SUBSTANCE-RELATED AND ADDICTIVE DISORDERS

Tobacco Use Disorder

TUD

DSM-5-TR 305.1 | ICD-10-CM F17.200, F17.210

Nicotine dependence sustained by rapid reinforcement and aversive withdrawal, and the leading preventable cause of death in the US.

US ADULT CIGARETTE USE	TYPICAL ONSET	ATTRIBUTABLE DEATHS	COURSE
~11% (2022)	Adolescence; most before 18	~480,000/yr in the US	Chronic; many quit attempts

CLINICAL PICTURE

- Smoking within 30 minutes of waking is the single best marker of dependence severity and reliably predicts difficulty quitting.
- Withdrawal starts within hours as irritability, anxiety, poor concentration, restlessness, increased appetite, and disrupted sleep.
- Most patients arrive having made multiple prior quit attempts and carry real demoralization about their capacity to succeed.
- Physical findings include chronic cough, reduced exercise tolerance, delayed wound healing, and accelerated skin and dental aging.
- Use is tightly cue-bound to coffee, driving, phone calls, alcohol, and work breaks rather than to blood nicotine level alone.
- Vaping and dual use are now common, so ask specifically about e-cigarette nicotine strength and pod or disposable device use.

DIAGNOSTIC CRITERIA AT A GLANCE

- Requires at least 2 of 11 criteria in 12 months, with DSM-5-TR using a single tobacco use disorder rather than an abuse and dependence split.
- Severity is mild 2-3, moderate 4-5, or severe 6 or more criteria, which maps loosely onto traditional nicotine dependence severity.
- Tobacco withdrawal requires 4 or more characteristic symptoms within 24 hours of abrupt cessation or reduction after daily use.
- Risky-use and social-impairment criteria discriminate less well than for other substances because tobacco is legal and rarely intoxicating.
- The **Fagerstrom Test for Nicotine Dependence** and time-to-first-cigarette usefully complement DSM criteria for treatment planning.

NEUROBIOLOGY & PHYSIOLOGY

- Nicotine agonizes **alpha4beta2** nicotinic acetylcholine receptors on VTA neurons, releasing dopamine in the nucleus accumbens within seconds.
- Inhaled delivery reaches the brain in about 10 to 20 seconds, producing rapid, highly repeatable reinforcement thousands of times per year.
- Chronic exposure upregulates nicotinic receptors, and desensitization between cigarettes generates the withdrawal and craving cycle.
- **CYP2A6** metabolism rate determines the nicotine metabolite ratio, which predicts relative response to varenicline versus the patch.
- **CHRNA5-A3-B4** gene cluster variants raise heavy smoking and lung cancer risk independent of self-reported consumption levels.
- Combustion products rather than nicotine cause most harm, including cardiovascular disease, COPD, and cancers of many organ systems.

PSYCHOLOGICAL MECHANISMS

- Massed conditioning pairs each cigarette with reinforcement hundreds of times monthly, creating exceptionally durable cue reactivity.
- Patients report smoking to relieve stress, but relief of withdrawal accounts for most of the perceived calming effect they describe.
- Weight gain concern, averaging about 4 to 5 kg after quitting, is a major barrier especially for women and should be addressed directly.
- Low self-efficacy after prior failed attempts predicts relapse, so reframe earlier quits as practice attempts yielding usable data.
- Smoking is embedded in social routine and identity, so replacing the ritual matters as much as replacing the nicotine itself.

DIFFERENTIAL & COMORBIDITY

- Prevalence is two to four times higher in schizophrenia, bipolar disorder, depressive disorders, and other substance use disorders.
- Smoking induces **CYP1A2**, so quitting can raise clozapine and olanzapine levels by 30% to 50% and requires prompt dose review.
- Cessation does not worsen psychiatric illness, and the EAGLES trial found no excess neuropsychiatric events with varenicline or bupropion.
- Screen for COPD and coronary disease, and check eligibility for low-dose CT lung cancer screening in adults with 20 pack-years.
- Co-occurring alcohol use disorder sharply raises relapse risk, and treating both conditions concurrently improves both outcomes.

Treatment EVIDENCE-BASED MANAGEMENT

PHARMACOLOGIC

- **Varenicline 1 mg BID** started about one week before quit day is the most effective single agent; nausea and vivid dreams are common.
- Combination **nicotine replacement** pairing a 21 mg patch with as-needed gum or lozenge outperforms any single-form product.
- **Bupropion SR 150 mg BID** roughly doubles quit rates and blunts post-cessation weight gain, but avoid it with any seizure history.
- Varenicline plus the patch may exceed either alone, and extending treatment to 12 to 24 weeks meaningfully reduces late relapse.
- **Cytisinicline** and preloading strategies are emerging options, and EAGLES confirmed the neuropsychiatric safety of first-line agents.

PSYCHOTHERAPY

- Combining medication with behavioral counseling produces the highest quit rates, and either component used alone is clearly inferior.
- The **5 A's** framework of ask, advise, assess, assist, and arrange should be applied at essentially every clinical encounter.
- **CBT** and behavioral counseling of 4 or more sessions totaling over 90 minutes shows a clear and reproducible dose-response effect.
- **Motivational interviewing** helps patients who are not yet ready to quit and increases the likelihood of future quit attempts.
- Quitlines such as 1-800-QUIT-NOW and text-message programs deliver effective counseling at scale with proactive follow-up contact.

ADJUNCT & SUPPORTIVE

- Reduce-to-quit works: patients unwilling to set a quit date still benefit from **NRT**-supported gradual reduction over several weeks.
- Recheck psychiatric medication levels after quitting, especially clozapine and olanzapine, and review caffeine intake as well.
- Address weight concerns with activity planning and realistic expectations rather than postponing the quit attempt indefinitely.
- Switching completely to e-cigarettes reduces toxicant exposure relative to smoking but is not FDA-approved cessation therapy.
- Track exhaled carbon monoxide and schedule contact within the first week, when the large majority of lapses actually occur.

CLINICAL PEARLS

- Time to first cigarette under 30 minutes is the fastest measure of dependence.
- Quitting removes CYP1A2 induction: clozapine and olanzapine levels rise sharply.
- Combination NRT beats single-form NRT; do not settle for the patch alone.

References

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NOTE

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