



“FARMACI PER IL TABAGISMO: IL TRATTAMENTO EVIDENCE-BASED DEL TABAGISMO”

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TRATTAMENTO FARMACOLOGICO DEL DISTURBO DA USO DI TABACCO

EFFICACIA

Quanto funziona?



CERTEZZA

Quanto ci possiamo
fidare dell'evidenza?



NRT

Terapia sostitutiva
nicotinica



VARENICLINA

Agonista parziale
 $\alpha 4 \beta 2$ nicotinico



CITISINA

Agonista parziale
 $\alpha 4 \beta 2$ nicotinico



BUPROPIONE

Antidepressivo –
modulazione
dopamina/noradrenalina



WHO 2024

WHO Clinical Treatment Guideline for Tobacco Cessation in Adults – 2024

L'OMS raccomanda vareniclina, NRT, bupropione e citisina
come trattamenti farmacologici efficaci per la **cessazione del fumo di tabacco**.



Esiste una gerarchia di efficacia pur essendo tutti trattamenti efficaci?

FOCUS DELLA NOSTRA ANALISI

Efficacia nelle principali **MONOTERAPIE** nella popolazione generale
(in assenza di comorbidità note)

EVIDENZA CONSOLIDATA

Shang et al., 2022

Frontiers in Pharmacology

Network meta-analysis di 159 studi
(60.285 fumatori), 15 interventi farmacologici

*Focus selezionato: confronto tra le principali
monoterapie farmacologiche*

- Vareniclina vs NRT in monoterapia:
OR 1,42 (IC 95% 1,16–1,73)
- Vareniclina vs bupropione:
OR 1,52 (IC 95% 1,22–1,89)
- Bupropione vs NRT in monoterapia:
nessuna differenza statisticamente significativa

Tra queste monoterapie emerge
una maggiore efficacia relativa
della **VARENICLINA**

Evidenze
consolidate



integrazione con
le evidenze più
recenti sulla
CITISINA



INTEGRAZIONE CON LA CITISINA

Puljević et al., 2024

Addiction

Systematic review and meta-analysis
(14 RCT, 9.637 fumatori adulti)

- Citisina vs placebo: **RR 2,65**
- Citisina vs NRT: **RR 1,36**
- Citisina vs vareniclina: **RR 0,96**
(nessuna differenza statisticamente dimostrata)

La citisina amplia il quadro:
superiore a placebo e NRT,
senza differenza dimostrata
rispetto alla vareniclina



> Front Pharmacol. 2022 Oct 24;13:1012433. doi: 10.3389/fphar.2022.1012433. eCollection 2022.

Save

Pharmacological interventions on smoking cessation: A systematic review and network meta-analysis

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Ziyi Wang^{1 2 3}, Yanan Wu^{1 2 3}, Meng Xu^{1 2 3}, Chaoqun Yang^{1 2 3}, Xiuxia Li^{1 2 3},
Kehu Yang^{1 2 3}

Affiliations + expand

PMID: 36353488 PMCID: PMC9638092 DOI: 10.3389/fphar.2022.1012433

Abstract

Objective: A network meta-analysis based on randomized controlled trials was conducted to investigate the effects of pharmacological interventions on smoking cessation. **Methods:** English databases were searched to obtain randomized controlled trials reporting the effect of pharmacological interventions on smoking cessation. The risk of bias for the included trials was assessed using Cochrane Handbook tool. Stata 15.1 software was used to perform network meta-analysis, and GRADE approach was used to assess the evidence credibility on the effects of different interventions on smoking cessation. **Results:** A total of 159 studies involving 60,285 smokers were included in the network meta-analysis. The analysis involved 15 interventions and which yielded 105 pairs of comparisons. Network meta-analysis showed that varenicline was more helpful for smoking cessation than other monotherapies, such as nicotine replacement therapy [Odds Ratio (OR) = 1.42, 95% confidence interval (CI) (1.16, 1.73)] and bupropion [OR = 1.52, 95% CI (1.22, 1.89)]. Furthermore, combined interventions were superior to monotherapy in achieving smoking cessation, such as varenicline plus bupropion over bupropion [OR = 2.00, 95% CI (1.11, 3.61)], varenicline plus nicotine replacement therapy over nicotine replacement therapy [OR = 1.84, 95% CI (1.07, 3.18)] and nicotine replacement therapy plus mecamylamine over naltrexone [OR = 6.29, 95% CI (1.59, 24.90)]. Finally, the surface under the cumulative ranking curve value indicated that nicotine replacement therapy plus mecamylamine had the greatest probability of becoming the best intervention. **Conclusion:** Most pharmacological interventions demonstrated a benefit in smoking cessation compared with placebo, whether monotherapy or combination therapy. Moreover, confirmed evidence suggested that some combination treatments, such as varenicline plus bupropion and nicotine replacement therapy plus mecamylamine have a higher probability of being the best smoking cessation intervention.



