



Institut Català de la Salut
Gerència Territorial Metropolitana Nord
Servei d'Atenció Primària
Vallès Oriental



VII Jornada Tabaquisme en
Atenció Primària

VI Trobada del Programa
d'Atenció Primària Sense Fum

Auditori Miquel Pont - CASTELLAR DEL VALLÈS

23 D'OCTUBRE DE 2014

Actualització en Tabaquisme

Pere GARCIA

Metge MFiC

Grapat, Xarxa PAPSf

Novetats en :

Pes al deixar de fumar

Fenotips

Tractament farmacològic:

- Eficàcia i seguretat dels tractaments
- TSN (sprai, embaràs)
- Varenicline + altres (TSN, Bupropion)
- línies d'investigació encara futures

“Paquetatge”

~~Cigarreta~~ electrònica.

RESEARCH

62 estudis

Weight gain in smokers after quitting cigarettes: meta-analysis

OPEN ACCESS

Henri-Jean Aubin *professor of psychiatry and addiction medicine*^{1,2}, Amanda Farley *research fellow*³, Deborah Lycett *National Institute for Health Research school for primary care research fellow*³, Pierre Lahmek *gastroenterologist*², Paul Aveyard *professor of behavioural medicine*³

¹Centre d'Enseignement, de Recherche et de Traitement des Addictions, Hôpital Paul Brousse, AP-HP, Univ Paris-Sud, INSERM U669, 94804 Villejuif, France; ²Centre de Traitement des Addictions, Hôpital Emile Roux, Limeil-Brévannes, France; ³UK Centre of Tobacco Control Studies, Primary Care Clinical Sciences, University of Birmingham, Birmingham, UK

Augment mig de 4-5kg (mitjana 4,7kg) a l'any de deixar de fumar

En especial en primers 3 mesos d'abstinència (*1kg per mes*)

Però: 16% perden pes

i 13% augmenten >10kg

= en els preocupats vs no preocupats pel pes

No clares diferències segons tractament fc* (TSN, Bupropion, Varenicline i fluoxetina

reducció mentre es prenen, però no a llarg plaç. Interventi for preventing weight gain after smoking cessation Review Cochrane 2012 Farley AC et al.

Searching for phenotypes in smoking cessation treatment

C. A. Jiménez-Ruiz,¹ J. F. Pascual Lledó,² A. Cicero Guerrero,¹ M. Mayayo Ulibarri,¹ M. Cristóbal Fernández,¹ L. Perera López¹

n= 3622patients Unitat Tabaquisme, Tractament fc + intervenció intensiva

Review criteria

We have reviewed the clinical records of 3622 smokers who attended a Smoking Cessation Service looking for help to quit.

Message for the clinic

There are some smoking phenotypes based on gender, age and tobacco dependence. These phenotypes may help us to choose the best treatment.

TSN menys efectiva en alta dependència, especial en dones molt dependents i/o amb "reforçament negatiu de fumar"

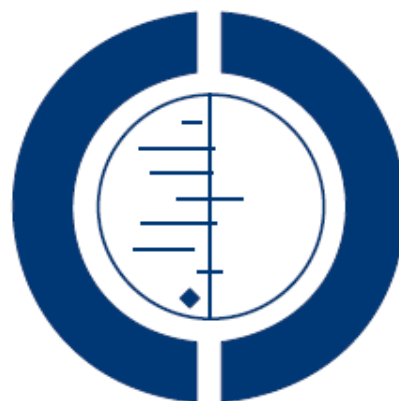
Molt Joves (<20anys) i dependència moderada-alta més resistents a tots els tractaments fc.

