UW Integrative Health

Department of Family Medicine and Community Health



Nicotine Use Disorder

Introduction

Negative health consequences of nicotine use disorder (NUD) are one of the greatest public health threats, with more than 20 million Americans having died as a result of NUD, particularly cigarette smoking, in the past 50 years.¹ and 16 million Americans experiencing smoking-related disease.² It is estimated that over 47 million U.S. adults currently use tobacco products, with over 34 million smoking cigarettes.³ These numbers may not well account for vaping of nicotine products that has recently been increasing in prevalence, thus underestimating the number of Americans affected by NUD. In the United States, tobacco use is the leading cause of preventable death and multiple serious health conditions, including smoking-related cancers; cardiovascular, pulmonary, and metabolic diseases; worsened pregnancy and birth outcomes; residential fires; and harms related to secondhand smoke exposure.⁴ It is estimated that, from 1965 through 2014, cigarette smoking prematurely claimed lives of more than 20,000,000 Americans—10 times more than the wars fought by the United States.¹

Evidence-Based Brief Interventions for NUD

There is strong evidence for Screening and Brief Intervention (SBI) as an effective screening and therapeutic approach to address NUD. Tobacco SBIs are recommended by the U.S. Preventive Services Task Force (USPSTF) as a routine component of primary care for all adults; with the recent emergence and rapid increase in e-cigarette use and vaping, recommendations to apply SBI toward non-combustible nicotine use are also emerging.^{5,6} The National Institute on Drug Abuse provides a clinical resource for SBI screening tools for nicotine, alcohol, and other drug misuse and use disorders.⁷ (This is included in the Resources section below).

SBI approaches, often based on Motivational Interviewing, have been shown to be effective for nicotine use reduction and cessation, including when delivered by primary care clinicians.^{5,6} For best effects, clinicians should schedule follow-up visits and reassess the patient's progress with smoking reduction/cessation efforts. The SBIs often include strategies such as the "5 As" (Ask, Assess, Advise, Assist, Arrange) or the FRAMES (Feedback, Responsibility, Advice, Menu of Strategies, Empathy, Self-Efficacy) methods⁸⁻¹⁰. The 5 As is a recommended method to assess readiness to quit smoking.^{11,12} For those unwilling to quit, Motivational Interviewing-based strategies (e.g., express empathy, develop discrepancy, roll with resistance, and support self-efficacy), can be useful to help increase patient motivation to reduce or quit nicotine use.^{9,13} This includes the "5 Rs" approach (Relevance, Risks, Rewards, Roadblocks, Repetition)

Although nicotine use cessation is the recommended "ideal" target, a reduction in the use of nicotine products can also be beneficial and decrease harm (a "harm reduction" approach). The Resources section, below, outlines additional strategies for nicotine use reduction/cessation and includes the National Institute of Drug Abuse (NIDA) clinical resource, which provides screening tools for substance misuse and use disorders.¹⁴

It is recommended that both SBI-based counseling and NUD-specific pharmacotherapy be offered, because combination therapy is more effective than either intervention alone.^{2,5,6,15-17} The USPSTF recommends that adults who are not pregnant receive both SBI and FDA-approved pharmacotherapy to treat NUD.^{5,6} SBI is the first-line approach to the treatment of NUD in pregnant patients.^{5,6,15,18} It is initiated at the initial prenatal visit and continued as needed throughout pregnancy and postpartum visits. However, if behavioral approaches are insufficient, clinicians may need to consider pharmacotherapy for NUD and weigh the benefits, risks, and patient preferences when making treatment recommendations for their individual pregnant patients.