Meta-Analysis > Addiction. 2024 Oct;119(10):1713-1725. doi: 10.1111/add.16592. Epub 2024 Jul 4.

Systematic review and meta-analyses of cytisine to support tobacco cessation

Cheneal Puljević¹, Daniel Stjepanović^{1 2}, Isabel Meciar¹, Heewon Kang^{1 3}, Gary Chan^{1 2},
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PMID: 38965792 DOI: [10.1111/add.16592](https://doi.org/10.1111/add.16592)

Abstract

Background and aims: Cytisine (also known as cytisinicline) is a low-cost partial agonist of nicotinic acetylcholine receptors used to assist tobacco cessation. We aimed to review the effectiveness of cytisine for tobacco cessation and the effects of dose and co-use of behavioural or other pharmacological interventions on cessation outcomes.

Methods: We searched seven databases, Google Scholar, and reference lists of included publications for randomised controlled trials investigating use of cytisine as a tobacco cessation aid. Studies were eligible if participants were ≥ 15 years old and used tobacco upon study enrolment. We conducted four random effects meta-analyses and sensitivity analyses with fixed effects models. We used the Cochrane risk-of-bias tool for randomised trials version 2 to assess risk of bias in included studies, with adjustments recommended by the Cochrane Tobacco Addiction Group.

Results: Participants using cytisine were significantly more likely to quit tobacco than participants who received placebo/no intervention/usual care (risk ratio [RR] = 2.65, 95% confidence interval [CI] = 1.50-4.67, 6 trials, 5194 participants) or nicotine replacement therapy (RR = 1.36, 95% CI = 1.06-1.73, $p = 0.0152$, 2 trials, 1511 participants). The difference in cessation rates among participants receiving cytisine versus varenicline was not statistically significant (RR = 0.96, 95% CI 0.63-1.45, $P = 0.8464$, 3 trials, 2508 participants). Two trials examined longer versus shorter treatment duration, finding higher abstinence rates with longer treatment (RR = 1.29, 95% CI = 1.02-1.63, 2 trials, 1009 participants). The differences in the number of adverse events reported by participants who received cytisine versus placebo (RR = 1.19, 95% CI = 0.99-1.41, $P = 0.0624$; 6 trials; 4578 participants) or cytisine versus varenicline (RR = 1.37, 95% CI = 0.57-3.33, $P = 0.4835$; 2 trials; 1345 participants), were not statistically significant. Most adverse events were mild (e.g. abnormal dreams, nausea, headaches).

Conclusions: Cytisine is an effective aid for tobacco cessation and appears to be more effective for tobacco cessation than placebo, no intervention, usual care and nicotine replacement therapy.



TERAPIE FARMACOLOGICHE COMBINATE: ESISTE UN VANTAGGIO RISPETTO ALLA MONOTERAPIA?

