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Cytisine in Tobacco Dependence Treatment

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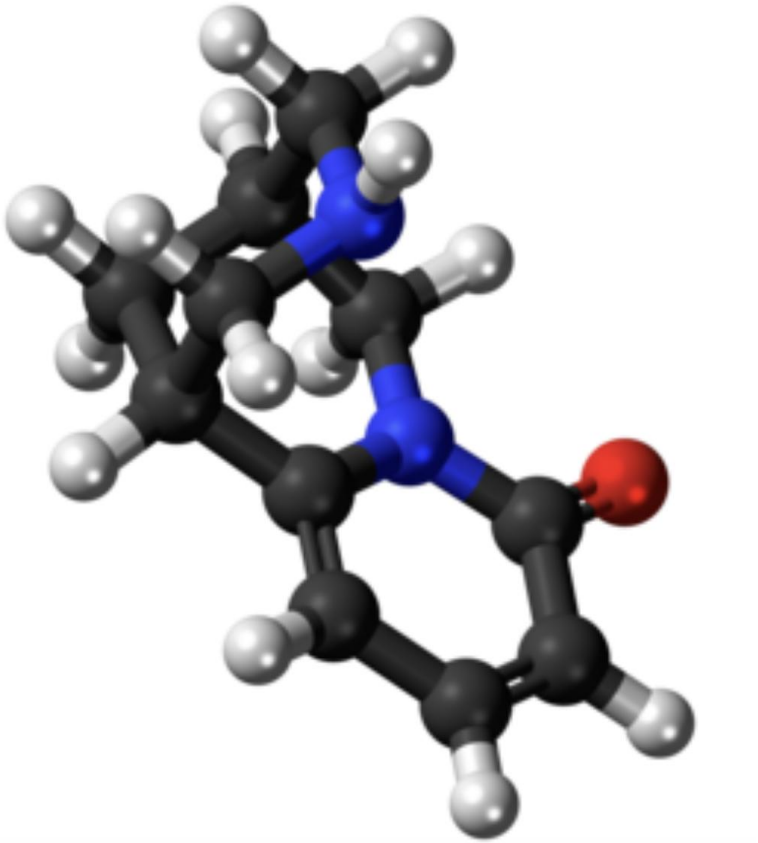

Cytisine Molecule. Image by Jynto, CC0, via Wikimedia Commons (https://commons.wikimedia.org/wiki/File:Cytisine_3D_ball.png)

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Disclosures

- None

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Learning Objectives

- Describe the mechanism of cytisine (cytisinicline)
- Summarize the clinical trial evidence comparing cytisine with NRT & varenicline
- Identify adverse effects and dosing regimens
- Discuss use in special populations (psychiatric illness, pregnancy, COPD)

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Pre-Test Questions

- Cytisine is a:
  A) Full agonist B) Partial agonist
  C) Dopamine reuptake inhibitor
- Most frequent adverse effects:
  A) Rash/anaphylaxis
  B) GI upset and sleep disturbance
  C) Hyponatremia
- Standard regimen length:
  A) 7 d B) 14 d C) 25 d

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Current Landscape

- 6 FDA-approved medications for tobacco treatment
- Varenicline the most effective
  - Expensive if not covered by insurance
  - Nausea, dreams can limit the uptake of the medication
- Having a wide variety of medications improves access for all

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Pharmacotherapy

Nicotine Replacement Therapy (NRT)

- **Any NRT product:** 133 trials, ~65K participants.

→ RR = 1.55 (1.49–1.61), **High** certainty.

- **Forms:** Patch (1.64 RR), Lozenge (1.52), Gum (1.49), Inhaler (1.90), Nasal spray (2.02), Mouth spray (2.48).

→ All show clear benefit.

Other Pharmacotherapies

- **Varenicline:** RR = 2.24 (2.06–2.43), **High** certainty.
- **Bupropion SR:** RR = 1.64 (1.52–1.77), **High** certainty.
- **Combination Pharmacotherapies:**
  - Short + long-acting NRT → RR = 1.25 (1.15–1.36).
  - Bupropion + NRT → RR = 1.19 (0.94–1.51).
  - Varenicline + NRT → RR ≈ 1.62–2.05 .
  - **Certainty:** Moderate

Behavioral therapy + pharmacotherapy: RR = 1.15 (1.08–1.22), **High** certainty.

Combined behavioral + pharmacological vs. brief advice: RR = 1.83 (1.68–1.98), **High** certainty.

