Advanced Pharmacotherapy:
Treating Tobacco Use Disorder within Mental Health and Substance Use Recovery Settings

Presented by Dr. Jill Williams,

Robert Wood Johnson Medical School-Division of Addiction Psychiatry, Rutgers University.

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Lung Mind Alliance

A commercial tobacco-free future for Minnesotans with mental illness or substance use disorders

Who We Are

The Lung Mind Alliance is a statewide coalition with the goal of **reducing disparities related to the impact of commercial tobacco* on people with mental illness and/or substance use disorders**.

The Lung Mind Alliance is led by the American Lung Association in Minnesota and includes partners from mental health, substance use treatment, and public health organizations, as well as the Minnesota Department of Health and the Department of Human Services.

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THE STATE UNIVERSITY OF NEW JERSEY

Advanced Pharmacotherapy:

Treating Tobacco Use Disorder within Mental Health and Substance Use Recovery Settings

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Disclosures

Jill Williams, MD has no relevant financial relationships.

The off-label use of medication will be discussed.

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Objectives

At the conclusion of this session, participants should be able to:

1. Be familiar with advanced topics in tobacco treatment including combination pharmacotherapy and guidelines for first line treatments.
2. Be familiar with off- label uses of medications in populations who may not be immediately ready to stop using tobacco or longer durations of treatment for relapse prevention.
3. Understand uses and guidelines in special populations.

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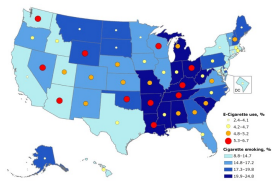
"Smoking is much more common in adults with mental illness than other adults"



US 11%

in 2022; NHIS

E cigs ~ 6%

Mental Health ~ 30%
SUD ~ 40-60%
SUD Staff ~ 30%

Centers for Disease Control and Prevention, 2015; Guydish 2022

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Clinical Conundrums for the Experienced Clinician

- Higher levels of dependence
- Combination NRT or varenicline as first line
- More advanced combination options
- Prescribing for tobacco user not ready to quit
- Longer durations
- Special populations
- Reduced risk products: Electronic cigarettes and vaping

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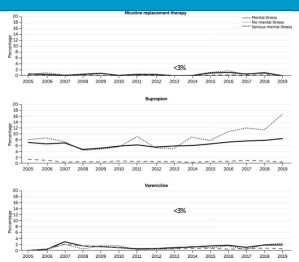
Access to Treatment Still Limited



The most common barrier to providing smoking cessation treatment noted by general internists (60%) and psychiatrists (80%) was patients' perception of **smoking as a coping mechanism for their mental illness**.

White et al., 2022, Psych Serv
Medical Expenditure Panel Survey (MEPS) data (2005–2019)

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What's New?

Emerging Evidence

- Cytisinicline (cytisine)
- Pre-quit NRT
- Reduce to Quit
- ACT
- Mobile Phone Apps
- Ecigarettes
- Incentives
- Transcranial Magnetic Stimulation

*FDA approved

No evidence of benefit

- Alternative Therapies
- Internet
- Exercise
- Acupuncture/ acupressure
- Hypnotherapy
- Mindfulness
- Naltrexone, selegiline, anxiolytics, lobeline, N-Acetylcysteine, St John's Wort, and selective serotonin reuptake inhibitors (SSRIs)

Patnode et al., AHRQ 2021; Jackson et al., 2022

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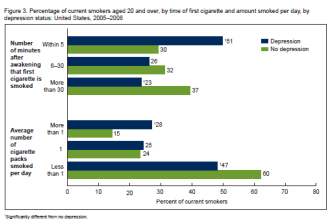
Measure of Tobacco Use Severity

Heaviness of Smoking Index

- **AM Time to first cigarette (TTFC)**
  - ≤ 30 minutes = moderate
  - ≤ 5 minutes = severe
- Cigarettes per day smoked

Implications for Treatment Outcome
Need for Medications
Implications for Dose



Heatherton 1991; Pratt & Brody, 2010

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Effectiveness of First Line Medications

Results from meta-analyses comparing to placebo (6 month F/U)

Medication	No. Studies	OR	95% CI
Nic. Patch (6-14 wks)	32	**1.9**	1.7-2.2
Nic. Gum (6-14 wks)	15	**1.5**	1.2-1.7
Nic. Inhaler	6	**2.1**	1.5-2.9
Nic. Spray	4	**2.3**	1.7-3.0
Bupropion	26	**2.0**	1.8-2.2
Varenicline (2mg/day)	5	**3.1**	2.5-3.8