STRATEGIA	EFFICACIA (vs monoterapia)	CERTEZZA DELL'EVIDENZA (GRADE)
 NRT COMBINATA (cerotto + forma rapida) vs NRT singola	RR 1,25 (IC95% 1,15–1,36) 14 studi – 11.356 partecipanti	 ALTA
 BUPROPIONE + VARENICLINA vs vareniclina	RR 1,21 (IC95% 0,95–1,55) 3 studi – 1.057 partecipanti	 MODERATA
 BUPROPIONE + NRT vs NRT singola	RR 1,17 (IC95% 0,95–1,44) 15 studi – 4.117 partecipanti	 BASSA



**La NRT combinata rappresenta una strategia efficace;
bupropione + vareniclina o bupropione + NRT possono essere considerati
in caso di risposta inadeguata ai trattamenti di prima linea.**



FOCUS SULLE PRINCIPALI COMORBIDITÀ



**LE EVIDENZE DI EFFICACIA E SICUREZZA SONO TRASFERIBILI
ALLE PRINCIPALI SOTTOPOPOLAZIONI?**



PSICHIATRICA

- Rischio di riacutizzazione dei sintomi e interazioni farmacologiche
- Evidenze specifiche di efficacia e sicurezza
- Scelta del trattamento in base alla patologia e alla terapia psicofarmacologica in atto



CARDIOVASCOLARE

- Rischio cardiovascolare di base e indotto dal trattamento
- Impatto del trattamento e sulla prognosi cardiovascolare
- Evidenze comparative di sicurezza e raccomandazioni specifiche



PNEUMOLOGICA

- BPCO, asma e altre patologie respiratorie
- Effetto del trattamento sulla funzione polmonare e sulle riacutizzazioni
- Benefici clinici e sicurezza nella pratica quotidiana



**Obiettivo: identificare il trattamento farmacologico più efficace e sicuro per
massimizzare i tassi di cessazione del fumo e migliorare gli esiti clinici in ogni sottopopolazione.**

*L'EBM non è solo scegliere il trattamento più efficace,
ma scegliere il trattamento più appropriato per il paziente.*



TABAGISMO E COMORBIDITÀ PSICHIATRICA



**I trattamenti farmacologici per la cessazione
mantengono efficacia e sicurezza nei pazienti con disturbi psichiatrici?**



UNA POPOLAZIONE AD ALTA PRIORITÀ

- Prevalenza del fumo più elevata nei disturbi psichiatrici
- Maggiore intensità della dipendenza nicotinic
- Minori probabilità di cessazione spontanea



IL PROBLEMA CLINICO

- Elevato carico di comorbidità e polifarmacoterapia
- Possibili interazioni farmacologiche
- Necessità di considerare stabilità psicopatologica e trattamento concomitante



IL PROBLEMA DELLA SICUREZZA

- Storiche preoccupazioni sugli eventi neuropsichiatrici associati alla farmacoterapia
- Necessità di distinguere gli eventi correlati al trattamento da quelli associati alla patologia di base o al processo di cessazione

GOVERNARE LA COMPLESSITÀ

I SERVIZI PER LE DIPENDENZE TRA INDIRIZZI ISTITUZIONALI,
EVIDENZE CLINICHE E BISOGNI EMERGENTI



NAPOLI
14-15-16
OTTOBRE
2026

Hotel Royal Continental

FARMACI PER IL TABAGISMO: IL TRATTAMENTO EVIDENCE-BASED DEL TABAGISMO

Lancet. 2016 Jun 18;387(10037):2507-20. doi: 10.1016/S0140-6736(16)30272-0. Epub 2016 Apr 22.

Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial.

Antenelli RM¹, Benowitz NL², West R³, St Aubin L⁴, McRae T⁴, Lawrence D⁴, Ascher J⁵, Russ C⁴, Krishen A⁶, Evins AE⁷.

Author information

Abstract

BACKGROUND: Substantial concerns have been raised about the neuropsychiatric safety of the smoking cessation medications varenicline and bupropion. Their efficacy relative to nicotine patch largely relies on indirect comparisons, and there is limited information on safety and efficacy in smokers with psychiatric disorders. We compared the relative neuropsychiatric safety risk and efficacy of varenicline and bupropion with nicotine patch and placebo in smokers with and without psychiatric disorders.