Table 1. Evidence-Based Treatments for Cigarette Smoking Cessation

Source	Treatment	No. Trials[b]	Participants	No. quit/study population total (%)[a] Intervention	Control	RR (95% CI) for ≥6-mo cessation	Certainty of the estimate of benefit
Pharmacotherapy							
Hartmann-Boyce et al,[21] 2018	Any NRT product	133	64 640	5574/32 918 (17)	3315/31 722 (10)	1.55 (1.49-1.61)	High
	Nicotine						
	Patch	51	22 581			1.64 (1.53-1.75)	
	Lozenge	8	4439			1.52 (1.32-1.74)	
	Gum	56	25 754			1.49 (1.40-1.60)	
	Inhaler	4	976			1.90 (1.36-2.67)	
	Nasal spray	4	887			2.02 (1.49-2.73)	
	Mouth spray[c]	1	479			2.48 (1.24-4.94)	
Cahill et al,[22] 2016	Varenicline	27	12 625	1695/6632 (26)	668/5993 (11)	2.24 (2.06-2.43)	High
Cahill et al,[22] 2016	Cytisine[c]	2	937	40/470 (8)	10/467 (2)	3.98 (2.01-7.87)	Low
Howes et al,[23] 2020	Bupropion SR	45	17 866	1846/9714 (19)	900/8152 (11)	1.64 (1.52-1.77)	High
Lindson et al,[24] 2019	Short- + long-acting NRT	14	11 356	881/5218 (16)	852/6138 (13)	1.25 (1.15-1.36) vs single form	High
Howes et al,[23] 2020	Bupropion + NRT	12	3487	360/1648 (21)	342/1839 (18), NRT only	1.19 (0.94-1.51) vs NRT only	Low
Chang et al,[25] 2015	Varenicline + NRT[d]	2	787	NA	NA	OR, 1.62 (1.18-2.23) vs varenicline only; OR, 2.05 (0.82-5.17) vs varenicline from network meta-analysis	Low
Howes et al,[23] 2020	Varenicline + bupropion	3	1057	136/525 (26)	114/532 (21), Varenicline alone	1.21 (0.95-1.55) vs varenicline	Moderate
Electronic nicotine delivery systems							
Hartmann-Boyce et al,[26] 2021	e-Cigarettes with nicotine	4 vs NRT	1924	183/1032 (18)	92/892 (10) NRT	1.53 (1.21-1.93) vs NRT	Moderate (vs NRT)
		5 vs nonnicotine	1447	75/947 (8)	22/500 (4) Nonnicotine	1.94 (1.21-3.13) vs nonnicotine e-cigarettes	Moderate (vs nonnicotine)
		6 vs no support	2886	38/1649 (2)	13/1237 (1) No support	2.61 (1.44-4.74) vs no support	Very low (vs non support)
Behavioral therapies							
Stead et al,[27] 2013	Physician brief advice	17	13 724	455/7913 (6)	216/5811 (4)	1.66 (1.42-1.94) vs minimal intervention	Moderate
Stead et al,[27] 2013	Physician brief counseling	11	8515	553/4670 (11)	246/3845 (6)	1.86 (1.60-2.15) vs no intervention	Moderate
Rice et al,[28] 2017	Nurse-delivered counseling	44	20 881	1607/11 319 (14)	1165/9562 (12)	1.29 (1.21-1.38)	Moderate
Hartmann-Boyce et al,[29] 2021; Livingstone-Banks et al,[30] 2019	Printed self-help materials						
	Nontailored	11	13 241	416/6723 (6)	331/6518 (5)	1.19 (1.03-1.37)	Moderate
	Tailored	10	14 359	501/6786 (7)	455/7573 (6)	1.34 (1.19-1.51)	
Hartmann-Boyce et al,[29] 2021; Matkin et al,[31] 2019	Telephone counseling						
	Quit line	14	32 484	2123/19 600 (11)	1004/12884 (8)	1.38 (1.19-1.61)	Moderate
	Nonquit line	65	41 233	2924/21 001 (14)	2229/20 232 (11)	1.25 (1.15-1.35)	
Tzelepis et al,[32] 2019	Real-time video counseling	2	608	30/301 (10)	22/307 (7)	2.15 (0.38-12.04) vs telephone counseling	Very low
Hartmann-Boyce et al,[29] 2021; Stead et al,[33] 2017	Group counseling (in person)	13					
			4395	239/2388 (10)	116/2007 (6)	1.88 (1.52-2.33) vs self-help	
			7601	547/4815 (11)	196/2471 (8)	1.22 (1.03-1.43) vs brief advice	Moderate
			1098	119/623 (19)	32/475 (7)	2.60 (1.80-3.76) vs no intervention	
Hartmann-Boyce et al,[29] 2021; Lancaster and Stead,[34] 2017	Individual counseling (in-person +/- telephone follow-up)	27	11 100	604/5519 (11)	392/5581 (7)	1.57 (1.40-1.77)	High
Lindson et al,[35] 2019	Motivational interviewing	4	684	73/367 (20)	71/317 (22)	0.84 (0.63-1.12)	Low
Hartmann-Boyce et al,[29] 2021; Whittaker et al,[36] 2019	Text messaging	13	14 133	694/7324 (9)	382/6809 (6)	1.54 (1.19-2.00)	Moderate
Hartmann-Boyce et al,[29] 2021; Whittaker et al,[36] 2019	Mobile phone apps	5	3079	111/1535 (7)	119/1544 (8)	1.00 (0.66-1.52)	Very low
Hartmann-Boyce et al,[29] 2021; Taylor et al,[37] 2017	Internet-based interventions						
	Adjunct to behavioral therapy	5	2334	164/1368 (12)	75/966 (8)	1.69 (1.30-2.18)	Moderate
	Without additional support	8	6786	516/4020 (13)	356/2766 (13)	1.15 (1.01-1.30)	
Notley et al,[38] 2019	Financial incentives[e]	30	20 097	1336/12 800 (10)	516/7260 (7)	1.49 (1.28-1.73)	High
Behavioral therapy plus pharmacotherapy							
Hartmann-Boyce et al,[19] 2019	Behavioral therapy as an adjunct to pharmacotherapy	65	23 331	2291/11 630 (20)	2006/11 701 (17)	1.15 (1.08-1.22) vs pharmacotherapy alone	High
Stead et al,[20] 2016	Combined behavioral + pharmacotherapy	52	19 488	1529/10 070 (15)	808/9418 (9)	1.83 (1.68-1.98) vs brief advice or usual care	High

Abbreviations: NA, not available; NRT, nicotine replacement therapy; OR, odds ratio; RR, risk ratio; SR, slow release.