None new since 2006

Fiore et al., 2008. PHS Guideline

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Combination Therapies

- Long acting (patch) + short acting (gum/lozenge)
- Delivers higher dose
- Immediate withdrawal and craving relief
- Enhances outcomes

	OR
Patch + gum or spray	**1.9** (1.3-2.7)
Patch + bupropion	**1.3** (1.0-1.85)

Varenicline and NRT **NOT** recommended- evidence conflicting

2008 PHS Guideline Update

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Oral Forms of NRT

From Nicorette.com

- Higher dose gum/ lozenge (4mg if TTFC, 30 mins)
- Minimum effective dose ~ 8
- Dose frequently – every 1-2 hours
- Slow, buccal absorption
- Acidic foods ↓ absorption
- Mild side effects – mouth, throat burning

- GI upset/ hiccups if swallowed
- Better for cravings vs patch
- Titrate to dose
- Rescue medicine
- Supplement the patch

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Nicotine Patch Treatment

- I often have pts tell me they are worried about smoking while on the patch due to the potential for agitation, jumpiness, from nicotine overload or toxicity.
  - Can you elaborate on how much of a concern this may be?

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S76 REVIEW: USE OF NICOTINE REPLACEMENT AND CIGARETTES

Table 2. Transdermal nicotine replacement

	N	Duration	Product	Percent Change		
				Nic. conc.	No. of Cigs.	CO
Instruction or intention to reduce						
Carpenter 2001	12	4W	Nicoderm 14, 21mg	5%[1]	−55%	−36%
Mahmarian 1997	40	3D	Nicoderm 14mg	50%	−65%	−39%
		3D	21mg	88%	−74%	−48%
Average				48%	−65%	−41%
Instruction to smoke ad libitum						
Zevin 1998	12	20D	Nicoderm 21mg	55%	NA	NA
			42mg	140%	NA	NA
			63mg	200%	NA	NA
Pickwort 1994	10	24D	Prostep 22mg	105%	−16%	−18%
			44mg	231%	−28%	−27%
Foulds 1992	30	2W	Nicorette 15mg	19%	−20%	−15%
Average			<23mg	60%	−21%	−20%
			>22mg	190%		
Total Average			<23mg	54%	−43%	−31%
			>22mg	190%		

D = Days W = Weeks 1. Cotinine in saliva

Nicotine & Tobacco Research (2002), S73–S79 Taylor & Francis healthsciences

Review

Nicotine concentrations with concurrent use of cigarettes and nicotine replacement: A review

Karl Olov Fagerström, John R. Hughes

[Received 18 June 2001; accepted 26 November 2001]

This paper reviews the data on blood nicotine or saliva cotinine concentrations with concomitant smoking and use of nicotine replacement (NR) products. Eleven studies that provided data on blood nicotine concentrations, carbon monoxide in exhaled air, and number of cigarettes smoked were reviewed. At least one day had to be spent on concurrent use of cigarette and NR products. With simultaneous use of smoking and acute NR products (gum and inhaler) the nicotine concentrations were unchanged, whereas they increased (+54%) with nicotine patches. With both types of NR products, the number of cigarettes smoked per day was reduced by approximately 50% and carbon monoxide (CO) by 30%. Where smokers had the intention or received instructions to reduce smoking, a greater reduction in cigarettes smoked and exhaled CO was observed. Despite substantially increased nicotine concentrations (e.g., up to 3 times the approved dose) there were no significant adverse reactions. Concurrent use of NR products and cigarette smoking appears to be safe.

- Subjects experienced almost no toxic effects from their cigarette smoking while wearing the patch (pl controlled)
- No increase in BP or pulse with 21mg dose
- 2 patients had nausea and vomiting

* Very few adverse effects even with nicotine levels that were 2-3 times higher compared with smoking

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Oral Tobacco Use Treatment

- How do you estimate NRT doses for oral tobacco products (snus, chew, and nicotine pouches)?

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Treatment Smokeless Tobacco

TTFU

Time to First Use

Lozenge 4mg dose

34 trials, > 16,000 participants.

Moderate quality evidence suggesting that **varenicline** increases ST abstinence rates (risk ratio [RR] 1.34, 95% confidence interval (CI) 1.08 to 1.68, 507 participants).