METHODS: We did a randomised, double-blind, triple-dummy, placebo-controlled and active-controlled (nicotine patch; 21 mg per day with taper) trial of varenicline (1 mg twice a day) and bupropion (150 mg twice a day) for 12 weeks with 12-week non-treatment follow-up done at 140 centres (clinical trial centres, academic centres, and outpatient clinics) in 16 countries between Nov 30, 2011, and Jan 13, 2015. Participants were motivated-to-quit smokers with and without psychiatric disorders who received brief cessation counselling at each visit. Randomisation was computer generated (1:1:1:1 ratio). Participants, investigators, and research personnel were masked to treatment assignments. The primary endpoint was the incidence of a composite measure of moderate and severe neuropsychiatric adverse events. The main efficacy endpoint was biochemically confirmed continuous abstinence for weeks 9-12. All participants randomly assigned were included in the efficacy analysis and those who received treatment were included in the safety analysis. The trial is registered at ClinicalTrials.gov (number [NCT01456936](#)) and is now closed.

FINDINGS: 8144 participants were randomly assigned, 4116 to the psychiatric cohort (4074 included in the safety analysis) and 4028 to the non-psychiatric cohort (3984 included in the safety analysis). In the non-psychiatric cohort, 13 (1·3%) of 990 participants reported moderate and severe neuropsychiatric adverse events in the varenicline group, 22 (2·2%) of 989 in the bupropion group, 25 (2·5%) of 1006 in the nicotine patch group, and 24 (2·4%) of 999 in the placebo group. The varenicline-placebo and bupropion-placebo risk differences (RDs) for moderate and severe neuropsychiatric adverse events were -1·28 (95% CI -2·40 to -0·15) and -0·08 (-1·37 to 1·21), respectively; the RDs for comparisons with nicotine patch were -1·07 (-2·21 to 0·08) and 0·13 (-1·19 to 1·45), respectively. In the psychiatric cohort, moderate and severe neuropsychiatric adverse events were reported in 67 (6·5%) of 1026 participants in the varenicline group, 68 (6·7%) of 1017 in the bupropion group, 53 (5·2%) of 1016 in the nicotine patch group, and 50 (4·9%) of 1015 in the placebo group. The varenicline-placebo and bupropion-placebo RDs were 1·59 (95% CI -0·42 to 3·59) and 1·78 (-0·24 to 3·81), respectively; the RDs versus nicotine patch were 1·22 (-0·81 to 3·25) and 1·42 (-0·63 to 3·46), respectively. Varenicline-treated participants achieved higher abstinence rates than those on placebo (odds ratio [OR] 3·61, 95% CI 3·07 to 4·24), nicotine patch (1·68, 1·46 to 1·93), and bupropion (1·75, 1·52 to 2·01). Those on bupropion and nicotine patch achieved higher abstinence rates than those on placebo (OR 2·07 [1·75 to 2·45] and 2·15 [1·82 to 2·54], respectively). Across cohorts, the most frequent adverse events by treatment group were nausea (varenicline, 25% [511 of 2016 participants]), insomnia (bupropion, 12% [245 of 2006 participants]), abnormal dreams (nicotine patch, 12% [251 of 2022 participants]), and headache (placebo, 10% [199 of 2014 participants]). Efficacy treatment comparison did not differ by cohort.

INTERPRETATION: The study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo. Varenicline was more effective than placebo, nicotine patch, and bupropion in helping smokers achieve abstinence, whereas bupropion and nicotine patch were more effective than placebo.



Randomized Controlled Trial > [Addict Behav.](#) 2024 Dec;159:108148. doi: 10.1016/j.addbeh.2024.108148. Epub 2024 Aug 29.

Mental health related adverse events of cytisine and varenicline in smokers with and without mental health disorders: Secondary analysis of a randomized controlled trial

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Affiliations + expand

PMID: 39213816 DOI: [10.1016/j.addbeh.2024.108148](#)

Free article

Abstract

Introduction: Little is known about the adverse events (AEs) of cytisine versus varenicline among individuals with mental health disorders (MHDs), highlighting the necessity for further exploration to inform clinical practice. This secondary analysis of clinical trial data aimed to investigate the effect of varenicline vs. cytisine regarding mental-health-related AEs (MH-related AEs) on smokers with and without MHDs.