Research supports individual, group, and telephone counseling for NUD treatment, with evidence suggesting that more intensive interventions are more efficacious than less intense interventions or self-help.^{11,19-21} Yet even a very brief, single SBI session can be beneficial.^{5,6} The use of incentives can add benefits.²² There is also some evidence that minimal intervention, such as written handouts, may be helpful for smoking cessation.^{5,6,23,24} Patients may be more likely to reduce/quit nicotine use when a clinician is involved in their NUD treatment efforts.¹²

NUD is more prevalent among individuals with mental health disorders, including SUDs, than in the general population.^{1,13,25} Untreated or undertreated mental health disorders may reduce the effectiveness of NUD treatment and increase the risk for relapse among those who have stopped nicotine use; patients may use nicotine to help cope with uncomfortable emotional states. Addressing co-occurring mental health conditions and SUDs, and providing additional support and motivation, can increase the chance for successful cessation of nicotine use.^{13,25,26}

Detailed reviews and recommendations about interventions for NUD treatment are available as part of the U.S. Preventive Services Task Force (USPSTF) Recommendations (refer to Clinician Resources section). The USPSTF recommends (Grade B) annual screening for lung cancer with low-dose computed tomography(CT) in adults ages 55-80 who have a 30 pack-year history of cigarette smoking and currently smoke or have quit within the past 15 years.²⁷ It also recommends (Grade B) a one-time screening for abdominal aortic aneurysm (AAA) by ultrasonography in men ages 65-75 years who have "ever smoked," a status that is commonly defined as someone who has smoked 100 or more cigarettes. The greater exposure, the greater risk of developing AAA (dose-response relationship).²⁸ According to the USPSTF, current evidence is insufficient to extend a recommendation to routinely screen "ever smoking" women for AAA.²⁸

Pharmacotherapy for NUD

A combination of NUD-specific pharmacotherapy and behavioral intervention, such as the brief interventions, is more effective than applying each modality alone.^{2,5,6,15-17} Pharmacotherapy can aid in decreasing symptoms of nicotine withdrawal, reducing the rewarding aspects of smoking, decreasing nicotine craving, and reducing relapse risk.²⁹ Nicotine replacement therapy (NRT), varenicline, and bupropion are evidence-based FDA-approved pharmacological interventions for NUD treatment.¹⁵ Research findings suggest that the rates of quitting smoking can reach 17%-19% with NRT or bupropion, and 28% with varenicline, compared to approximately 10%-12% abstinence rates without these medications at 6 or more months.^{5,6,30}

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Of note, electronic cigarettes (e-cigs), widely available and often marketed for smoking cessation, or an alternative to smoking, are not approved smoking cessation aids.^{5,6,31} E-cigarette use involves inhaling a vapor containing nicotine. Research on their efficacy for smoking cessation is very limited, and adverse effects related to e-cig use have been reported.^{12,32-34} It is not advisable for clinicians to endorse e-cig use as a safe and effective alternative to smoking for their patients at this time.

Withdrawal symptoms can be a challenge for those striving for cessation, with acute withdrawal symptoms peaking at 24-28 hours, then slowly decreasing over a the next few weeks; symptoms of mild depression, dysphoria, and anhedonia can last for months.³⁵ As with other medications, the decision about and the choice of pharmacotherapy for NUD should be tailored to each patient's needs and preferences, with treatment response then monitored longitudinally.¹³

Nicotine Replacement Therapy

Nicotine Replacement Therapy (NRT) has been shown effective as a treatment for NUD. Several different NRT preparations have been approved by the U.S. Food and Drug Administration, including nicotine-containing gums, lozenges, inhalers, nasal sprays, and patches.^{12,13,36} It is often recommended to combine "long-acting" preparations (patches) with short-acting nicotine replacement products (for an as-needed use) for optimum support with nicotine use cessation.^{13,15} NRT can be associated with adverse effects; for example, it may increase the risk of certain cardiovascular events.¹⁵ It is important to review the patient's clinical history to determine potential risk factors that may limit or even preclude the use of NRT in some individuals.¹⁵

Non-Nicotine-BASED Pharmacotherapy

Bupropion is an antidepressant that also reduces the symptoms of acute nicotine withdrawal.¹³ Varenicline is a partial agonist of nicotine receptors that reduces both symptoms of withdrawal and craving.¹³ Along with NRT, these two medications are considered first-line treatment for NUD and have shown to increase the likelihood of smoking cessation.¹⁵

These medications are usually prescribed a week before the chosen quit date so the medication is able to reach steady-state blood levels prior to the planned nicotine use reduction or cessation.¹⁵ Bupropion treatment should be started 1 week prior to quit date (typical minimum treatment length is 6-12 weeks); varenicline treatment should be started 1-5 weeks prior to quit date (typical treatment length is 12 weeks).¹³

