San Mateo County Health and BHRS Guidelines for Smoking Cessation

Purpose: The goal of these guidelines is to present updated practice standards for the management of smoking cessation in adults, in order to reduce practice variation, improve patient safety, increase patient and provider satisfaction, and use evidence-based treatment.

Background: Nicotine dependence is an addiction to the nicotine in tobacco products, including cigarettes, e-cigarettes, and other combustibles like cigars, pipe tobacco, and hookah. Clinician involvement can significantly increase the chances of a patient successfully quitting smoking. The goal is to routinely identify individuals who smoke tobacco products and offer them evidence-based help to quit. These guidelines provide an overview of the management of smoking cessation in adults.

Benefits of quitting smoking

- Within minutes, HR & BP drop, CO level returns to normal in days
- Circulation improves, lung function increases, coughing and shortness of breath decrease in 2-3 months
- Risk of heart attack drops dramatically in 1-2 years
- Risk of mouth, throat, larynx cancer and stroke decrease by half in 5-10 years
- Risk of lung cancer is half a smoker's and other cancers decrease after 10 years
- Risk of coronary heart disease is close to a non-smoker after 15 years
- Lowers risk of diabetes, improves blood vessel function, heart & lung health
- Adds up to 10 years to life, quitting at any age gives back years of life
- Tobacco treatment in addiction therapy increases long-term sobriety from alcohol and drugs by 25%, but only 64% of SUD patients are screened for tobacco use and fewer than 25% facilities offer effective quitting treatments
- For a healthy pregnancy and baby, quitting smoking is a crucial step for women who smoke. Ideally, women should quit before attempting to conceive, but quitting at any point during pregnancy can still improve both mother and baby's health
- Saves money, better tasting food, improved sense of smell, better smelling breath, hair, and clothes, and improved physical activity
- Stops damaging effects on appearance, including premature wrinkling, gum disease, and tooth loss

Clinical Support/Consultation

Evaluation:

The clinician's role in helping patients quit smoking involves providing clear advice to quit, treatment options, and follow-up, and documenting the patient's smoking status. The 5A's approach is a framework that guides this process, involving the routine identification of patients who smoke and the offering of evidence-based help to quit. This includes asking about tobacco use, advising quitting, assessing readiness to quit, assisting those ready to quit, and arranging follow-up.

The 5A's approach is a framework that involves regularly identifying patients who smoke and offering them evidence-based help to quit. The 5A's approach includes the following steps. It is presented in a simple algorithm in tables 1 and 2: asking about tobacco use, advising quitting, assessing readiness to quit, assisting smokers ready to quit, and arranging follow-up. The 5A's approach has been recommended in national guidelines since 2008 and is recommended by US Preventive Services Task Force guidelines.

To make the 5A's approach more practical for busy outpatient practices and involve more members of the care team, variations have been developed. The AAR method involves asking about tobacco use, assisting with advice and a plan to quit, and referring to behavioral support resources. Another variation, the proactive offer of treatment approach, offers treatment as an expectation rather than an option and still includes components of the 5A's approach, such as asking about use, assisting those ready to quit, and

arranging follow-up. These variations aim to improve the efficiency and effectiveness of the process by involving more members of the care team and presenting treatment as an expectation rather than an option.

For individuals who are not yet ready to quit smoking, clinicians can use motivational interviewing and harm reduction strategies, such as initiating pharmacotherapy, to encourage them to quit. This approach can help encourage individuals to quit smoking.