Methods: Australian daily smokers interested in quitting were randomised to varenicline (84 days) or cytisine (25 days) and categorised by self-reported MHD diagnosis or treatment in the past year (MHD or non-MHD groups). Treatment adherence was assessed by self-reported number of doses taken during the active treatment phase via two check-in calls (at one month), while AEs were evaluated through four phone interviews: two check-in calls (one month) and follow-up calls at four and seven months. Logistic regression analysis compared MH-related AEs between groups, including only participants taking at least one dose.

Results: Of 1452 smokers 246 reported MHDs, 725 received cytisine and 727 received varenicline. Median number of doses taken was comparable between MHD (34 cytisine and 12 varenicline) and non-MHD (33 cytisine and 13 varenicline) groups. MH-related AEs were: 14.1 % (n = 30) in MHD (12.5 % in cytisine and 15.4 % in varenicline), and 11.8 % (n = 126) in non-MHD group (10.9 % in cytisine and 13.7 % in varenicline). No significant difference in MH-related AE occurrence was identified between medication groups (aOR=0.96, 95 % CI 0.4 to 2.2, p-value = 0.94).

Conclusion: Comparable MH-related AEs were observed between smokers with and without MHDs, suggesting that cytisine, like varenicline, may be well-tolerated by those with MHDs. However, larger clinical trials focused on MH-related AEs are needed for more conclusive evidence.

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Keywords: Cytisine; Mental health; Neuropsychiatric adverse events; Smoking cessation; Varenicline.



TRATTAMENTO FARMACOLOGICO NEL PAZIENTE CARDIOVASCOLARE

PubMed

Efficacy and Safety of Smoking Cessation Interventions in Patients With Cardiovascular Disease: A Network Meta-Analysis of Randomized Controlled Trials

Karine Suissa et al. Circ Cardiovasc Qual Outcomes. 2017 Jan;10(1):e002458.

Abstract

Background: Smoking cessation reduces cardiovascular risk, but the comparative efficacy and safety of available pharmacotherapies in patients with cardiovascular disease (CVD) are uncertain.

Methods: We performed a systematic review and network meta-analysis of randomized controlled trials (RCTs) evaluating smoking cessation interventions in patients with established CVD. We searched MEDLINE, EMBASE, PsycINFO, PubMed, and the Cochrane Tobacco Addiction Specialized Register from inception to July 2015. RCTs were eligible if they included adult smokers with CVD and reported biochemically validated smoking abstinence at 6 or 12 months. We compared pharmacotherapies (varenicline, bupropion, nicotine replacement therapy [NRT]) using a random-effects network meta-analysis. Behavioral interventions were also evaluated but are not the focus here.

Results: Seven pharmacotherapy RCTs (n = 2809) met the inclusion criteria. Network meta-analysis showed greater abstinence than placebo with varenicline (RR 2.64; 95% CI 1.34–5.21) and bupropion (RR 1.42; 95% CI 1.01–2.01). Evidence for nicotine replacement therapy was inconclusive (RR 1.22; 95% CI 0.72–2.06). Results were consistent at both 6 and 12 months. No significant increase in serious cardiovascular adverse events was observed for any pharmacotherapy compared with placebo.

Conclusions: Varenicline and bupropion are effective and appear to be safe for smoking cessation in patients with cardiovascular disease, supporting their use in this high-risk population.

EFFICACIA

Astinenza vs placebo

VARENICLINA

RR 2,64

IC95% 1,34 – 5,21

BUPROPIONE

RR 1,42

IC95% 1,01 – 2,01

NRT

RR 1,22

IC95% 0,72 – 2,06 • inconclusivo

MESSAGGIO CHIAVE

**Vareniclina: maggiore efficacia stimata
nella popolazione cardiovascolare.**



CITISINA NEL PAZIENTE CARDIOVASCOLARE: QUALI EVIDENZE?

Clinical Study > Intern Emerg Med. 2025;20:817–828.
doi: 10.1007/s11739-025-03888-5. Epub 2024 Aug 28.

Cytisine for smoking cessation in hospitalised smokers with cardiovascular diseases: an observational study

Tedesco E et al.