Pooling five studies of nicotine **lozenges** did increase tobacco abstinence (RR 1.36, 95% CI 1.17 to 1.59, 1529 participants) but confidence in this estimate is low

Pooled results from two trials of bupropion did not detect a benefit of treatment at six months or longer (RR 0.89, 95% CI 0.54 to 1.44, 293 participants)

Neither nicotine patch (five trials, RR 1.13, 95% CI 0.93 to 1.37, 1083 participants) nor nicotine gum (two trials, RR 0.99, 95% CI 0.68 to 1.43, 310 participants) increased abstinence. Ebbert et al., Cochrane. 2015

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Pharmacotherapy for Smokeless Tobacco

- 34 trials, limited data
- Varenicline increases abstinence (RR 1.34)
- ? Bupropion, lozenges, counseling may help
- Nicotine patch or gum not helpful

Ebbert, Cochrane et al., 2015

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Varenicline

Partial Agonist ($\alpha4\beta2$ receptor subtype)

- Blocks nicotine binding $\alpha4\beta2$ receptor; Some DA release at NAcc
- Reduces withdrawal and craving
- Superiority to bupropion or nicotine patch (nicotine monotherapy) psychiatric and nonpsychiatric smokers
- Comparable efficacy to combination NRT
- No significant differences in rates of moderate and severe neuropsychiatric events (vs bup or NP or placebo)
- Side effects: Nausea, insomnia, abnormal dreams, headache
- Effective in AA vs plc (50% smoked light <10)
- Voluntary recall over (manufacturing problem/ nitrosamine)

Anthenelli et al., Lancet 2016; Cox et al., JAMA 2022

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Safety Varenicline: Neuropsychiatric

- Meta analysis 39 RCTs (10,761 participants)
  - **No** increased risk of suicide, suicidal ideation, depression, irritability, aggression
- RCT. MDE, Schizophrenia, Bipolar
  - No worsening illness (MADRS, PANSS)
- EAGLES study : N= 8144 (4416 stable, psych outpatients)
  - **No increased risk of moderate/ severe adverse effects** vs NP or Bup or Placebo (Anxiety/ Panic, Depression, Feeling abnormal, Hostility, Agitation, Aggression, Delusions, Hallucinations/ Paranoia/ Psychosis, Homicidal ideation, Mania, Suicidal ideation or behavior)
- Predictors of moderate to severe NPSAEs : current anxiety or prior suicidal ideation at baseline and White. In smokers with psych, female sex, younger age, and greater severity of nicotine dependence were also predictive (not medication type)

Chengappa et al., 2014; Anthenelli et al, 2013, 2016, 2019; Thomas et al., 2015; Williams et al., 2012;

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Best Practices
Current Recommendations

Varenicline* or combination NRT + behavioral support should be considered **first line**

*American Thoracic Society (2020) (including for psychiatric patients)

Leischow, JAMA 2019

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Varenicline Treatment

- How long do we maintain a patient on varenicline (Chantix)?
  - 12-24 weeks?
  - Can we do a longer treatment?

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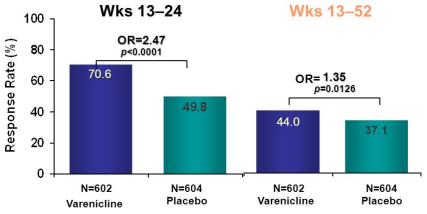
Varenicline Maintenance of Abstinence Study



Tonstad et al. JAMA 2006;296:64-71

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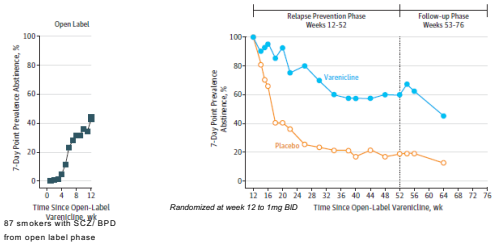
Maintenance Varenicline Greater Abstinence at 1 Year in SCZ/ BPD



Evins, 2014; Pachas et al., 2012

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Can Medications for Tobacco Use Disorder be Used Long-Term (up to 6 Months)?

- Yes. Better relapse prevention
- This does not present a known health risk
- Developing dependence on medications is uncommon.
- FDA approved use of bupropion SR, varenicline, and NRT for 6-month use.

Fiore et al., 2008. PHS Guideline

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Combination Varenicline and Bupropion

- Meta-analysis: 4 RCT with a total of 1230 smokers.
- Combination varenicline and bupropion significantly improves the abstinence rate at end of treatment (RR 1.2, 95% CI 1.0 to 1.3, P = 0.024) vs varenicline alone
- The benefit existed at 6 months follow-up (RR 1.2, 95% CI 1.0 to 1.5, P = 0.033), and mainly concentrated in **highly dependent smokers** (RR 1.6, 95% CI 1.3 to 2.1, P < 0.001) and **heavy smokers** (RR 1.5, 95% CI 1.2 to 1.9, P < 0.001)
- For safety outcomes, the combination treatment was associated with **more anxiety** (RR 1.7, 95% CI 1.2 to 2.5,P = 0.005) and **insomnia** (RR 1.3, 95% CI 1.1 to 1.5, P = 0.005) symptoms vs varenicline monotherapy.