[a] As calculated from Cochrane meta-analyses.

[b] Number of trials represents those included in relevant evidence synthesis and comparison is to placebo or minimal control unless stated otherwise.

[c] Not approved by the US Food and Drug Administration as smoking cessation medication.

[d] No published reviews include RR calculation for this combination.

[e] Cash payments, vouchers, or return of money deposited by participants.

Rigotti NA, Kruse GR, Livingstone-Banks J, Hartmann-Boyce J. Treatment of Tobacco Smoking: A Review. JAMA. 2022;327(6):566–577. doi:10.1001/jama.2022.0395

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Cytisine

- Cytisine: plant-derived alkaloid from *Cytisus laburnum*
- Partial agonist at α4β2 nicotinic acetylcholine receptors (nAChRs)
- Competes with nicotine for α4β2 binding sites

- Achieve Life Sciences called this drug Cytisinicline for US trials

West R et al. *N Engl J Med*. 2011;365(13):1193–200
Laburnum anagyroides (syn. Cytisus laburnum). (n.d.). Adobe. https://stock.adobe.com/images/laburnum-anagyroides-syn-cytisus-laburnum-the-common-laburnum-golden-chain-or-golden-rain-it-is-native-to-central-and-southern-europe/503474102

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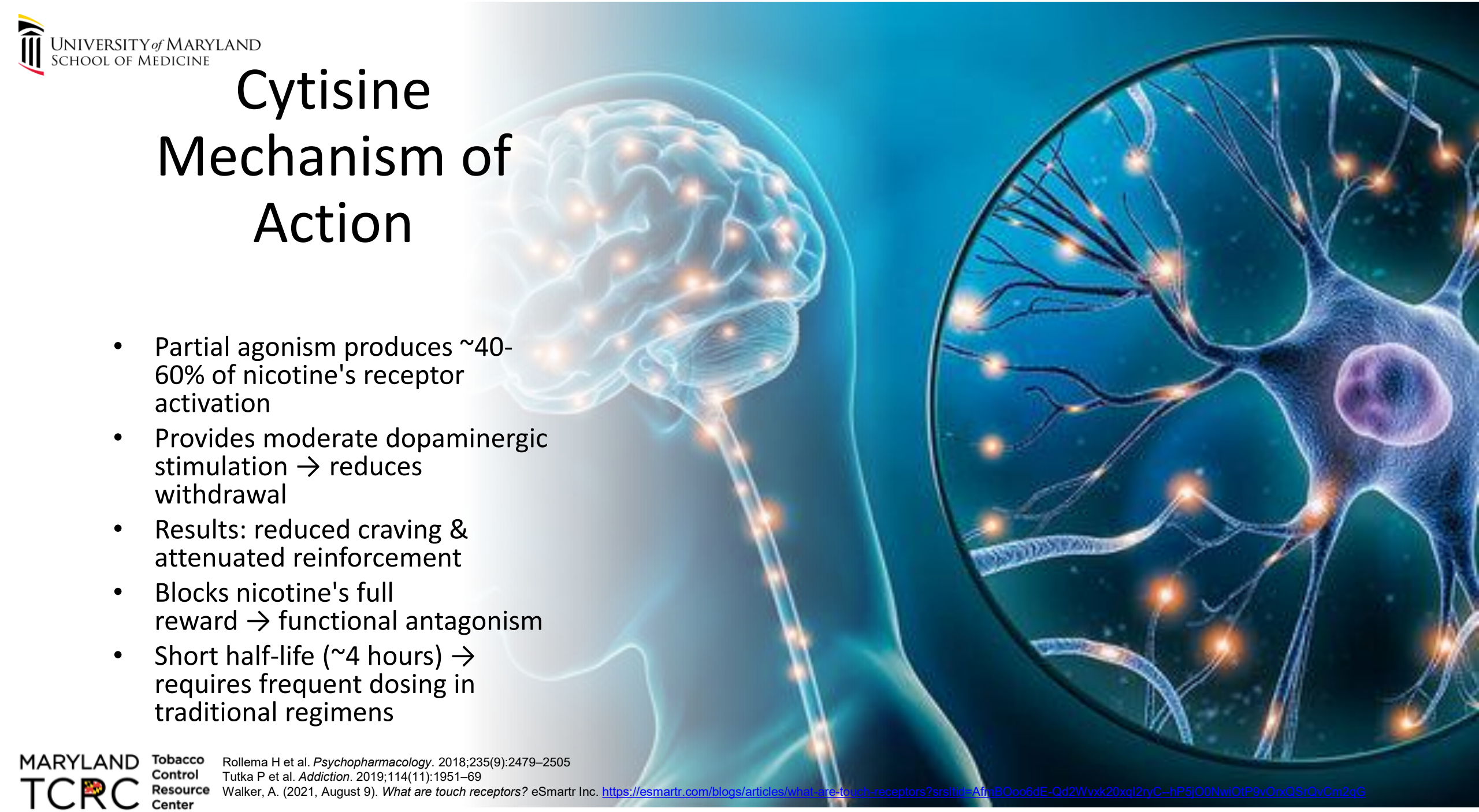
Cytisine Mechanism of Action