PMID: 39939444 DOI: [10.1007/s11739-025-03888-5](https://doi.org/10.1007/s11739-025-03888-5)

Abstract

BACKGROUND: Smoking cessation in patients with cardiovascular disease (CVD) is crucial but challenging. Cytisine, a partial agonist of nicotinic acetylcholine receptors, may aid cessation.

METHODS: We conducted a prospective, real-world, observational study on smokers hospitalized in Cardiology Unit and treated with cytisine for 25 days, plus behavioral support. Follow-up was at 1, 3, 6 and 12 months.

RESULTS: Thirty-six patients were included (mean age 60.5 ± 9.8 ; 72% male). At first follow-up, 13 (36%) patients were abstinent (CO-verified). Point-prevalence abstinence rates were 50%, 47% and 36% at 3, 6 and 12 months, respectively. Nine (25%) patients reported adverse reactions, all mild to moderate. No serious or unexpected suspected adverse drug reactions were identified. No cardiovascular adverse reactions were attributed to cytisine.

CONCLUSIONS: Cytisine may be effective and safe for smoking cessation in patients with CVD. Further randomized controlled trials with larger samples are needed.

CVD = malattia cardiovascolare, CO = monossido di carbonio

TEDESCO ET AL., 2025 *Internal and Emergency Medicine*



36 pazienti con patologia
cardiovascolare ricoverati in Cardiologia



Cytisine per 25 giorni
+ supporto comportamentale



Nessuna reazione avversa
cardiovascolare attribuita alla citisina



Nessuna sospetta reazione avversa
grave o inattesa attribuita alla citisina



Reazioni avverse: 9/36 pazienti (25%),
tutte lievi-moderate



ASTINENZA DAL FUMO (follow-up)

3 mesi: 50%

6 mesi: 47%

12 mesi: 36%

**DATI PROMETTENTI DI EFFICACIA E SICUREZZA,
MA EVIDENZA ANCORA LIMITATA DALLA RIDOTTA
NUMEROSITÀ E DAL DISEGNO OSSERVAZIONALE.**



BPCO: CESSAZIONE DEL FUMO E TERAPIE FARMACOLOGICHE COSA DICONO LE EVIDENZE?

Review > Cochrane Database Syst Rev. 2016 Aug 5;2016(8):CD010744.
doi: 10.1002/14651858.CD010744.pub2.

Smoking cessation for people with chronic obstructive pulmonary disease

Digna J van Eerd¹, Suzanne A Smith, Niels H Chavannes, Nathalie van der Meer, Enriqueta G Blom, Paul W Jones, J Eduardo R van Beek

Affiliations + expand

PMID: 27545342 DOI: [10.1002/14651858.CD010744.pub2](https://doi.org/10.1002/14651858.CD010744.pub2)

Abstract

BACKGROUND: Smoking cessation is the most effective intervention to slow the decline in lung function in people with COPD.

OBJECTIVES: To assess the effects of interventions for smoking cessation for people with COPD.

SEARCH METHODS: We searched the Cochrane Tobacco Addiction Group's Specialised Register, CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL, AMED and trial registries (up to March 2016).

SELECTION CRITERIA: Randomised controlled trials (RCTs) evaluating pharmacological and/or behavioural interventions for smoking cessation in people with COPD, with a minimum follow-up of six months.

RESULTS: Sixteen RCTs (13,123 participants) were included. Compared with placebo, the following pharmacotherapies increased long-term abstinence: varenicline (RR 3.34, 95% CI 1.88 to 5.92), nicotine replacement therapy – sublingual nicotine (RR 2.60, 95% CI 1.29 to 5.24), and bupropion (RR 2.03, 95% CI 1.26 to 3.28). Four studies (1,540 participants) could be pooled: pharmacotherapy plus behavioural support versus placebo plus behavioural support increased abstinence (RR 2.53, 95% CI 1.83 to 3.50; high-quality evidence).

AUTHORS' CONCLUSIONS: There is high-quality evidence that pharmacotherapy, when combined with intensive behavioural support, is effective for smoking cessation in people with COPD. There is no convincing evidence for the superiority of one pharmacological treatment over another.