Table 1

Intervention	Technique
Ask	Implement an officewide system that ensures that, for every patient at every clinic visit, tobacco-use status is queried and documented. Repeated assessment is not necessary in the case of the adult who has never used tobacco, or has not used tobacco for many years, and for whom this information is clearly documented in the medical record.
Advise	Strongly urge all tobacco users to quit in a clear, strong, personalized manner.
	Advice should be:
	Clear - "I think it is important for you to quit smoking now and I can help you." "Cutting down while you are ill is not enough."
	Strong - "As your clinician, I need you to know that quitting smoking is the most important thing you can do to protect your health now and in the future. The clinic staff and I will help you."
	Personalized - Tie tobacco use to current health/illness and/or its social and economic costs, motivation level/readiness to quit, and/or the impact of tobacco use on children and others in the household.
Assess	Determine the patient's willingness to quit smoking within the next 30 days:
	If the patient is willing to make a quit attempt at this time, provide assistance.
	If the patient will participate in an intensive treatment, deliver such a treatment or refer to an intensive intervention.
	If the patient clearly states that they are unwilling to make a quit attempt at this time, provide a motivational intervention and/or offer the option of initiating pharmacotherapy rather than waiting until they are ready to quit.
	If the patient is a member of a special population (eg, adolescent, pregnant smoker), provide additional information specific to that population.
Assist	Provide aid for the patient to quit. These actions are summarized in the accompanying table.
Arrange	Schedule follow-up contact, either in person or by telephone. Follow-up contact should occur soon after the quit date, preferably during the first week. A second follow-up contact is recommended within the first month. Schedule further follow-up contacts as indicated.
	Congratulate success during each follow-up. If tobacco use has occurred, review circumstances and elicit recommitment to total abstinence. Remind the patient that a lapse can be used as a learning experience. Identify problems already encountered and anticipate challenges in the immediate future. Assess pharmacotherapy use and problems. Consider use or referral to more intensive treatment.

Table 2

Action	Strategies for implementation
Help the patient with a quit plan	Set a quit date. Ideally, the quit date should be within 2 weeks.
	Tell family, friends, and coworkers about quitting and request understanding and support.
	Anticipate challenges to planned quit attempt, particularly during the critical first few weeks. These include nicotine withdrawal symptoms.
	Remove tobacco products from your environment. Prior to quitting, avoid smoking in places where you spend a lot of time (eg, work, home, car).
Provide practical counseling (problem solving/training)	Abstinence - Total abstinence is essential. "Not even a single puff after the quit date."
	Past quit experience - Review past quit attempts, including identification of what helped during the quit attempt and what factors contributed to relapse.
	Anticipate triggers or challenges in upcoming attempt - Discuss challenges/triggers and how patient will successfully overcome them. Advise patient to remove all tobacco from home, car, and work environment.
	Alcohol - Because alcohol can cause relapse, the patient should consider limiting/abstaining from alcohol while quitting.
	Other smokers in the household - Quitting is more difficult when there is another smoker in the household. Patients should encourage housemates to quit with them or not smoke in their presence.
Provide intra-treatment social support	Provide a supportive clinical environment while encouraging the patient in their quit attempt. "My office staff and I are available to assist you."
Help the patient obtain extra-treatment social support	Help the patient develop social support for their quit attempt in their environments outside of treatment. "Ask your spouse/partner, friends, and coworkers to support you in your quit attempt."
Recommend the use of approved pharmacotherapy, except in special circumstances	Recommend the use of pharmacotherapies found to be effective. Explain how these medications increase smoking cessation success and reduce withdrawal symptoms.
Provide supplementary materials	Sources - Federal agencies, nonprofit agencies, or local/state health departments. Offer a free telephone quitline (in the United States, 1-800-QUIT-NOW or 1-800-784-8669 can be used).
	Type - Culturally/racially/educationally/age appropriate for the patient.
	Location - Readily available at every clinician's workstation.

Treatments

The most effective treatment for smoking cessation is a combination of behavioral and pharmacotherapy. Meta-analyses of clinical trials have shown that combining these two treatments is more effective than using either one alone. Varenicline, combination NRT, and bupropion are first-line pharmacotherapies for smoking cessation. The choice of medication is generally based on patient preference after discussion with a clinician. While financial incentives, acupuncture, and hypnotherapy have been tried for smoking cessation, their efficacy is inconsistent.