- Partial agonism produces ~40-60% of nicotine's receptor activation
- Provides moderate dopaminergic stimulation → reduces withdrawal
- Results: reduced craving & attenuated reinforcement
- Blocks nicotine's full reward → functional antagonism
- Short half-life (~4 hours) → requires frequent dosing in traditional regimens

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Rollema H et al. *Psychopharmacology*. 2018;235(9):2479–2505
Tutka P et al. *Addiction*. 2019;114(11):1951–69
Walker, A. (2021, August 9). *What are touch receptors?* eSmartr Inc. https://esmartr.com/blogs/articles/what-are-touch-receptors?srsltid=AfmBOoo6dE-Qd2Wvxk20xqI2ryC--hP5jO0NwjOtP9vOrxQSrQvCm2qG

Comparative Pharmacology

Feature	Cytistine	Cytisinicline	Varenicline
Receptor	α4β2 partial agonist	α4β2 partial agonist	α4β2 partial agonist
Half-Life (h)	4	6-8	24
Metabolism	Minimal hepatic	Minimal hepatic	Renal
Course Length (weeks)	3.5	6-12	12
Cost (USD)	<30	Expected 100-200	>400

Pfizer Chantix PI 2024
Rigotti NA et al. *JAMA*. 2023;330(2):152–160
Tutka P et al. *Addiction*. 2019;114(11):1951–69

EVIDENCE BASE (EARLY EFFICACY)

West et al., NEJM 2011 RCT

- Design/pop: double-blind RCT (740 smokers, Poland)
- Intervention: Cytisine 25-day course + brief counseling
- Comparator: placebo + counseling
- Primary outcome: 12-month continuous abstinence
- Results: 8.4 % vs 2.4 % ($p < 0.001$); RR 3.4 (95 % CI 1.9–6.3)
- Adverse Events: GI symptoms 10%; no serious AEs difference
- Conclusion: Cytisine tripled long-term quit rates vs placebo

West R et al. *N Engl J Med*. 2011;365(13):1193–200

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Cytisine versus Nicotine for Smoking Cessation.

1310 adult daily smokers with 25-day course of Cytisine / 8 weeks of NRT and low-intensity telephone behavioral support.

Primary outcome :self-reported continuous abstinence at 1 month

Secondary outcomes : abstinence at later time points and adverse events.

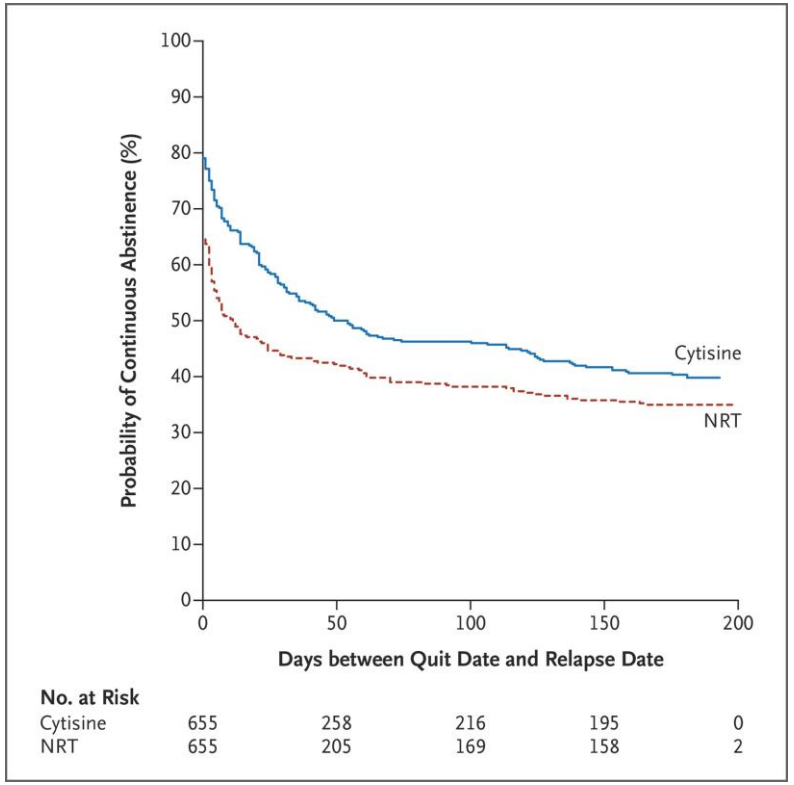
Cytisine demonstrated superior effectiveness over NRT for continuous smoking cessation: at 1 month,

40% of cytisine recipients vs. 31% in the NRT group (risk difference 9.3 percentage points, 95% CI 4.2–14.5).

Persisted at 1 week, 2 months, and 6 months.

Median time to relapse of 53 days (Cytisine) vs. 11 days for NRT.

Adverse events were more frequent with cytisine (primarily nausea, vomiting, and sleep disorders, generally mild to moderate).



Conclusion: Cytisine superior to NRT for 1- and 6-month abstinence; NNT ≈ 11

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Walker N, Howe C, Glover M, McRobbie H, Barnes J, Nosa V, Parag V, Bassett B, Bullen C. Cytisine versus nicotine for smoking cessation. N Engl J Med. 2014 Dec 18;371(25):2353-62. doi: 10.1056/NEJMoa1407764. PMID: 25517706.