VAN EERD ET AL., 2016

Cochrane Database of Systematic Reviews



Revisione sistematica e meta-analisi di
16 RCT (13.123 partecipanti) su interventi
per la cessazione del fumo in pazienti con BPCO
con follow-up ≥ 6 mesi

FARMACOTERAPIA vs PLACEBO (ASTINENZA A LUNGO TERMINE)



VARENICLINA

RR 3,34
(IC95% 1,88 – 5,92)



NRT – NICOTINA SUBLINGUALE

RR 2,60
(IC95% 1,29 – 5,24)



BUPROPIONE

RR 2,03
(IC95% 1,26 – 3,28)



I dati non dimostrano la superiorità di una
specifica farmacoterapia rispetto alle altre
nella popolazione con BPCO.



CITISINA E BPCO: QUALI EVIDENZE?

ANALISI POST HOC DEGLI STUDI ORCA-2 E ORCA-3

PubMed®
Advanced User Guide

Prochaska J et al.

Thorax. 2026;81:164–169

doi: 10.1136/thorax-2025-223880

**Cytisinicline for smoking
cessation in individuals
with self-reported COPD:
a post hoc analysis
of the ORCA-2 and
ORCA-3 trials**



DUE TRIAL DI FASE 3

ORCA-2: 810 partecipanti • ORCA-3: 792 partecipanti
Randomizzati, in doppio cieco, controllati con placebo.



SOTTOGRUPPO CON BPCO

145 partecipanti con BPCO riferita; diagnosi non confermata con spirometria.



TRE BRACCI DI TRATTAMENTO

1 • Cytisinicline

3 mg tre volte al giorno
per 6 settimane

2 • Cytisinicline

3 mg tre volte al giorno
per 12 settimane

3 • Placebo

per 12 settimane

Supporto comportamentale in tutti i bracci.



ASTINENZA CONTINUA VERIFICATA BIOCHIMICAMENTE

Valutata durante le ultime 4 settimane di ciascun trattamento.

Trattamento	Finestra di astinenza	Cytisinicline	Placebo	OR (IC95%)
6 settimane	Settimane 3–6	17,3%	2,1%	9,7 (1,2–75,0)
12 settimane	Settimane 9–12	19,1%	4,3%	5,3 (1,1–26,2)

Due gruppi distinti: non due controlli successivi dello stesso gruppo.



TOLLERABILITÀ

nessun evento avverso grave
correlato al trattamento riportato.