Pharmacotherapy for Nicotine Dependence[1]

Type / HPSM Formulary Status	Dosing & instructions	Side effects/concerns	Comments
Nicotine Replacement Therapy (NRT)[2,3]			
Patch (OTC & Rx) Formulary with quantity limits	≥ 40 cpd = 42 mg/day 21-39 cpd = 28-35 mg/day 10-20 cpd = 14-21 mg/day <10 cpd = 14 mg/day ▪ apply on the quit day as soon as pt wakes up. May start before quit date ▪ Tapering dose is not necessary ▪ individualize based on pt characteristics (previous patch experience, degree of dependence, experiencing WDL or AEs) ▪ treatment of ≤ 8 weeks has been shown as efficacious as longer treatment ▪ If a dose > 42mg/day is needed, contact the prescriber. Taper Q2-4 weeks in 7-14 mg steps based on withdrawal symptoms, urges, & comfort after 4-6 weeks of abstinence	▪insomnia &/or vivid dreams ▪ local skin reaction usually self-limiting, hydrocortisone 1% or triamcinolone 0.5% cream & rotating patch sites may help (require discontinuation in <5%	▪ Effective, 1st line agent (strength of evidence: A) ▪ continuous nicotine delivery, require 6-8 hrs to achieve peak serum concentrations ▪ delivers nicotine to the CNS more slowly than any other NRT. Provides steady nicotine level, easiest to use ▪ remove the 24-hr patch prior to bedtime or use 16-hr patch in case of sleep disruption ▪ patch use almost doubles the likelihood of long-term abstinence vs placebo ▪ Reaches effective levels within 30 minutes to 3 hours after reapplication, if removed before bedtime
Gum (OTC) Formulary with quantity limits	2 mg: smoking < 25 cigarettes/d 4 mg: ≥25 cigarettes/d ▪ every 1 hr prn for the first 6 weeks, may be used for up to 12 weeks ▪ Max: 24 pieces a day ▪ Chew slowly until peppery/flavored taste is noted. Then "park" between cheek & gum for absorption until the tingling is almost gone. Repeat for about 30 min ▪ Avoid eating or beverages other than water 15-30 min before or during (pH changes affect absorption)	mouth soreness, hiccups, dyspepsia, nausea (GI AEs usually due to vigorous chewing) & jaw ache (mild & transient, improved by correcting chewing technique) CI: use in temporomandibular joint disease	▪ Effective 1st line option (strength of evidence: A) ▪ gum use may increase the likelihood of long-term abstinence by ~50 % compared to placebo ▪ control over nicotine dose, oral substitute for cigarettes ▪ Unpleasant taste, may damage dental work/difficult for denture wearers. Proper "chew & park" technique must be used
Lozenge (OTC) Formulary with quantity limits	2 mg: if 1st cigarette > 30 min after waking. 4 mg: if 1st cigarette within 30 min of waking ▪ Max 5 lozenges in 6 hours or 20 lozenges/d ▪ clts often do not use enough prn NRT to gain optimal effects. Generally, smokers should use 1 lozenge Q 1 to 2 hrs first 6 weeks, Q 2-4 hrs during weeks 7-9, followed by Q 4–8 hrs during weeks 10-12 ▪ must be sucked (vs bitten or chewed) ▪ Avoid eating or beverages other than water 15-30 min before or during (pH changes affect absorption) ▪ taper over 6-12 weeks (can be longer)	▪ mouth irritation, heartburn, hiccups, & nausea ▪ HA & cough (4 mg dose)	Effective, 1st line med (strength of evidence: B) ▪ control over nicotine dose, oral substitute for cigarettes ▪ Option for smokers with dentures or poor dentition ▪ Unpleasant taste