ORCA 2 TRIAL

JAMA

QUESTION Is cytisinicline an effective and safe pharmacotherapy to promote smoking cessation?

CONCLUSION This randomized clinical trial found that 2 cytisinicline schedules, with behavioral support, vs placebo demonstrated smoking cessation efficacy and excellent tolerability.

POPULATION

442 Women
368 Men

Adults ≥18 years who smoked 10 or more cigarettes per day, had expired air carbon monoxide ≥10 ppm, and were ready to quit

Mean age: 52.5 years

LOCATIONS

17
Sites in the US

INTERVENTION

810 Participants randomized
618 Participants completed trial

270 Cytisinicline for 12 weeks
Cytisinicline, 3 mg, 3 times daily for 12 weeks plus behavioral support

269 Cytisinicline for 6 weeks
Cytisinicline, 3 mg, 3 times daily for 6 weeks then placebo 3 times daily for 6 weeks plus behavioral support

271 Placebo
Placebo 3 times daily for 12 weeks plus behavioral support

PRIMARY OUTCOME

Biochemically confirmed continuous smoking abstinence during the last 4 weeks of the 6-week treatment and the last 4 weeks of the 12-week treatment

FINDINGS

Biochemically confirmed continuous smoking abstinence

	Cytisinicline for 12 weeks	Cytisinicline for 6 weeks	Placebo
Weeks 3-6	22.2% (60/270)	25.3% (68/269)	4.4% (12/271)
Weeks 9-12	32.6% (88/270)	22.3% (60/269)	7.0% (19/271)

Cytisinicline for 6 weeks vs placebo:
Odds ratio, 8.0 (95% CI, 3.9-16.3)

Cytisinicline for 12 weeks vs placebo:
Odds ratio, 6.3 (95% CI, 3.7-11.6)

Rigotti NA, Benowitz NL, Prochaska J, et al. Cytisinicline for smoking cessation: a randomized clinical trial. *JAMA*. Published July 11, 2023. doi:10.1001/jama.2023.10042

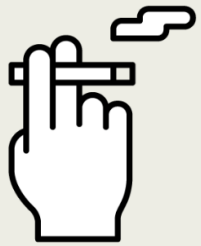
JAMA Internal Medicine

ORCA 3 Trial

RCT: Cytisinicline for Smoking Cessation

POPULATION

439 Females, 353 Males



Adults who smoked ≥10 cigarettes daily and were ready to quit

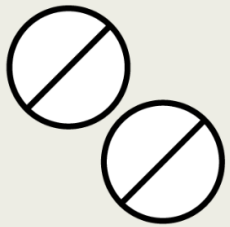
Mean age, 52 y

SETTINGS / LOCATIONS

20 Clinical sites in the US

INTERVENTION

792 Participants randomized



264 Cytisinicline for 12 wk
Cytisinicline, 3 mg, 3 times daily for 12 wk plus behavioral support

263 Cytisinicline for 6 wk
Cytisinicline, 3 mg, 3 times daily for 6 wk then placebo 3 times daily for 6 wk plus behavioral support

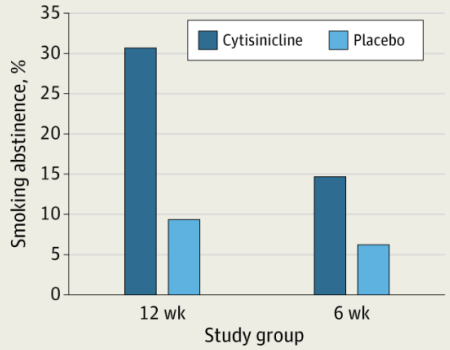
265 Placebo
Placebo 3 times daily for 12 wk plus behavioral support

PRIMARY OUTCOME

Biochemically confirmed continuous smoking abstinence during the last 4 wk of the 6-wk and 12-wk treatments

FINDINGS

Biochemically confirmed continuous smoking abstinence was significantly higher for both cytisnicline groups compared with the placebo group



Smoking abstinence in the 12-wk treatment
Cytisinicline: 30.3%
Placebo: 9.4%
Odds ratio, 4.4; 95% CI, 2.6-7.3; *P* < .001

Smoking abstinence in the 6-wk treatment
Cytisinicline: 14.8%
Placebo: 6.0%
Odds ratio, 2.9; 95% CI, 1.5-5.6; *P* < .001

Rigotti NA, Benowitz NL, Prochaska JJ, et al. Cytisinicline for smoking cessation: the ORCA phase 3 replication randomized clinical trial. *JAMA Intern Med.* Published online April 21, 2025. doi:10.1001/jamainternmed.2025.0628

Cytisine VS, Varenicline for Tobacco Treatment

JAMA Network

QUESTION Is cytisine noninferior to varenicline regarding smoking cessation?

CONCLUSION The clinical trial findings failed to demonstrate noninferiority of cytisine compared with varenicline regarding smoking cessation in adult daily smokers.