Bupropion i Varenicline anirien millor en alt dependents de més edat

Baixa dependència responen a tots els tractaments però si són >60anys millors resultats amb bupropion i varencline

Nicotine receptor partial agonists for smoking cessation (Review)

Cahill K, Stead LF, Lancaster T



**THE COCHRANE
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Abril 2012

Varenicline dosis estàndard (1mgr 2 vegades dia) es més del doble d'eficaç per deixar de fumar a llarg plaç en comparació a placebo

Varenicline a dosis baixes ($\leq 1\text{mgr/d}$) sembla ser similar eficaç a Bupropion i TSN i amb menor incidències d'efectes adversos en les primeres setmanes de tractament

Hi ha evidència limitada que Varenicline pot tenir un paper en la prevenció de recaigudes. (no amb bupropion i no hi ha dades amb TSN

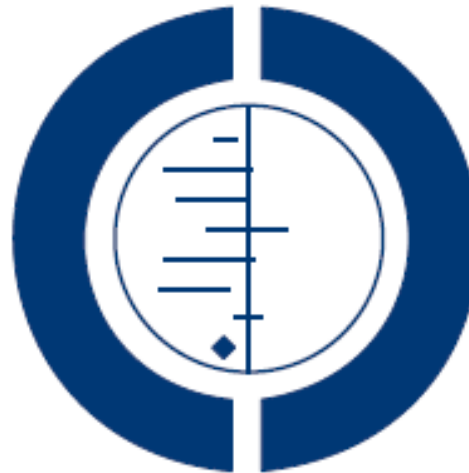
Relapse prevention interventions for smoking cessation Peter Hajek¹ et al Cochrane Tobacco Addiction Group 20 AUG 2013)

El pacients tractats amb Varenicline poden presentar més efectes adversos greus (1/3 més d'efectes adv greus) que els no tractats

Però No hi ha prous evidències per concloure l'associació de Varenicline i efectes adversos cardiovasculars , hi ha una petita evidència en els psiquiàtrics

**Pharmacological interventions for smoking cessation: an
overview and network meta-analysis (Review)**

Cahill K, Stevens S, Perera R, Lancaster T



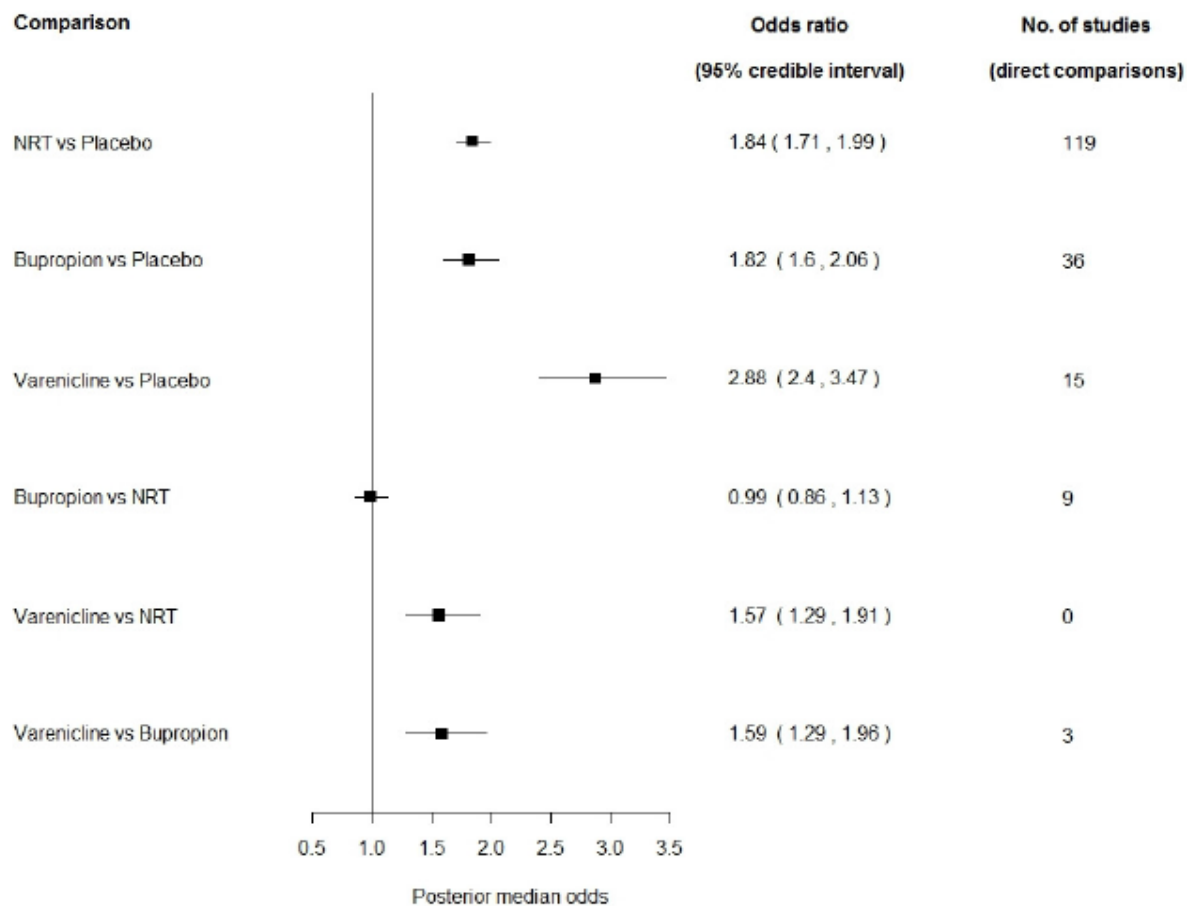
**THE COCHRANE
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Maig 2013