Both bupropion and varenicline may be associated with adverse effects, most of which are minor and self-limited. However, they also have the potential for more severe negative effects. Bupropion can increase the risk of seizures and is contraindicated in patients with a seizure history, head trauma with associated skull fracture or prolonged unconsciousness, and use of monoamine oxidase inhibitors, or medications that decrease the threshold for seizures.¹³ Bupropion may also contribute to reduced appetite and may not be the best choice in patients with eating disorders.¹³ Varenicline may exert cardiovascular adverse effects.¹⁵ Both bupropion and varenicline, particularly the latter, can lead to worsened depression and suicidality.^{12,13,15} It is important to review the patient's medical and mental history to determine potential risk factors and help determine the best pharmacotherapy choice for each patient.¹⁵

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E-Cigarettes/Vaping

E-cigarettes or other similar "electronic nicotine delivery systems" (ENDS), including vaporizers or so called vapes, are battery-operated devices used to deliver nicotine via inhalation.^{31,37} The use of ENDS involves heating a liquid containing nicotine, flavoring, and chemicals. The vapor is inhaled deep into the lungs, a process known as "vaping."^{31,37} Vaping can be done using a wide variety of ENDS, some of which may resemble actual cigarettes (e-cigarettes), USB drives, pens, or larger modular devices; the term "vaping" is typically used to describe the use of refillable devices that do not resemble a cigarette.³¹

Nearly 7 million (2.8%) U.S. adults use e-cigarettes, which have often been marketed by producers as safe alternatives to smoking and effective modalities for smoking cessation, despite insufficient evidence to support such claims.^{3,5,6} Research on their efficacy for smoking cessation is very limited and inconclusive; more high-quality research is needed. ^{5,6,12,32,34,35,38,39}

While nicotine delivery via ENDS might be less harmful than cigarette smoking, there are health risks including lung injury, potential cardiorespiratory effects, possible decrease in the ability to fight off infection, and fetal harm. Defective ENDS batteries have caused burns, fires, and explosions.^{10,31,33,40} ENDS are not approved by the FDA for smoking cessation.³¹ The inhaled vapor, in addition to varied concentrations of nicotine, may include volatile organic compounds, heavy metals, and chemicals associated with cancer and lung disease.^{10,31,41}

E-cigarette or vaping use-associated lung injury (EVALI), which can be fatal, has been reported, particularly in relation to vaping tetrahydrocannabinol (THC); however, cases of EVALI have been reported in relation to nicotine-only use as well.^{33,42,43} Vitamin E acetate, a common additive in the vaping liquid, may have contributed to this potentially deadly complication.^{33,42,43} The CDC and FDA recommend avoidance of vaping products containing THC or vitamin E.^{33,42,43}

Other Interventions

Biomedical risk assessment may sometimes be useful for motivating a patient to change and reduce or quit nicotine use. Various biomedical assessments have been evaluated as interventions to improve NUD treatment engagement and efficacy (e.g., spirometry, ultrasonography of arteries, carotid plaque screening, and carbon monoxide feedback). While they may provide a deeper understanding of the effects of smoking and other nicotine use on a patient's health, they are expensive, and evidence is insufficient to recommend their routine use as a part of smoking cessation efforts.⁴⁴ There is also insufficient evidence to support aversive smoking, which involves smoking in a concentrated or unpleasant way.^{45,46}

Complementary and Integrative Health Modalities

Only preliminary research has focused on the evaluation of complementary and integrative health (CIH) approaches (e.g., black pepper,^{47,48} angelica,⁴⁸ cannabidiol,⁴⁹ melatonin,⁵⁰ Guided Imagery,⁵¹ and Transcendental Meditation[™])⁵² as treatments for NUD. Limitations in methodological quality or sample sizes prevent drawing conclusions about their efficacy.⁵³⁻⁵⁸ Rigorous research is needed to assess the potential benefits.

Resource Box 1, below, lists available evidence for the efficacy of CIH modalities that have some evidence supporting their use in NUD; however, conclusions cannot yet be drawn about most due to a lack of sufficient research.