Zhong et al., 2019

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Combination therapy of Varenicline and NRT

- **Generally not recommended**
- Mixed study results
- More side effects
- Unclear mechanism
- ? Most severe dependence

- 12 or 24 weeks ; including placebos
- N=1251, >5cpd; 2 week pretx NP
- 6 sessions, 15min counseling

Nausea 24-31%
Insomnia 24-31%
Changes in mood 16-18%

	7dPP, 52W
VAR monotherapy for 12 weeks	25.1
VAR + NP for 12 weeks	23.6
VAR monotherapy for 24 weeks	24.4
VAR + NP for 24 weeks	25.1

Baker et al., JAMA 2021

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Gender and Quitting

- **Women in a given quit attempt women are less likely to successfully quit smoking than men**
  - ? Negative affect/ depression/ socioeconomic issues/ less likely meds/ beliefs about weight and appetite
- Women in placebo group less likely than men to quit
- **Varenicline was more effective than TNP for women** (OR=1.51; 95%CI=0.12,2.05; p=0.007) but not men (OR=0.92; 95%CI=0.65,1.31; p=0.64).
- The advantage of varenicline over bupropion SR and TN is greater for women than men
- Clinical trials and epidemiologic studies

McKee et al., 2016; Smith PH et al., 2017; Smith et al., 2016

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Pregnancy Options

- Some Evidence
- NRT - Difference in smoking rates favoring use of NRT (risk ratio (RR) 1.41, 95% (CI) 1.03 to 1.93, eight studies, 2199 women
- Bupropion v Placebo
  - Limited studies, no benefit

Exposure to Medications

- NRT-no differences in rates of miscarriage, stillbirth, premature birth, birthweight, low birthweight, admissions to neonatal ICU, congenital abnormalities or neonatal death
- Bupropion- no increased risk of congenital malformations
- Varenicline- no risk for congenital abnormalities

Coleman et al., 2015; Nanovskaya et al., 2016; Richardson et al., 2017; Coleman et al., 2015

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ACOG Recommendations- Smoking Cessation During Pregnancy

Current evidence is insufficient to assess the balance of benefits and harms of nicotine replacement products or other pharmaceuticals for smoking cessation aids during pregnancy.

There is **conflicting evidence as to whether or not NRT increases abstinence rates in pregnant smokers**, and it does not appear to increase the likelihood of permanent smoking cessation during postpartum follow-up of these patients.

Use of NRT should be undertaken with close supervision and after careful consideration and discussion with the patient of the known risks of continued smoking and the possible risks.

Alternative agents include varenicline and bupropion. There is insufficient evidence to evaluate the safety and efficacy of these treatments in pregnancy and lactation.

American College of Obstetricians and Gynecologists; Siu 2015; Fiore 2008

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Incentives

- Financial incentives (monetary or vouchers)
- 33 studies (N> 21k participants)- High and low value USD 45 to 1000; quitting validated with CO
- **RR quitting with incentives at longest follow-up (6 months or more) vs controls was 1.49** (95% CI 1.28 to 1.73)
- Sustained effectiveness even after the withdrawal of incentives

- 9 studies of ~ 2500 pregnant women
- **RR at longest follow-up (up to 6 months post-partum) of 2.38** (95% CI 1.54 to 3.69), in favor of incentives

Notley et al., Cochrane 2019

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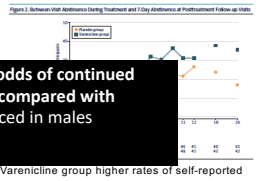
Varenicline for Adolescent Smoking Cessation

- N = 157; aged 14 to 21 years; Tobacco use 11.5 cpd at baseline
- Dose adjustment for weight (some 0.5 BID)
- The v… cotini… (vare… of 45…
- 59.2% canna…

Baseline cannabis users (68%) had 2X odds of continued cigarette smoking throughout the trial compared with noncannabis users, which was pronounced in males



Varenicline group higher rates of self-reported weekly abstinence during the full course of treatment (RR, 1.81; 95%CI, 1.09-2.99; P = .02) and at follow-up

Gray et al., 2019;