Eficàcies TSN, Bupropion i Varenicline....

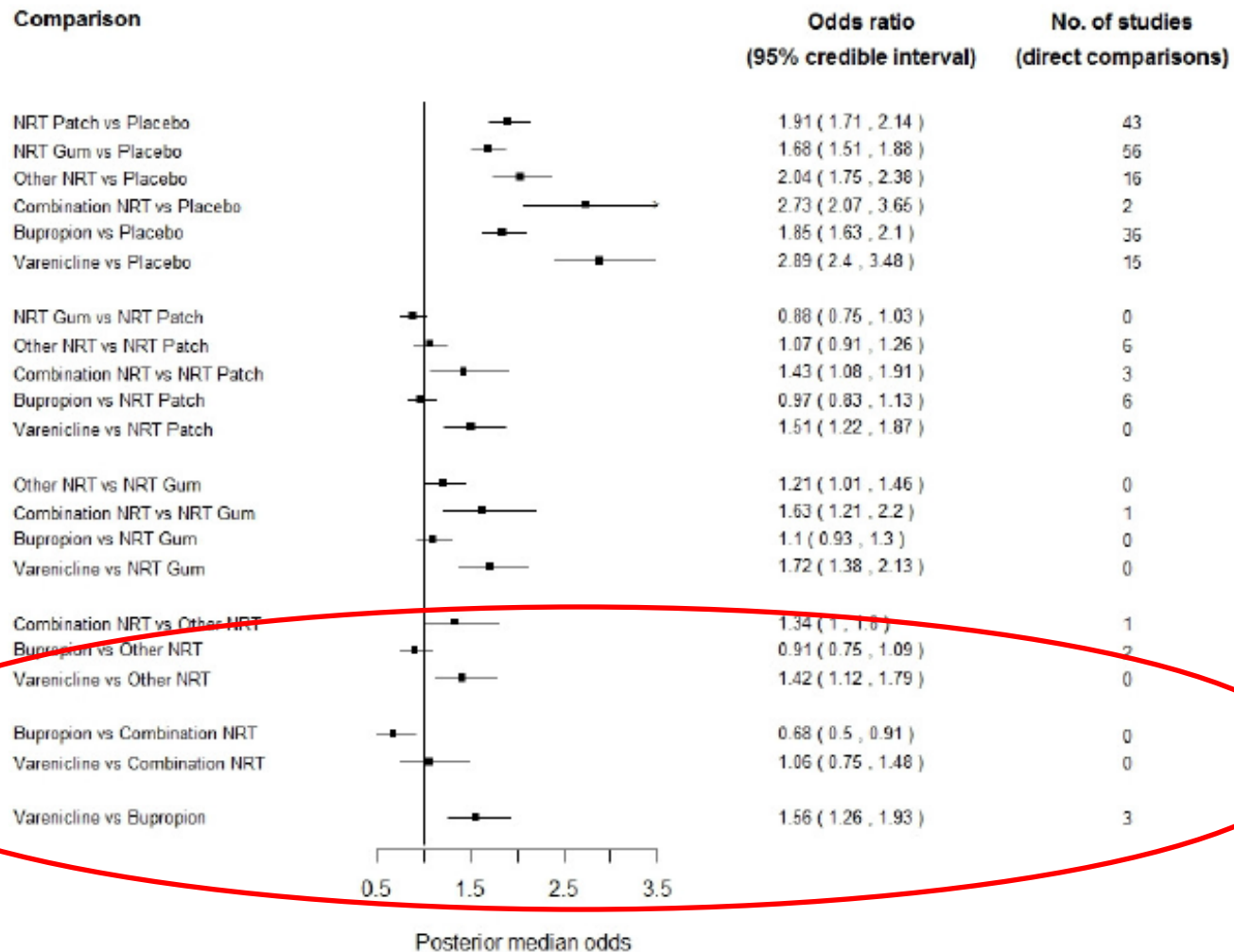
Similar Eficàcia de Bupropion i de TSN una sola presentació