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Overall, although many CIH practices are safe for most people, it is best for people to consult with a clinician prior to engaging in a particular CIH modality. As with any therapy, there may be risks to consider for some individuals treated with certain medications or with certain physical or mental health conditions.

Note: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

Resource Box 1. Complementary and Integrative Health (CIH) Interventions for Nicotine Use Disorders

Acupuncture

Existing research has yielded inconsistent results, with some studies suggesting efficacy and others not finding a beneficial effect of acupuncture for long-term nicotine use cessation.. ⁵⁹⁻⁶¹

Cytisine

An organic heterotricyclic compound found in some plants that exerts acetylcholine agonist effects.⁶²

Cytisine is used in some European countries to assist with smoking cessation. It is not currently approved for this use in the United States, however preliminary research suggests it may be effective in assisting with smoking cessation.⁶⁰

Exercise

There is mixed evidence regarding the efficacy of exercise as treatment for NUD.⁶³⁻⁶⁵ One systematic review found that negative affect and nicotine withdrawal symptoms were reduced with light-to-moderate intensity exercise, but increased during high-intensity exercise.⁶⁶ Other systematic reviews and meta-analyses found evidence that physical activity may reduce nicotine craving⁶⁷ ⁶⁶

Hypnotherapy

Hypnosis under the care of a trained clinician can be used to help guide the mind to facilitate changes, which, in turn, may help individuals progress toward their goals. There is mixed preliminary evidence regarding the effectiveness of hypnotherapy for smoking cessation, with some evidence suggesting benefit and other evidence showing no benefit.^{60,68} Two randomized controlled trials showed potential benefit for hypnotherapy for smoking cessation/relapse prevention in veterans; however more research is needed.⁶⁹

Although clinical hypnosis is considered overall safe, research on its safety is limited. Clinicians should first assess the patient for the appropriateness of this treatment before recommending or applying hypnosis as a therapeutic modality.⁷⁰



L-Tryptophan

An amino acid found in proteins, L-Tryptophan has shown *possible effectiveness* as an adjunct treatment for smoking cessation when taken orally and is considered *possibly safe* when taken in approved therapeutic amounts for the short term. However, there have also been cases of eosinophilia-myalgia syndrome reported as a result of L-Tryptophan use, potentially because of a specific contaminated product. More research is needed to determine its efficacy and safety for long-term use. L-Tryptophan should not be taken during pregnancy as it may cause an inutero respiratory depression.⁷¹ Patients should discuss with their clinicians the potential risks and benefits of L-Tryptophan prior to its use.

Mindfulness meditation

Research shows that mindfulness meditation–based interventions, such as mindfulness-based stress reduction (MBSR), may be beneficial in assisting with smoking cessation; however, more rigorous research is needed.^{60,72-75} In general, caution should be taken with any type of meditation practice (e.g., mindfulness meditation, TM) in those with underlying substantial mental health issues (e.g., untreated, active post-traumatic stress disorder or mania); these patients should consult with a clinician before beginning a meditation program.

St. John's wort

Preliminary research evidence does not support St. John's wort efficacy as treatment for NUD.^{76,77}

Yoga (e.g., Hatha, Vinyasa, Ashtanga)

Research indicates yoga may be beneficial in assisting with smoking cessation, abstinence, and craving; however, more rigorous research is needed.^{60,78-81}

Resources for More Information on Integrative Health Approaches to Tobacco Use

Resource Box 2. Links and Other Resources for Clinicians Guides/ Resources

- <u>American Academy of Family Physicians—Tobacco and Nicotine Prevention and</u> <u>Control</u>: https://www.aafp.org/patient-care/public-health/tobacco-nicotine.html
- <u>National Institute on Drug Abuse (NIDA). Screening Tools and Prevention. 2019</u>.
 *Screening for alcohol, tobacco and substance abuse
 https://www.drugabuse.gov/nidamed-medical-health-professionals/screening-tools prevention
- U.S. Department of Health and Human Services. Public Health Service. <u>Treating</u> <u>Tobacco Use and Dependence: 2008 Update</u>. Clinical Practice Guideline: https://www.ncbi.nlm.nih.gov/books/NBK63952/
- U.S. National Library of Medicine: Medline Plus—Smoking: http://www.nlm.nih.gov/medlineplus/smoking.html
- U.S. Preventive Services Task Force. <u>Tobacco Smoking Cessation in Adults, Including</u> <u>Pregnant Women: Behavioral and Pharmacotherapy Interventions 2015 Final</u> recommendation statement:

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https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions

- U.S. Preventive Services Task Force. <u>Tobacco Smoking Cessation in Adults, Including</u> <u>Pregnant Persons: Interventions</u>. 2020 Draft recommendation statement. https://www.uspreventiveservicestaskforce.org/uspstf/draft-recommendation/tobacco-smoking-cessation-in-adults-including-pregnant-women-interventions
- World Health Organization. Tobacco Free Initiative (TFI). <u>Toolkit for Delivering the 5As</u> and 5Rs Brief Tobacco Interventions in Primary Care. https://www.who.int/tobacco/publications/smoking cessation/9789241506953/en/

Education/Training

- <u>Motivational Interviewing Network of Trainers</u>: https://motivationalinterviewing.org/
- Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Substance Abuse Treatment—<u>Enhancing Motivation to Change in Substance Abuse</u> <u>Treatment, Treatment Improvement Protocol</u> (TIP) Series, 35: **Chapter 2 provides information on the FRAMES approach* https://store.samhsa.gov/sites/default/files/d7/priv/tip35_final_508_compliant_-__02252020_0.pdf
- U.S. Department of Veterans Affairs: Community Provider Toolkit—<u>Smoking and</u> <u>Tobacco Use Treatment and Training</u>: https://www.mentalhealth.va.gov/communityproviders/clinic tobacco.asp

Information and Organizations

- Centers for Disease Control and Prevention—<u>Smoking & Tobacco Use: Healthcare</u> <u>Provider Resources</u>: https://www.cdc.gov/tobacco/basic_information/for-health-care-providers/index.html
- National Center for Complementary and Integrative Health (NCCIH)—Quitting Smoking: https://www.nccih.nih.gov/health/quitting-smoking
- National Institute on Drug Abuse (NIDA)—<u>DrugFacts—Cigarettes and Other Tobacco</u> <u>Products</u>: http://www.drugabuse.gov/publications/drugfacts/cigarettes-other-tobaccoproducts
- National Institute on Drug Abuse (NIDA)—<u>DrugFacts—Vaping Devices (Electronic Cigarettes</u>): https://www.drugabuse.gov/publications/drugfacts/vaping-devices-electronic-cigarettes
- National Institute on Drug Abuse (NIDA)—<u>Tobacco, Nicotine, and E-Cigarettes</u> <u>Research Report</u>: https://www.drugabuse.gov/publications/research-reports/tobacconicotine-e-cigarettes
- <u>University of Wisconsin Center for Tobacco Research and Intervention</u>: https://ctri.wisc.edu/
- U.S. Centers for Disease Control and Prevention—<u>Smoking & Tobacco Use—Office on</u> <u>Smoking and Health</u>: https://www.cdc.gov/tobacco/about/osh/index.htm?s_cid=osh-stuhome-nav-001
- U.S. Centers for Disease Control and Prevention—<u>Smoking & Tobacco Use—About</u> <u>Electronic Cigarettes (E-Cigarettes)</u>: https://www.cdc.gov/tobacco/basic_information/ecigarettes/about-e-cigarettes.html
- U.S. Centers for Disease Control and Prevention: <u>Smoking & Tobacco Use—Fast Facts</u> and Fact Sheets: https://www.cdc.gov/tobacco/data_statistics/fact_sheets/index.htm

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- U.S. Food and Drug Administration—Center for Tobacco Products: https://www.fda.gov/about-fda/fda-organization/center-tobacco-products
- U.S. National Library of Medicine: Medline Plus—Smoking: • http://www.nlm.nih.gov/medlineplus/smoking.html