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Mental Health Populations

- Treatments work and well tolerated
- Overall cessation on a given attempt can be less than populations without mental illness
- Many studies- no worsening of depression, psychosis in quit attempt
- No worsening of neuropsychiatric: varenicline
- Modified counseling approaches with pharmacotherapy

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Substance Using Populations

- Treatments work and well tolerated
- Cessation (h/o alcohol) –equal success despite higher dependence
- Cigarette smoking associated increased risk of SUD relapse
- Smoking cessation improves abstinence outcomes
- Varenicline reduces drinking (modulate reward)
  - In heavy drinkers
  - In smokers trying to quit smoking
  - In lab studies of animals and humans

Weinberger et al., 2017; Erwin & Slaton, 2014; Mitchell et al., 2012; Hurt et al., 2018; McKelvey 2017

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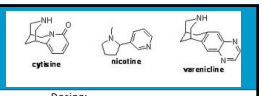
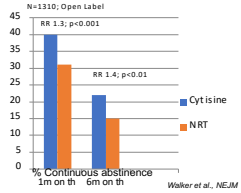
Cytisinicline/Cytisine



- Nicotine partial agonist
- Eastern Europe since 1960s (Tabex); Not licensed US

Dosing:
1.5mg 6times daily, decreasing for 25 days

Varenicline vs Nicotine Patch
N=1310; Open Label



Walker et al., NEJM 2014

Varenicline vs Cytisine
N=1452; Open Label- 25d C, 84 d (12W) V; telephone counseling

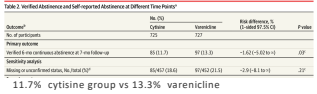


Table 2. Verified Abstinence and Self-reported Abstinence at Different Time Points*

Outcome†	No. (%)		Risk difference, % (1-sided 97.5% CI)	P value
	Cytisine	Varenicline		
No. of participants	725	727		
Primary outcome				
Verified 6-mo continuous abstinence at 7-mo follow-up	85 (11.7)	97 (13.3)	−1.62 (−5.02 to ∞)	.03‡
Sensitivity analysis				
Missing or unverified status, No./total (%)§	85/457 (18.6)	97/452 (21.5)	−2.9 (−8.1 to ∞)	.23‡

11.7% cytisine group vs 13.3% varenicline

Courtney RJ et al, JAMA 2021

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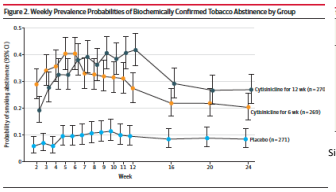
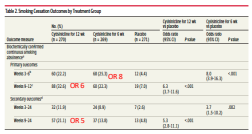
Cytisinicline/Cytisine

- N=810 (19.4 cpd), motivated to quit, brief counseling
- Cytisinicline 3mg TID for 12W; Cytisinicline 3mg TID (6W, then 6W pl); or Placebo TID for 12W





Side effects (<10%) : nausea, abnormal dreams, insomnia

Rigotti et al., JAMA, 2023

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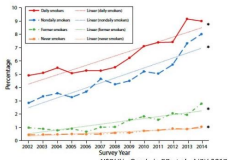
Cannabis and Tobacco Co-Use

- Trends
  - Combustible vs Vaping/Ecigs/ Other
  - Co-Use Delivery
- Impact of Co-Use
  - Mental Health
  - Physical Health
  - Quitting tobacco
  - Quitting cannabis
  - Pregnancy
- Policy and Public Health Implications
  - Indoor Air/ Public Spaces

Daily cannabis increased in last decade in smokers



NSDUH; Goodwin RD et al., AJPH 2017

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Cannabis and Tobacco Co-Use

- More psychiatric problems
- More health risks
- Higher risk for SUD of other

- More difficulty quitting
- Motivation differs tobacco> cannabis
- Severity of withdrawal
- ?Drug substitution
- ?Interventions for both
- Sequential or simultaneous
- Few trials, gender effects, mental health comorbidity

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Medication Interaction Tobacco and Treatments

Nicotine	CYP2A6	None
Bupropion	CYP2B6 CYP2D6 inhibitor	Many
Varenicline	Excreted in urine	None
Tobacco Smoke (Cannabis smoke)	CYP1A2 inducer	Reduces level of olanzapine, clozapine, tricyclic ADs, caffeine, duloxetine, mirtazapine, fluvoxamine

https://smokingcessationleadership.ucsf.edu/factsheets/drug-interactions-tobacco-smoke-rx-change-2022

Oliveira et al, 2017; Desai et al., 2001

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Should We Use Medications For People Who Aren't Ready to Quit?