POPULATION

742 Women
710 Men

Adult daily smokers willing to make a quit attempt

Mean age: 43 years

LOCATIONS

Australia

INTERVENTION

1452 Patients randomized
1108 Patients completed final follow-up

725

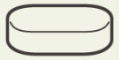
Cytisine

1.5-mg capsules taken 6 times daily initially, then reduced over 25-day course

727

Varenicline

0.5-mg tablets titrated to 1 mg twice daily for 12 weeks



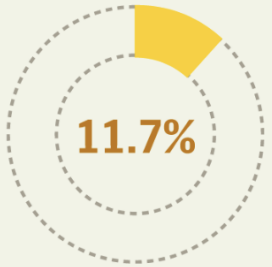
PRIMARY OUTCOME

6-month continuous abstinence verified using carbon monoxide breath test at 7-month follow-up, and noninferiority set at 5%

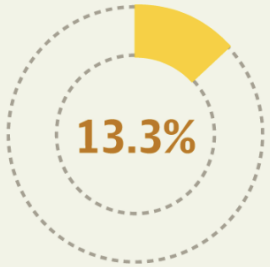
FINDINGS

6-month biochemically verified continuous abstinence rate

Cytisine
85 of 725 patients



Varenicline
97 of 727 patients



Cytisine was not noninferior to varenicline:

between-group difference, **−1.62%**
(1-sided 97.5% CI, −5.02% to ∞)

Courtney RJ, McRobbie H, Tutka P, et al. Effect of cytisine vs varenicline on smoking cessation: a randomized clinical trial. *JAMA*. Published July 6, 2021. doi:10.1001/jama.2021.7621

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Cytisine vs. Varenicline in Primary Care (Croatia & Slovenia)

- Randomized, open-label, non-inferiority trial, conducted across multiple primary care centers in Europe
    - Adult smokers motivated to quit N = 377 participants: 186 assigned to Cytisine, 191 to varenicline
- Intervention:
    - Cytisine group: 25 days of cytisine treatment vs. Varenicline group: 12 weeks of varenicline treatment
    - All participants received behavioral support
- Primary End point: Continuous abstinence from smoking at 24 weeks, biochemically verified (e.g., via exhaled CO or cotinine).
- 24-week (≈6-month) abstinence rate:
  - Varenicline group: **62/191 = 32.46%**
  - Cytisine group: **43/186 = 23.12%**
  - Odds ratio (Cytisine vs varenicline): **OR = 0.63** (95% credible interval [CI]: 0.39 to 0.98)
- Adherence:
  - Varenicline group: 113/191 = **59.16%** adhered (≥80%)
  - Cytisine group: 131/186 = **70.43%** adhered
  - OR for adherence (Cytisine vs varenicline) = **1.65** (95% CI: 1.07 to 2.56)
  - **Participants assigned to Cytisine had fewer total adverse-events compared to varenicline: incidence rate ratio (IRR) = 0.59 (95% CI: 0.43 to 0.81)**

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Oreskovic T, Percac-Lima S, Ashburner JM, Tiljak H, Rifel J, Klemenc Ketiš Z, Oreskovic S. Cytisine Versus Varenicline for Smoking Cessation in a Primary Care Setting: A Randomized Non-inferiority Trial. Nicotine Tob Res. 2023 Aug 19;25(9):1547-1555. doi: 10.1093/ntr/ntad065. Erratum in: Nicotine Tob Res. 2024 May 22;26(6):792. doi: 10.1093/ntr/ntae015. PMID: 37291049.

Meta-Analysis	Comparator(s)	Pooled RR (95% CI)	Interpretation
Cochrane 2023 (Livingstone-Banks et al.)	Placebo	2.25 (1.79-2.82)	Significant benefit to placebo
Addiction 2024 (Puljević et al.)	NRT	1.32 (1.05-1.67)	Cytisine superior to NRT
Network 2024 (Ofori et al.)	Varenicline	0.94 (0.78-1.14)	Comparable efficacy

Livingstone-Banks J, Hartmann-Boyce J, Walker N, et al. *Cochrane Database Syst Rev*. 2023;5:CD006103.
Ofori S, et al. *Drug Alcohol Depend*. 2023;251:110936.
Puljević C, Sankaranarayanan A, et al. *Addiction*. 2024;119(10):1713-1725.

DOSING & ADMINISTRATION

Day Range	Dosage Schedule
1-3	1 tab (1.5 mg) q2 h ≈ 6 tabs/day
4-12	1 tab q2.5 h ≈ 5 tabs/day
13-16	1 tab q3 h ≈ 4 tabs/day
17-20	1 tab q4–5 h ≈ 3 tabs/day
21-25	1–2 tabs daily

Parameter	Cytisinicline (ACHL-490)
Dose	3 mg TID (6 weeks) ± extend to 12 weeks
Initiation	Set quit date within 1 week of start
Formulation	Standardized synthetic API
Adherence	>90% in ORCA-3 trial
Key Advantage	Simplified schedule vs 25-day taper

- **Standard Cytisine Regimen (25 days)**
- **Start 5 days before quit date; max 25 days course**

Cytisinicline Modern Dosing (ORCA Protocol)

Tutka P et al. *Addiction*. 2019;114(11):1951-69

SAFETY & TOLERABILITY

Adverse Events Profile

Event	Cytisine %	Comparator %
Nausea	8-13	25 (varenicline)
Sleep Disturbance / Dreams	5-8	18 (varenicline)
GI Upset	10	9 (placebo/NRT)
Headache	6	6 (placebo)
Serious AEs	<1	<1