Figure 2. Network meta-analysis of smoking cessation with each first-line pharmacotherapy versus placebo and versus each other



Però Similar eficàcia TSN combinades presentacions i Varenicline, sent superiors a Bupropion

Figure 4. Network meta-analysis of first-line pharmacotherapies versus placebo and versus each other, with NRT split by type



- Bupropion demonstrates no excess of neuropsychiatric events (RR 0.88 (95% CI 0.31 to 2.50)) or of cardiovascular events (RR 0.77 (95% CI 0.37 to 1.59)).
- Varenicline demonstrates no excess of neuropsychiatric events (RR 0.53 (95% CI 0.17 to 1.67)), and a marginal but non-significant increase in cardiovascular events (RR 1.26 (95% CI 0.62 to 2.56)).

Bupropion demostra no excés d'events psiquiàtrics ni cardiovasculars

Varenicline demostra no excés d'events psiquiàtrics, si cardiovasculars de forma no significativa

Table 3. Estimated RR and 95% CrI From Random-Effects Network Meta-Analysis for Cardiovascular Events in Smoking Cessation RCTs

Comparison	All CVD events	MACEs
All trials		
NRT vs placebo →	2.29 (1.39–3.82)	1.95 (0.92–4.30)
Bupropion vs placebo	0.98 (0.54–1.73)	0.45 (0.21–0.85)
Varenicline vs placebo	1.30 (0.79–2.23)	1.34 (0.66–2.66)
Bupropion vs varenicline	0.76 (0.33–1.73)	0.33 (0.16–0.87)
Bupropion vs NRT	0.43 (0.19–0.91)	0.23 (0.08–0.63)
Varenicline vs NRT	0.56 (0.25–1.27)	0.67 (0.26–1.90)
High-risk populations (sensitivity analysis)		
NRT vs placebo	1.31 (0.58–3.32)	1.53 (0.38–6.24)
Bupropion vs placebo	1.06 (0.59–2.04)	0.48 (0.18–1.21)
Varenicline vs placebo	0.99 (0.45–1.88)	1.22 (0.44–2.90)
Bupropion vs varenicline	1.09 (0.46–2.92)	0.39 (0.11–1.49)
Bupropion vs NRT	0.81 (0.26–2.26)	0.31 (0.05–1.68)
Varenicline vs NRT	0.92 (0.34–2.19)	0.81 (0.13–4.20)

CrI indicates credibility interval; CVD, cardiovascular disease; MACE, major adverse cardiovascular event; NRT, nicotine replacement therapy; RCT, randomized, clinical trial; and RR, relative risk.

pharmacotherapies: A

by Judith J. Prochaska

December 9, 2013;

TSN augment events CV a
 expenses d'events lleus
 (taquicàrdia i palpitations)

No evidència d'augment
 d'events cardiovasculars
 Varenicline ni Bupropion

Table 2| Risks of suicide and non-fatal self harm, treated depression, and all cause mortality at three months in patients prescribed varenicline, bupropion, and nicotine replacement therapy (NRT)