RISULTATI FAVOREVOLI, DA CONFERMARE

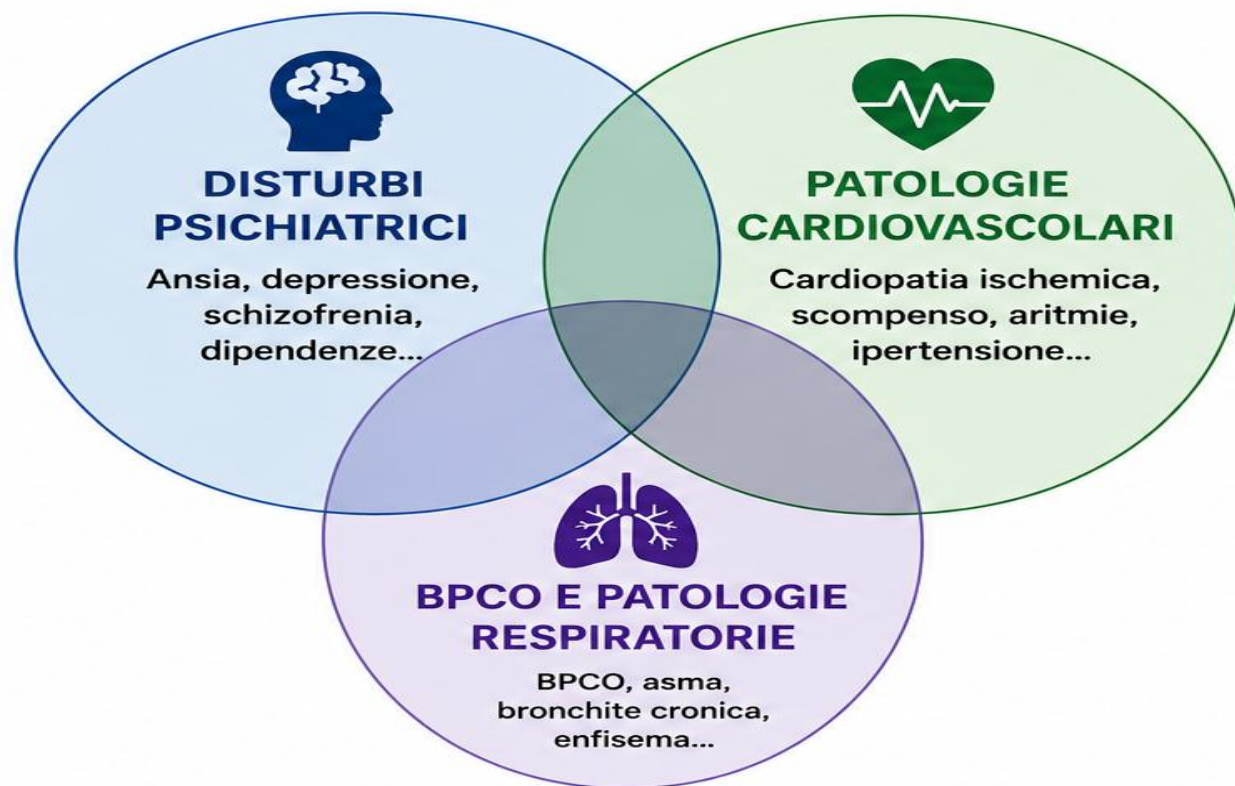
analisi post hoc, sottogruppo piccolo, BPCO riferita
e intervalli di confidenza ampi.



La citisina non era inclusa nella Cochrane Review 2016 sulla BPCO.



DALLE COMORBIDITÀ ALLA MULTIMORBIDITÀ



Le tre condizioni possono coesistere nello stesso grande fumatore.

Negli studi e nelle linee guida le popolazioni vengono analizzate separatamente per ragioni metodologiche e didattiche.



Nella pratica clinica il paziente è spesso multimorbido e assume contemporaneamente:

- psicofarmaci
- terapie cardiovascolari
- terapie pneumologiche



Il paziente reale è complesso e unico.

La valutazione deve tenere conto dell'interazione tra condizioni cliniche, terapie e fattori individuali.



**La terapia con maggiore efficacia nella singola sottopopolazione
NON È NECESSARIAMENTE quella più appropriata nel paziente multimorbido.**



DALLA GERARCHIA DELLE EVIDENZE ALLA SCELTA

Le evidenze orientano, il clinico decide

**MAGGIORE
EFFICACIA**



VARENICLINA

Migliore efficacia nei trial e nelle revisioni sistematiche



NRT COMBINATA

Cerotto + forma rapida (maggiore efficacia rispetto a NRT singola)



CITISINA

Efficacia paragonabile alla vareniclina in più studi e meta-analisi

OPZIONI A MAGGIORE EFFICACIA



BUPROPIONE

Efficace, ma mediamente meno performante delle opzioni sopra



NRT SINGOLA

Efficace, ma mediamente meno performante rispetto a NRT combinata

EFFICACI, MA MEDIAMENTE MENO PERFORMANTI

**LA GERARCHIA DI EFFICACIA ORIENTA LA SCELTA,
MA NON LA DETERMINA.**



SICUREZZA

Controindicazioni e precauzioni



COMORBIDITÀ E INTERAZIONI

Profilo clinico e terapie concomitanti



STORIA TERAPEUTICA

Precedenti tentativi e aderenza



CARATTERISTICHE DEL PAZIENTE

Motivazione, modalità di fumo, preferenze



CONCLUSIONI

DALL'EVIDENZA ALLA DECISIONE CLINICA

Il modello di David L. Sackett



MOST EFFECTIVE

*Quello che ci indicano
le evidenze*



MOST APPROPRIATE

*Quello che scegliamo
per quel paziente*