
- Tailored nicotine patch therapy
 - Craving reduction
 - Short-term (end-of-treatment) abstinence
- Nicotine lozenge (short-term abstinence)
- Nicotine gum (craving reduction)
- Varenicline









Treatment Not Recommended for ST Users

- Nicotine inhaler
 - Designed to replicate the tactile sensation of a cigarette

Nicotine nasal spray



 Speed of intranasal delivery designed to the speed of delivery of a cigarette



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