- Yes.
- Lessen dependence
- Minimize withdrawal
- Harm reduction
- Smoke less
- Higher OR for future quitting

Fiore et al., 2008. PHS Guideline

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Nicotine for Temporary Abstinence

- Withdrawal relief
- May facilitate subsequent cessation
- Nicotine patch use significantly reduced agitation in smokers with schizophrenia treated in an ER setting
- Smokers who were not given a prescription NRT >2X more likely to be discharged early/ AMA from the inpatient psychiatric hospital
- Packaging smaller quantities

Prochaska, 2004; Allen 2011

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Should Patients Reduce to Quit?

- 51 trials with 22,509 participants
- Low-certainty evidence that reduction-to-quit interventions may be more effective when **pharmacotherapy** is used as an aid, particularly fast-acting NRT or varenicline (moderate-certainty evidence).
- Reduction-to-quit may be equivalent to abrupt quitting for fast-acting NRT or varenicline but not for nicotine patch, combination NRT or bupropion (**abrupt quitting may be better**)

Lindson et al, Cochrane Review, 2019

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NRT Assisted Reduction

- 7 Smoking Reduction trials (four Nicotine gum, two inhalers, and one free choice NRT)
- 2767 smokers
- NRT for 6-18 months
- 6.75% of smokers receiving NRT had sustained abstinence for six months, 2X more those receiving placebo
- No statistically significant differences in adverse events and discontinuation because of adverse events
- except nausea →more with NRT
- **Whether smokers are motivated to reduce then quit or simply motivated to reduce may make little difference to the efficacy of NRT for smoking cessation**

Moore et al., BMJ, 2009

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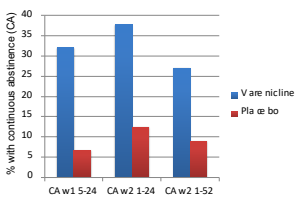
Smoking Reduction with Varenicline

- 52-week DB-PC study of 1,510 subjects who were not able/willing to quit smoking within four weeks, but were willing to gradually reduce their smoking over 12 weeks
- Varenicline 1 mg BID or placebo for 24 weeks
- Instructed to reduce cpd by 50% end of first four weeks of treatment, followed by further 50% from week 4-8, with the goal of reaching complete abstinence by 12 weeks.

Package Inset: *Consider a gradual approach to quitting smoking with CHANTIX for patients who are sure that they are not able or willing to quit abruptly. ….Continue treatment for an additional 12 weeks, for a total of 24 weeks.*



Ebbert et al., 2015

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Pre-Quit NRT

- Rationale: get used to dose/ side effects, familiarize, less enjoyment smoking
- Usual 2 weeks before QD
- Not all studies show effect (patch)
- Well tolerated
- Meta-analysis of 4 studies, pre-loading with the nicotine patch doubled the odds of quitting at 6 weeks (OR = 1.96; 95% CI, 1.31–2.93) and at 6 months (OR = 2.17; 95% CI, 1.46–3.22)
- A meta-analysis of 6 trials (N=1772), some benefit of pre-loading with a nicotine patch (OR=1.34; 95% CI, 1.08-1.65

Rose et al., 2009; Shiffman & Ferguson, 2008; Stead et al., 2012

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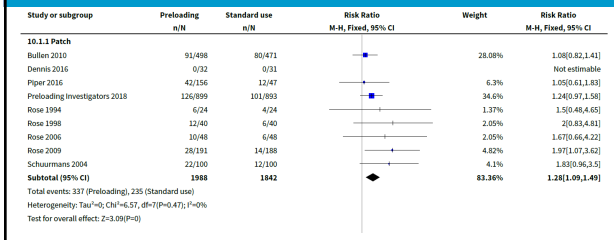

Study or subgroup	Preloading n/N	Standard use n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
10.1.1 Patch					
Bullen 2010	91/498	80/471		28.08%	1.08[0.82,1.41]
Dennis 2016	0/32	0/31			Not estimable
Piper 2016	42/156	12/47		6.3%	1.05[0.61,1.83]
Preloading Investigators 2018	126/899	101/893		34.6%	1.24[0.97,1.58]
Rose 1994	6/24	4/24		1.37%	1.5[0.48,4.65]
Rose 1998	12/40	6/40		2.05%	2[0.83,4.81]
Rose 2006	10/48	6/48		2.05%	1.67[0.66,4.22]
Rose 2009	28/191	14/188		4.82%	1.97[1.07,3.62]
Schuurmans 2004	22/100	12/100		4.1%	1.83[0.96,3.5]
Subtotal (95% CI)	**1988**	**1842**		**83.36%**	**1.28[1.09,1.49]**
Total events: 337 (Preloading), 235 (Standard use)					
Heterogeneity: Tau^2=0; Chi^2=6.57, df=7(P=0.47); I^2=0%					
Test for overall effect: Z=3.09(P=0)					