Nasal Spray (Rx) Nonformulary	▪ 0.5 mg per spray administered via each nostril (total 1 mg) ▪ Apply 1 spray to each nostril Q1 to 2 hours prn ▪ max: 80 sprays/d (10 sprays/hr) ▪ administer with the head tilted slightly back ▪ do not sniff, swallow, or inhale through the nose during administration to minimize irritating effects ▪ duration of therapy: 3 to 6 months	▪ nasal & throat irritation, rhinitis, sneezing, cough, watery eyes, flushing, nasal congestion, transient changes in sense of smell & taste ▪ AEs common cause of discontinuation ▪ avoid use in clts with severe reactive airway disease	▪ Effective, 1st line agent (strength of evidence: A) ▪ highest dependence potential (higher peak nicotine levels compared to other NRTs) ▪ avoid use in individuals with other SUDs that involve snorting (reinforces the behavior) ▪ fastest-acting (but much slower than cigarettes), faster relief of nicotine withdrawal symptoms (Tmax: 4-15 min) ▪ control over nicotine dose ▪ local irritation of nasal mucosa could be difficult to tolerate
Inhaler (Rx) Nonformulary	Dose: Inhale as needed (such as Q1 to 2 hours) ▪ each cartridge delivers 4 mg nicotine over 80 inhalations ▪ Max: 16 cartridges a day ▪ cartridge placed inside hollow cigarette like plastic rods, produce nicotine vapor ▪ best effects attained by frequent inhalation & using ≥ 6 cartridges/d ▪ avoid beverages other than water 15 min before or during inhaler use (pH changes affect absorption) ▪ duration of therapy: up to 6 months, taper during the last 6-12 weeks	▪ mouth & throat irritation, cough & rhinitis ▪ frequency of symptoms declined with continued use ▪ tolerance usually develops within 1-2 days	▪ Effective, 1st line agent (strength of evidence: A) ▪ Facilitates/reinforces hand to mouth behaviors of smoking ▪ not a true pulmonary inhaler, nicotine absorbed across oropharynx mucosa ▪ inhaler use almost doubles the likelihood of long-term abstinence compared to placebo ▪ nicotine delivery declines significantly at T<40°F. Keep inhaler & cartridges in an inside pocket or other warm area in cold weather ▪ control over nicotine dose, oral substitute for cigarettes ▪ Use caution in pts with reactive airway disease ▪ Frequent puffing needed to achieve adequate nicotine delivery
Other Medications for Nicotine Dependence			
Buproprion SR (Zyban) Formulary	Initial: 150 mg QAM Max: 300 mg/d (150 mg/d for 3 days, then 150 mg BID) A lower dose of 150 mg/d is an option for pts who do not tolerate full dose ▪ begin treatment 1–2 weeks prior to quit date to allow steady state concentrations ▪ Duration of treatment: up to 6 months for long-term therapy MOA: DA & NE reuptake inhibitor, some nicotinic acetylcholinergic receptor blocking activity	insomnia, dry mouth, HA, jitteriness, agitation, nausea & constipation ▪ CIs: h/o seizures or eating disorders, clts on another form of bupropion, MAOI use in the past 14 days ▪ clts with conditions that increase seizure risk such as arteriovenous malformation, severe head injury, stroke, brain tumor, CNS infection should not take bupropion	Effective, 1st line med (strength of evidence: A) ▪ as effective as single NRT in increasing ≥6 months smoking cessation rates & reducing weight gain ▪ FDA approved since 1997 ▪ taking PM dose earlier (≥ 8 hrs after AM dose) may help with insomnia ▪ option to use in combination with NRTs ▪ limited data available for use in adolescents ≥14 yrs & ≥40.5 kg; shown to be effective short-term in 104 adolescents treated for 7 weeks with cessation counseling ▪ Pregnancy: limited human data suggest low risk ▪ Abruptly quitting smoking is preferred, but if not possible, reduce smoking by 50% by week 4, another 50% by week 8, and aim to quit by week 12 ▪ can help prevent post-cessation weight gain