Other Useful Resources

- American Heart Association: https://www.heart.org/en
- American Lung Association: http://www.lung.org/
- American Stroke Association: https://www.stroke.org/en •
- National Cancer Institute: http://www.cancer.gov/ •
- National Center for Complementary and Integrative Health (NCCIH)-Relaxation • Techniques for Health: https://www.nccih.nih.gov/health/relaxation-techniques-for-health
- National Emphysema Foundation: http://www.emphysemafoundation.org/ •
- National Heart Lung and Blood Institute: http://www.nhlbi.nih.gov/ •
- Substance Abuse and Mental Health Services Administration: http://www.samhsa.gov/ •
- University of Wisconsin Center for Tobacco Research and Intervention: https://ctri.wisc.edu/
- The "Substance Use Disorders" Whole Health overview has additional information: • https://wholehealth.wisc.edu/overviews/substance-use/

General Health Resources

- U.S. Center for Disease Control and Prevention: http://www.cdc.gov/
- U. S. Department of Health and Human Services Office of the Surgeon General: http://www.surgeongeneral.gov/

Resource Box 3. Patient Resources

- American Academy of Family Physicians—Quit Smoking Guide: https://www.aafp.org/dam/AAFP/documents/patient care/tobacco/stop-smokingauide.pdf
- American Cancer Society—How to Quit Smoking or Smokeless Tobacco: https://www.cancer.org/healthy/stay-away-from-tobacco/guide-guitting-smoking.html
- American Family Physician-Smoking: Do I Want to Quit: • https://www.aafp.org/afp/2002/1101/p1747.html
- American Heart Association, (smoking cessation patient resource): https://www.heart.org/en/healthy-living/healthy-lifestyle/guit-smoking-tobacco
- American Lung Association—How to Quit Smoking: https://www.lung.org/quit-smoking/i-• want-to-quit/how-to-quit-smoking
- A Report of the Surgeon General—How Tobacco Smoke Causes Disease...What it • Means to You:
 - http://www.cdc.gov/tobacco/data statistics/sgr/2010/consumer booklet/index.htm
- Centers for Disease Control and Prevention-Smoking & Tobacco Use: Quit Smoking: • https://www.cdc.gov/tobacco/quit smoking/index.htm
- Centers for Disease Control and Prevention—Tips from Former Smokers: Military Service Members and Veterans:

https://www.cdc.gov/tobacco/campaign/tips/groups/military.html

 <u>Centers for Disease Control and Prevention—Tips from Former Smokers: How to Quit</u> <u>Smoking</u>: https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html

- <u>FamilyDoctor.org—Infographic: Top Tools for Quitting</u>: https://familydoctor.org/wpcontent/uploads/2016/11/Infographic_Smoking_.pdf
- <u>FamilyDoctor.org—Tobacco Addiction</u>: https://familydoctor.org/condition/tobaccoaddiction/?adfree=true
- FamilyDoctor.org—Why Do I Smoke Quiz: https://familydoctor.org/why-do-i-smoke-quiz/
- North American Quitline Consortium (Quitline services by state): http://map.naquitline.org/
- <u>Nicotine Anonymous:</u> https://www.nicotine-anonymous.org/
- <u>SMART Recovery</u>: http://www.smartrecovery.org/
- Smokefree.gov: http://smokefree.gov/
- <u>Smokefree (UK)</u>: http://www.nhs.uk/smokefree
- <u>Smokefreevet</u>: https://veterans.smokefree.gov/
- <u>TRICARE</u>—<u>Tobacco Cessation Services</u>: https://www.tricare.mil/CoveredServices/IsItCovered/TobaccoCessationServices
- <u>University of Wisconsin Center for Tobacco Research and Intervention:</u> https://ctri.wisc.edu/
- <u>U.S. Department of Veterans Affairs—Tobacco and Health</u> (*smoking cessation, includes workbooks*): https://www.mentalhealth.va.gov/quit-tobacco/index.asp
- U.S. Department of Veteran's Affairs: Veteran's Health Library—Tobacco and Your Health:

https://www.veteranshealthlibrary.va.gov/HealthyLiving/TobaccoFree/Health/142%2CTO BACCOblurb_VA

- U.S. National Library of Medicine—Medline Plus: Smoking: https://medlineplus.gov/smoking.html
- You Can Quit Too: https://www.ycq2.org/

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