Smoking cessation product	Total person time (person years)	No of events/No of patients prescribed product	Hazard ratio (95% CI)	
			Basic model*	Fully adjusted model†
Main cohort: treatment initiators				
Fatal and non-fatal self harm				
NRT	19 196	69/78 407	1	1
Bupropion	1622	4/6568	0.62 (0.22 to 1.70)	0.83 (0.30 to 2.31)
Varenicline	7363	19/30 352	0.70 (0.41 to 1.18)	0.88 (0.52 to 1.49)
Treated depression‡				
NRT	10 315	799/42 475	1	1
Bupropion	961	40/3910	0.56 (0.41 to 0.77)	0.63 (0.46 to 0.87)
Varenicline	4435	255/18 386	0.69 (0.60 to 0.80)	0.75 (0.65 to 0.87)
All cause mortality				
NRT	19 947	292/81 496	1	1
Bupropion	1665	5/6740	0.31 (0.13 to 0.74)	0.39 (0.16 to 0.95)
Varenicline	7575	33/31 227	0.37 (0.26 to 0.54)	0.44 (0.30 to 0.63)
Secondary cohort: first time users				
Fatal and non-fatal self harm				
NRT	11 565	41/47 376	1	1
Bupropion	846	2/3427	0.64 (0.15 to 2.66)	0.87 (0.21 to 3.66)
Varenicline	4495	10/18 591	0.57 (0.28 to 1.17)	0.74 (0.36 to 1.52)
Treated depression‡				
NRT	6887	529/28 415	1	1
Bupropion	554	22/2255	0.56 (0.37 to 0.86)	0.63 (0.41 to 0.96)
Varenicline	2971	179/12 346	0.72 (0.60 to 0.86)	0.77 (0.65 to 0.92)
All cause mortality				
NRT	12 006	186/49 195	1	1
Bupropion	867	2/3512	0.23 (0.06 to 0.92)	0.29 (0.07 to 1.19)
Varenicline	4614	15/19 084	0.28 (0.16 to 0.48)	0.32 (0.19 to 0.55)

SEARCH

depression,
Research

M Martin professor

No evidència d'augment d'events fatals ni no fatals (siucidi, intents, depressió que requereixi tractament, mortalitat per qualsevol causa) en els tractats amb Bupropion o Varenicline, respecte els tractats TSN

Hazard ratios calculated using Cox proportional hazards regression model

*Basic model includes age, sex, and year of first prescription

†Fully adjusted model includes sex; age; previous psychiatric illness or consultation; previous use of psychotropic drugs such as hypnotics, antipsychotics, and antidepressants

‡Includes previous psychiatric self harm, no previous psychiatric illness, number of general practitioner consultations in the year before the prescription exposure to the drug before or after 2008; year of first prescription; and previous use of a smoking cessation product.

§Restricted to those with no previous antidepressant use.

Efficacy of interventions to combat tobacco addiction: Cochrane update of 2013 reviews

Jamie Hartmann-Boyce, Lindsay F. Stead, Kate Cahill & Tim Lancaster

Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

Actualització de
revisions 2013
Cochrane

al Maig 2014

No eficàcia de Naltrexona (sola o associada a TSN), No eficàcia ISRS, ni d' Herba de St Joan

En Embarassades: “Counselling” e intervencions psicològiques eficaces en cessació i en disminuir baix pes al néixer i prematurs.

Tractaments en fumadors/es amb depressió

Smoking cessation interventions for smokers with current or past DEPRESSION (Review) Van der Meer RM et al. Agost 2013

Per abstinència tabac a llarg plaç:

*Evidència eficaçia d'aplicar model “control de l'estat d'ànim” psicosocial.

*Evidència debil d'eficaçia de bupropion pacients amb depressió passada, (no evidència en depressió actual, ni sol ni associat a TSN).

*No es valora Varenicline** i no prou evidències per valorar IRSS;*

TSN (xiclets) efecte positiu però no significatiu

THE COCHRANE
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Novetats en productes TSN comercialitzats a Espanya:

Sprai bucal de nicotina

*

Envàs de 150 pufs (cost aprox 27,7€)

1-2 pufs/vegada, màx 4pufs/h i 64pufs/d

Efectes adversos: Singlot i irritació faríngia

(Tonnesen 2012)




Noves dosi de comprimits nicotina comercialitzades:

*Dosis 1,5mgr i 4mgr

n=403, en 23 maternitats de França

RESEARCH

Nicotine patches in pregnant smokers: randomised, placebo controlled, multicentre trial of efficacy