Varenicline (Chantix) Formulary with quantity limits	▪ Start with 0.5 mg, then titrate up to 1 mg bid 0.5 mg/d for 3 days, then 0.5 mg bid for 4 days, then 1 mg bid ▪ Renal dose adjustment needed for CrCl < 30 ml/min ▪ Start 1–2 weeks prior to quit date to allow steady state concentrations. may start up to 5 weeks before the quit date. ▪ Starter pack available ▪ Take after eating with a full glass of water MOA: Selective partial agonist activity at α4β2 neuronal nicotinic acetylcholine receptors (mediates dopamine release relieving cravings/withdrawal sx), competitively blocks exogenous nicotine binding. Higher affinity for α4β2 receptor vs. nicotine; reduced reward associated with smoking	▪ N/V, abnormal dreams, HA, sleep disturbances, constipation & flatulence ▪ Neuropsychiatric sx, exacerbations of pre-existing psychiatric disorders, suicidal thoughts, & increased rate of CV events ▪ Data from a retrospective study (n ~ 165,000) suggests varenicline was not associated with an increased risk of any CV or neuropsychiatric event compared to NRT or bupropion	▪ Data including long-term trials up to 1 yr indicates varenicline to be more effective than single NRT or bupropion and as effective as combination NRT in improving smoking cessation rates ▪ data also shows increased smoking cessation rates in pts with psych disorders without causing significant neuropsychiatric AEs ▪ a double-blind comparative trial (n=8144) found varenicline to be the most effective treatment, whereas bupropion & nicotine patch were similar in efficacy ▪ FDA approved in ages ≥17 yo, did not demonstrate efficacy for ≤16 yo ▪ no clinically significant DDIs ▪ Abruptly quitting smoking is preferred, but if not possible, reduce smoking by 50% by week 4, another 50% by week 8, and aim to quit by week 12 ▪relieves nicotine withdrawal and blocks the reward from smoking. ▪ Needs renal dose adjustment. Avoid use in pts with unstable psychiatric status or a history of suicidal thoughts or PTSD. Monitor for neuropsychiatric symptoms. ▪ Pregnancy: limited human data, animal data suggest low risk

Combination Strategies

Nicotine Patch plus	Gum
	Lozenge
	Inhaler
	Spray
Bupropion SR plus	Patch
	Gum
	Lozenge
Varenicline Plus	Gum
	Lozenge
	Inhaler
	Spray

1: please refer to Table A regarding effectiveness & abstinence rates. First-line medications are listed by size of the odds ratio; 2: reduces the severity of nicotine withdrawal symptoms. Not an independent risk factor for acute myocardial events, use with caution in cardiovascular pts (within 2 weeks post MI, serious arrhythmias, & unstable angina pectoris); 3: NRT Pregnancy Recommendation (Briggs Drugs in Pregnancy and Lactation): Compatible if maternal Benefit >> embryo/fetal risk. Contraindicated with any tobacco use. Non-pharmacologic approaches are the safest option, but if failed, NRT use during pregnancy might be reasonable. Pt education must include that if they continue to smoke while using NRT, the embryo/fetus risk might be greater than when either is used alone. Breast-feeding Recommendation: No human data, potential toxicity Strength of evidence: - A: Multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings; B: Some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optimal. For instance, few randomized trials existed, the trials that did exist were somewhat inconsistent, or the trials were not directly relevant to the recommendation; C: Reserved for important clinical situations in which the Panel achieved consensus on the recommendation in the absence of relevant randomized controlled trials

Pregnancy
There is strong evidence that behavioral interventions can help pregnant individuals quit smoking and prevent low birth weight in infants. However, there is limited evidence on the benefits of pharmacotherapy, including NRT, bupropion SR, varenicline, or e-cigarettes, for smoking cessation in pregnant individuals or improving infant outcomes.
Without clear evidence on the risks and benefits of pharmacotherapy in pregnant women, clinicians should consider the severity of tobacco dependence in each patient and engage in shared decision-making to determine the best individualized treatment plan

Discontinuation / Duration of Pharmacotherapy

The use of pharmacotherapy for smoking cessation should be continued for at least three months to reduce the risk of relapse. While the optimal duration of treatment has not been determined, research suggests that continued treatment for up to 18 months may be beneficial. Insurance coverage for smoking cessation medications typically lasts for three months, but some companies are now offering coverage for up to six months. There is no evidence to suggest that longer treatment with these pharmacotherapies is harmful.

When it comes to stopping NRT, it is generally recommended to gradually taper off after a certain period of time, as prolonged use has not been shown to significantly increase quit success rates. However, it is still preferable to continue using NRT rather than returning to smoking. If you wish to use NRT for a different duration, it is advisable to consult with a healthcare provider. Ongoing research is being conducted to better understand the use of NRT. It is important to note that NRT can potentially lead to long-term dependence, as nicotine is addictive and users may transfer their dependence from tobacco to NRT.