Lindson et al., 2019

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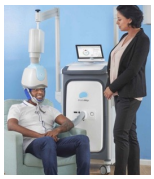
Transcranial magnetic stimulation



- Non-invasive technique to apply brief magnetic pulses to the brain. (passing high currents (pulse) through an electromagnetic coil (scalp) that induces electric/ magnetic field in brain tissue, activating neurons in targeted areas)
- Randomized, sham controlled; n=262
- 15 sessions (18 mins), 5/week for 3 weeks
- Targeting bilateral insula and prefrontal cortex (craving and consumption)
- 4 week continuous QR
  - 17% DTMS vs 8% Sham
  - Reduced cpd, and craving
- Side effects; Scalp discomfort, muscle twitching, headache
- FDA approved- smoking cessation

Zangen et al., World Psychiatry, 2021*

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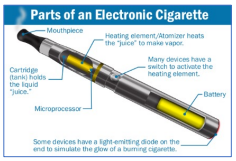
E-Cigarettes and Vaping

- Concern over youth uptake
  - **E-cigarette use is associated with increased risk for cigarette initiation and use, in low-risk youths**
- Controversy - older smoker for cessation
- Non- combustible
  - Safer than smoking doesn't mean safe?
- Not regulated/ Wide variability
- Nicotine addiction: ? same treatments
- Vaping culture- co use with THC/ cannabis
- Most EVALI cases: THC
- Public health support – UK, others
  - Continuum of risk ?



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E cig Controversies

Increasing Adult Cessation

Prevent Youth Uptake

Continuum of Risk

Combustible Tobacco | Electronic Cigarette | Nicotine Replacement Therapy

Policy Agenda

- Decreasing the addictiveness of combusted tobacco while ensuring the availability of reduced-risk nicotine products
- Imposing large taxes on combustible products and smaller taxes on e-cigarettes
- Limiting the sale of all tobacco/nicotine products to adult-only retailers
- Developing communications that accurately portray e-cigarettes' risks to youth and benefits for adult smokers

Warner et al., 2022

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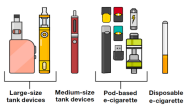
Tobacco and Nicotine Products

- Combustible

Hookah

- Non-Combustible



Snus, chew, and nicotine pouches

- Medicinal

Nicotine Replacement Therapy (NRT)

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FDA Marketing Authorization

Vuse Solo (RJR) and pods

Logic (Vapeleaf, Power, Pro)

VLN (King or Moonlight)- 95% less nicotine

NJOY (Daily Rich) Disposable

Not Sold in US
IQOS (PM)/ Marlboro Heatsticks

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Synthetic Nicotine

- Tobacco derived S-nicotine enantiomer
- Synthetic blend of R and S (R 10x weaker agonist)
- Industry innovations to reduce cost and increase S
- Marketing strategy
- FDA can regulate nicotine from any source (April 14, 2022)

- "Tobacco-free" synthetic nicotine pouches (since 2016)
  - No spitting, discrete
  - Nicotine salt
  - Zyn 3,6,8 mg

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E-Cigarettes for Adult Cessation

Motivated

- RCT : refillable vs combi NRT
  - 1year SA: 18% ecig v 10% NRT ; Abstinent: 80% using at 1 yr v 9% NRT
- NP vs NP/ Ecig vs NP/PI Ecig (no nic); RR ~1.5-2

	NP/Ecig	NP/PI Ecig	NP
3mos	33%	23%	17%
6 mos	24%	17%	11%

Unmotivated

- RCT: High nic Ecig vs No nic Ecig vs plastic
  - Abstinence 24 weeks (10.8% vs 0.8%) vs 3.1%

Hajek et al., NEJM 2019; Walker et al., 2020; Fould et al, NTR, 2021

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E-Cigarettes Population Study

- 1600 smokers, not intending quit; 50% >20 cpd
- 6% quit smoking over 5 years
- 11% quit daily smoking

- 28% quit if used ecig daily (vs no ecigs 6%); 8X↑
- 46% quit daily smoking if used ecig daily (vs no ecigs 10%)
- Non daily ecig (occasional) has no impact on quitting

Kasza et al, JAMA Network Open, 2021

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E-Cigarettes for Adult Cessation

Cochrane Library

Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

Main results

We included 88 completed studies (10 new to this update), representing 27,235 participants, of which 47 were randomized controlled trials (RCTs). Of the included studies, we rated ten (all but one contributing to our main comparisons) at low risk of bias overall, 58 at high risk overall (including all non-randomized studies), and the remainder at unclear risk.