- **Comparable to placebo/NRT; better tolerability than varenicline**

Tutka P et al. *Addiction*. 2019;114(11):1951-69

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Discontinuations and Contraindications

- Discontinuation for AEs: <5% (all trials)
- Main reasons: nausea, insomnia, GI upset
- No cardiovascular or neuropsychiatric signal detected
- Contraindications: hypersensitivity to cytisine; use caution in severe renal impairment

Courtney RJ, McRobbie H, Tonkin A, et al. *JAMA*. 2021;326(1):56-64
FDA NDA Briefing Doc 2025
Rigotti NA et al. *JAMA*. 2023;330(2):152–160

SPECIAL POPULATIONS

Safety in Special Groups (Overview)

Pharmacokinetic stability across age groups; no dose adjustment needed.
Safe in mild–moderate renal impairment (GFR > 30 mL/min).
Low CNS penetration → reduced dizziness, confusion risk in elders.

- Psychiatric comorbidity: No increased AEs vs control (ORCA-3 subgroup)
- Cardiac Disease: No hemodynamic changes reported
- Pregnancy/Lactation: Insufficient data – avoid unless risk > benefit
- COPD/Asthma: Improved quit success vs placebo (secondary analysis)
- Older Adults: Well tolerated; no dose adjustment required
- No human RCTs of cytisine in pregnancy
- Animal data show no teratogenicity at therapeutic doses
- WHO and ACOG: NRT preferred; cytisine not contraindicated but insufficient data
- Breastfeeding: limited excretion; avoid unless necessary

Rigotti NA et al. *JAMA*. 2023;330(2):152–160
Livingstone-Banks J, Hartmann-Boyce J, Walker N, et al. *Cochrane Database Syst Rev*. 2023;5:CD006103
Tutka P et al. *Addiction*. 2019;114(11):1951-69

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REGULATORY & GLOBAL ACCESS

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AB Posters. (n.d.). *Planet Earth with clouds: Europe and part of Asia and Africa [Photograph].* https://www.abposters.com/planet-earth-with-clouds-europe-and-part-of-asia-and-africa-pianeta-terra-con-f130242519?srsltid=AfmBOor7t0bzuW8GW-W4cqhDrAXUQjX5X2pQzMMXBA7q8Lus-agkLYZv

Europe and UK

REGION	STATUS	NOTES
Eastern Europe	OTC for >50 years	Legacy formulation (Tabex®)
EU (EMA)	Not centrally approved	Country-level sales permitted
UK (MHRA)	Licensed 2019; launched 2024	Prescription-only

UK MHRA Press Release 2019; Market Launch 2024.
WHO Model List of Essential Medicines, 2025.

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WHO Model List of Essential Medicines (2025)

- Added to WHO EML (23rd List, 2025).
- Recognized as effective, low-cost, and globally scalable cessation therapy.
- Enables international procurement by LMICs.
- Marks first addition of a new pharmacotherapy for tobacco dependence since varenicline (2006).

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World Health Organization. *Model List of Essential Medicines*, 23rd Edition, 2025.
https://www.emro.who.int/health-topics/essential-medicines/

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United States (FDA Status)

- FDA accepted NDA for cytisinicline (Achieve Life Sciences) — Sept 2025.
- **PDUFA target date:** June 20, 2026.
- Proposed trade name: *Cytisinicline™*.
- Expected indication: “Aid to smoking cessation in adults.”
- Postmarketing pharmacovigilance plan submitted to FDA.

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FDA Center for Drug Evaluation and Research. NDA 216987, Cytisinicline. September 2025.
https://www.nbcnews.com/storyline/smart-facts/what-fda-n957886
The Food and Drug Administration campus in Silver Spring, Maryland on Oct. 14, 2015. (2019, January 18). NBC News.
https://www.nbcnews.com/storyline/smart-facts/what-fda-n957886

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CLINICAL INTEGRATION & IMPLEMENTATION

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Integration with Behavioral Support

- Cytisine and cytisinicline effective alone but enhanced with behavioral interventions.
- Brief motivational interviewing + pharmacotherapy yields 2–3× higher quit odds.
- Ideal for primary care, pharmacy-based, or telehealth models.
- Cost-effectiveness supports use in resource-limited settings.

Livingstone-Banks J et al. *Cochrane Database Syst Rev*. 2023;5:CD006103
Ofori S et al. *Drug Alcohol Depend*. 2023;251:110936
Puljević C et al. *Addiction*. 2024;119(10):1713–25
The 4 Processes of Motivational Interviewing. (2022, November 1). PsychCentral. https://psychcentral.com/pro/the-four-processes-of-motivational-interviewing

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Future Directions

- FDA approval of cytisinicline anticipated 2026 → US market entry.
- Combination studies underway (cytisine + NRT patch).
- Trials in pregnancy, COPD, and indigenous populations ongoing (ANZCTR 2025).
- Expansion to e-cigarette cessation expected.

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Achieve Life Sciences. *ClinicalTrials.gov* Identifier: NCT05652519.
WHO EML 2025.

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Key Takeaways

Cytisine and cytisinicline: effective, safe, and affordable first-line cessation therapies.

Comparable to varenicline, superior to NRT, excellent tolerability.

Increasing global recognition: UK, Australia, Canada, pending FDA.