Preventing Relapse
To ensure successful smoking cessation, it is crucial to provide ongoing support and relapse prevention to patients, particularly during the first three months when most relapses tend to occur. When following up with a patient who has recently quit smoking, it is important to congratulate and encourage them for their continued abstinence, identify any issues they may be experiencing, assess their use and effectiveness of medications, and remind them of the resources available for support. It is also important to emphasize that even a single puff on a cigarette can potentially lead to relapse.

If a patient has successfully quit smoking but still feels at risk for relapse due to their previous quit attempts, all pharmacologic agents can be extended for an additional 12 weeks, or even longer up to one year. The use of nicotine replacement therapy (NRT) may be continued indefinitely.

Electronic Nicotine Delivery Systems

Electronic cigarettes, also known as e-cigarettes, are not approved by the Food and Drug Administration (FDA) as a tool for smoking cessation. They are marketed as a safer, more convenient and socially acceptable alternative to tobacco cigarettes. However, according to the Centers for Disease Control and Prevention (CDC), as of October 15, 2019, there have been 1,479 cases of lung injury and 33 deaths associated with the use of e-cigarette or vaping products. Most of these cases involved the use of products containing the psychoactive compound tetrahydrocannabinol (THC). The cause of the lung injuries is likely due to chemical exposure, as no consistent evidence of infectious disease has been identified.

In 2020, the Surgeon General's report on smoking cessation found insufficient evidence to conclude that e-cigarettes increase smoking cessation rates. The report also noted some suggestive but not sufficient evidence about the impact of specific e-cigarette use behaviors on smoking cessation.

Exclusions: Patients who may not be suitable for the following pharmacotherapy or who may require additional monitoring include:

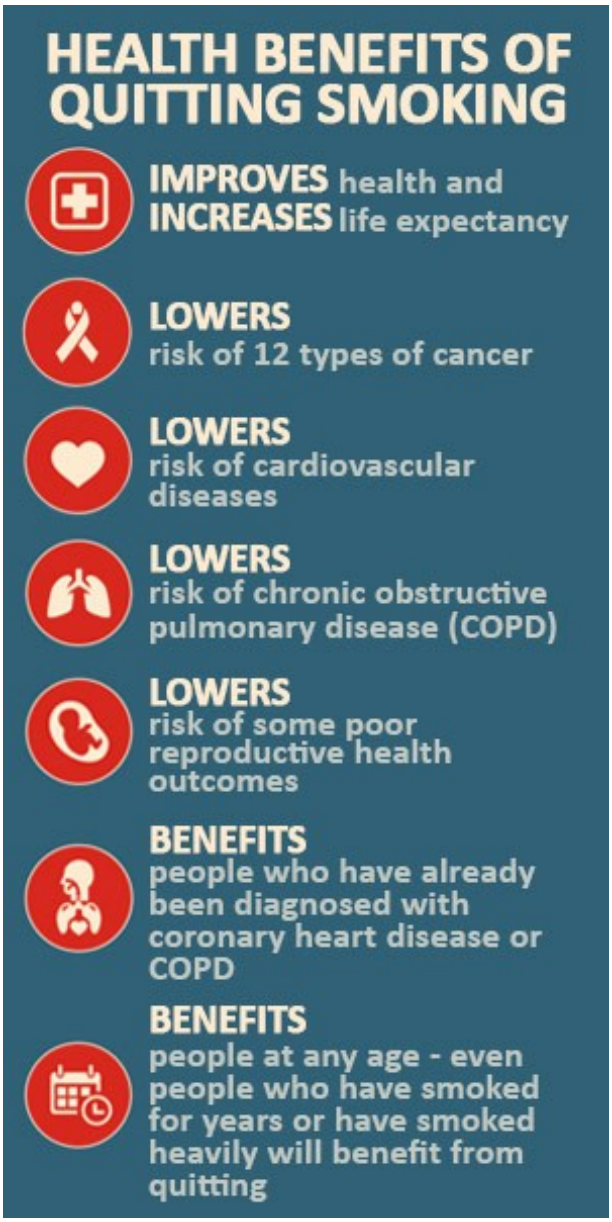
- Allergy to the medication
- Buproprion SR (Zyban)
    - Contraindications include h/o seizures or eating disorders, clts on another form of bupropion, and MAOI use in the past 14 days
    - Monitor for neuropsychiatric symptoms including behavioral changes, hostility, agitation, depressed mood, and suicidal thoughts or behavior. Clts with conditions that increase seizure risk such as arteriovenous malformation, severe head injury, stroke, brain tumor, CNS infection should not take bupropion
- Chantix
    - Avoid use in patients with unstable psychiatric status or a history of suicidal thoughts or PTSD. Monitor for neuropsychiatric symptoms.