There is high certainty that nicotine EC increases quit rates compared to nicotine replacement therapy (NRT) (RR 1.59, 95% CI 1.29 to 1.93; I^2 = 0%; 7 studies, 2544 participants). In absolute terms, this might translate to an additional four quitters per 100 (95% CI 2 to 6 more). There is moderate-certainty evidence (limited by imprecision) that the rate of occurrence of AEs is similar between groups (RR 1.03, 95% CI 0.91 to 1.17; I^2 = 0%; 5 studies, 2052 participants). SAEs were rare, and there is insufficient evidence to determine whether rates differ between groups due to very serious imprecision (RR 1.20, 95% CI 0.90 to 1.60; I^2 = 32%; 6 studies, 2761 participants; low-certainty evidence).

Key messages

Nicotine e-cigarettes can help people to stop smoking for at least six months. Evidence shows they work better than nicotine replacement therapy, and probably better than e-cigarettes without nicotine.

They may work better than no support, or behavioural support alone, and they may not be associated with serious unwanted effects.

However, we still need more evidence, particularly about the effects of newer types of e-cigarettes that have better nicotine delivery than older types of e-cigarettes, as better nicotine delivery might help more people quit smoking.

Lindson et 2024

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Nicotine Vaping Dose Equivalency

- How do you "convert" nicotine vaping amounts to the traditional PPD for deciding what dose of the nicotine patch to start?
  - Or does it not really matter and just typically start with 21 mg plus gum/lozenge as rescue?
  - Is there a conversion in figuring out one cartridge equaling a certain number of cigs?

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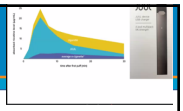
Electronic Cigarette Dependence



Penn State Electronic Cigarette Dependence Index

Roswell ENDS Nicotine Dependence Scale (Roswell eND Scale)

1. Do you vape more frequently during the first few hours after awakening than during the rest of the day?
   a. Yes < 1 >
   b. No < 0 >
2. How soon after you wake up do you vape?
   a. 0 – 5 m < 3 >
   b. 6 – 30 m < 2 >
   c. 31 – 60 m < 1 >
   d. 61+ m < 0 >
3. Of all the times that you vape, which time would you hate most to give up?
   a. 1st of Day < 1 >
   b. All Others < 0 >
4. How many pods, cartridges, or refills do you typically use each week?
   a. Less than 1 per week < 0 >
   b. 1 – 4 per week < 1 >
   c. 5 or more per weeks < 2 >
5. How often do you vape?
   a. 1 day or less each week < 0 >
   b. 2 – 3 days each week < 1 >
   c. 4 – 6 days each week < 2 >
   d. 7 days each week < 3 >

Score 0-10

Each JUUL pod (5.0% strength nicotine salt) contains ~ 40 mg of nicotine

Each pod ~20 cigarettes (200 puffs)

4 cartridges/ week (estimated to be equivalent of 12 cigs/day)

Sheffer et al., Drug Alc Dep, 2023

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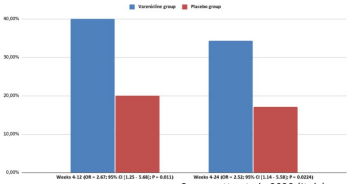
Quitting E Cigs

- Varenicline 1BID vs Pl (both counseling)
- DB-PC; N=140; motivated to stop ecigs



Caponnetto et al., 2023 (Italy)

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Cytisine for Ecig Cessation

N=160

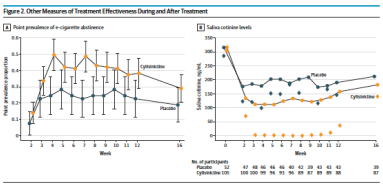
Vape nicotine daily, no cigs, wanting to quit

3mg TID for 12 weeks

QD 7-14 days after starting med

Behavioral support

No serious adverse events



Rigotti et al., JAMA Int Med, 2024

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Conclusions

- More cannabis co-use
- Combination NRT or varenicline as first line treatments
- Medications for those not immediately ready to quit/ Reduce to quit
- Reduced risk/ HR products

LungMindAlliance.org

Free Resources/ Technical Assistance

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