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Rigotti NA et al. *JAMA*. 2023;330(2):152–160
Walker N et al. *N Engl J Med*. 2014;371(25):2353–62
WHO Model List of Essential Medicines, 2025

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Post-Test Questions

- Cytisine is a:
  A) Full agonist B) Partial agonist
  C) Dopamine reuptake inhibitor
- Most frequent adverse effects:
  A) Rash/anaphylaxis
  B) GI upset and sleep disturbance
  C) Hyponatremia
- Standard regimen length:
  A) 7 d B) 14 d C) 25 d

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Post-Test Answers

- Cytisine is a: B) Partial agonist
- Most frequent adverse effects: B) GI upset and sleep disturbance
- Standard regimen length: C) 25 d

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How Marylanders Access Quitline Services

Phone

(800) QUIT-NOW (800) 784-8669
(855) DEJELO-YA
Asian Smokers Quitline- https://www.asiansmokersquitline.org
TTY(711) line for deaf and hard of hearing callers
We offer interpretation services into over 300 languages.

Web

Callers can enroll at quitnow.net/Maryland

Referral

Tobacco users may be referred from their health provider, which triggers an outbound call
We support fax referrals, e-referrals, online referrals and referrals via secure email

Text to Enroll

Marylanders can text “READY” to 34191 to enroll

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Maryland DEPARTMENT OF HEALTH

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UMMC Nicotine Health Clinic

- Director: pulmonologist Dr. Janaki Deepak
- Clinic integrated w/ pulmonary clinic - comprehensive lung health exam
- Lung Cancer Screening
- Free sample meds
- Combination med therapies + coaching
- Most insurances accepted, no referral needed
- Appointments: call 410-328-8141 or email Sherri Webster: SWebster@som.umaryland.edu

UMMC NHC is located at the Midtown Campus:
800 Linden Ave, 9th Floor, Baltimore, MD 21201

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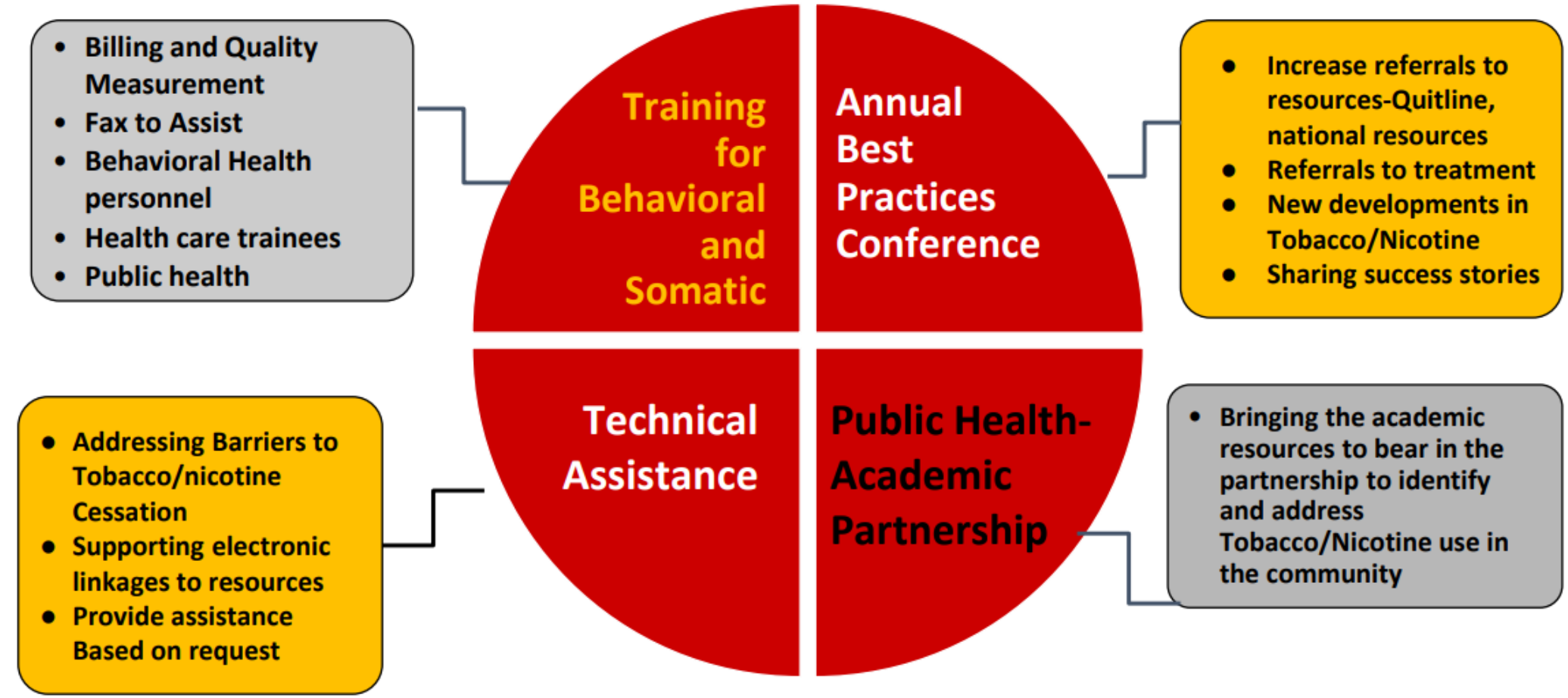
Maryland Tobacco Control Resource Center Activities



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Thank you!

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