Additional Resources

- **Highly recommended resource for quitting smoking, with our clinicians having excellent experiences and highlighting its benefits and value: California Smokers Helpline- 1-800-NO-BUTTS. Kick It California** is a free program offering tobacco cessation information and support to Californians. They provide free, personalized one-on-one coaching and self-help tools, all based on science. Contact a Quit Coach via phone or chat or refer patients to the service. They have been helping people quit smoking for nearly 30 years.
  https://kickitca.org/
- Centers for Disease Control and Prevention
  Health care clinician resources for treatment of tobacco use and dependence
  https://www.cdc.gov/tobaccoHCP
- Tips From Former Smokers
  https://www.cdc.gov/tobacco/campaign/tips/partners/health/index.html
- US Department of Health and Human Services
  SmokeFree.Gov Health Professionals Page
  https://smokefree.gov/help-others-quit/health-professionals
- SmokeFreeWomen
  http://women.smokefree.gov/pregnancy-motherhood
- https://www.cardiosmart.org/topics/healthy-living/stop-smoking?_ga=2.60477357.1269482144.1671834574-1920080473.1671834574
- Million Hearts tools for clinicians for tobacco cessation
  https://millionhearts.hhs.gov/tools-protocols/tools/tobacco-use.html
- Centers for Disease Control and Prevention state and community resources for tobacco control programs
  https://www.cdc.gov/tobacco/stateandcommunity/index.htm
- The US Department of Veterans Affairs (VA) Primary Care & Tobacco Cessation Handbook
  https://www.mentalhealth.va.gov/quit-tobacco/docs/IB_10-565-Primary-Care-Smoking-Handbook-PROVIDERS-508.pdf
- World Health Organization's toolkit for delivering brief smoking interventions in primary care
  http://www.who.int/tobacco/publications/smoking_cessation/9789241506953/en/

Attachments

- Kick It California
- SAMHSA Tobacco-free Toolkit for Behavioral Health Agencies
- Tobacco Use Assessment
- ASAM Integrating Tobacco Use Disorder Interventions in Addiction Treatment. A guide for addiction treatment clinicians and programs



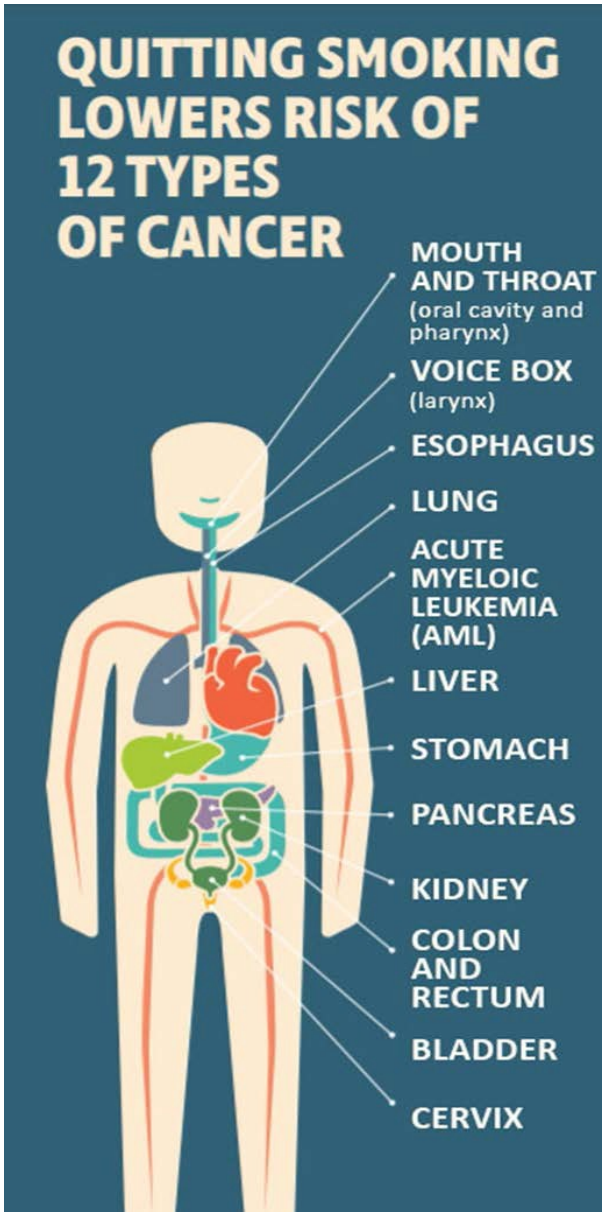


Table A: Meta-analysis (2008): Effectiveness and abstinence rates for various medications and medication combinations compared to placebo at 6-months post quit (n = 83 studies)[*#]

Medication	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	80	1.0	13.8
Monotherapies			
Varenicline (2 mg/day)	5	3.1 (2.5–3.8)	33.2 (28.9–37.8)
Nicotine Nasal Spray	4	2.3 (1.7–3.0)	26.7 (21.5–32.7)
High-Dose Nicotine Patch (> 25 mg) (These included both standard or long-term duration)	4	2.3 (1.7–3.0)	26.5 (21.3–32.5)
Long-Term Nicotine Gum (> 14 weeks)	6	2.2 (1.5–3.2)	26.1 (19.7–33.6)
Varenicline (1 mg/day)	3	2.1 (1.5–3.0)	25.4 (19.6–32.2)
Nicotine Inhaler	6	2.1 (1.5–2.9)	24.8 (19.1–31.6)
Clonidine	3	2.1 (1.2–3.7)	25.0 (15.7–37.3)
Bupropion SR	26	2.0 (1.8–2.2)	24.2 (22.2–26.4)
Nicotine Patch (6–14 weeks)	32	1.9 (1.7–2.2)	23.4 (21.3–25.8)
Long-Term Nicotine Patch (> 14 weeks)	10	1.9 (1.7–2.3)	23.7 (21.0–26.6)
Nortriptyline	5	1.8 (1.3–2.6)	22.5 (16.8–29.4)
Nicotine Gum (6–14 weeks)	15	1.5 (1.2–1.7)	19.0 (16.5–21.9)
Combination therapies			
Patch (long-term; > 14 weeks) + *ad lib* NRT (gum or spray)	3	3.6 (2.5–5.2)	36.5 (28.6–45.3)
Patch + Bupropion SR	3	2.5 (1.9–3.4)	28.9 (23.5–35.1)
Patch + Nortriptyline	2	2.3 (1.3–4.2)	27.3 (17.2–40.4)
Patch + Inhaler	2	2.2 (1.3– 3.6)	25.8 (17.4–36.5)
Patch + Second generation antidepressants (paroxetine, venlafaxine)	3	2.0 (1.2–3.4)	24.3 (16.1–35.0)
Medications not shown to be effective			
Selective Serotonin Re-uptake Inhibitors (SSRIs)	3	1.0 (0.7–1.4)	13.7 (10.2–18.0)
Naltrexone	2	0.5 (0.2–1.2)	7.3 (3.1–16.2)

*# Go to www.surgeongeneral.gov/tobacco/gdlnrefs.htm for the articles used in this meta-analysis.

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