 OPEN ACCESS

Ivan Berlin *senior lecturer, hospital practitioner*¹, Gilles Grangé *hospital practitioner*², Nelly Jacob *hospital practitioner*³, Marie-Laure Tanguy *statistician*⁴

What is already known on this topic

Smoking during pregnancy increases the risk of adverse pregnancy and birth outcomes

Guidelines suggest adding nicotine replacement therapies (NTR) to behavioural smoking cessation interventions in pregnant smokers because of their excellent safety profile and proved efficacy in other populations of smokers

Evidence about the efficacy of NTR in pregnant smokers at the level of both maternal abstinence and birth weight is not conclusive

What this study adds

Compared with placebo and despite individual dose adjustment, longer treatment duration, higher daily nicotine dose than previously used, nicotine patches did not increase smoking cessation rate or birth weight

Diastolic blood pressure was higher with the nicotine patch than with placebo, suggesting that further studies with nicotine in pregnant smokers should control for blood pressure

Augment TAd: 0,02mmHg/dia (aprox 3-4mmHg)

Varenicline + pegats nicotina és més eficaç que vareniline sola ?

BMC Medicine

BioMed Central
The Open Access Publisher

This Provisional PDF corresponds to the article as it appeared upon acceptance. Fully formatted PDF and full text (HTML) versions will be made available soon.

Combining varenicline and nicotine patches: a randomized controlled trial study in smoking cessation

BMC Medicine 2014, 12:172 doi:10.1186/s12916-014-0172-8

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Published online: 08 October 2014

Unitat Tabac Bellvitge

170p V+Pegat Nicotina

171p V+Pegat placebo

Fumadors 20cig o + /dia

Varecline dosi estàndard + pegat
21mgr/24h

Seguiment fins 24set

Table 2 Smoking abstinence by group

Group	Continuous abstinence ^a			Seven-day point-prevalence abstinence		
	Abstainers (%)	Crude OR (95%CI)	OR ^b (95%CI)	Abstainers (%)	Crude OR (95%CI)	OR ^b (95%CI)
Varenicline + nicotine patch (N = 170)	72 (42.2%)	1.08 (0.7 to 1.7)	1.04 (0.4 to 2.1)	80 (47.2%)	1.06 (0.7 to 1.6)	1.02 (0.3 to 1.6)
Varenicline + placebo (N = 171)	69 (40.4%)	1	1	78 (45.7%)	1	1
Week 24						
Varenicline + nicotine patch (N = 170)	66 (39.1%)	1.37 (0.8 to 2.1)	1.24 (0.8 to 2.6)	68 (40.2%)	1.37 (0.8 to 2.1)	1.20 (0.7 to 2.1)
Varenicline + placebo (N = 171)	54 (31.8%)	1	1	56 (38.5%)	1	1
Week 24						
Varenicline + nicotine patch (N = 170)	56 (32.8%)	1.25 (0.8 to 2.0)	1.17 (0.4 to 1.9)	60 (35.1%)	1.28 (0.8 to 2.0)	1.15 (0.4 to 2.0)
Varenicline + placebo (N = 171)	48 (28.2%)	1	1	51 (33.4%)	1	1

^aContinuous abstinence from weeks 2 to 8, 12 and 24 weeks; ^badjusted by age, gender and therapist. CI, confidence interval; N, number; OR, odds ratio.

No més efectiva que Varenicline sola

* Potser si més efectiva la combinació en fumadors de >29cig/d

Table 3 Smoking abstinence by group and cigarette consumption

Group	Smokers ≤ 29 cigarettes/day			Smokers > 29 cigarettes/day		
	Abstainers/N (%)	Crude OR (95%CI)	OR ^a (95%CI)	Abstainers/N (%)	Crude OR (95%CI)	OR ^a (95%CI)
Weeks 2 to 8						
Varenicline + nicotine patch	38/78 (48.7%)	1.05 (0.7 to 1.4)	1.0 (0.5 to 1.3)	34/92 (36.9%)	1.13 (0.7 to 1.6)	1.07 (0.6 to 1.8)
Varenicline + placebo	39/84 (46.4%)	1	1	29/87 (33.3%)	1	1
Weeks 2 to 12						
Varenicline + nicotine patch	35/78 (43.6%)	1.14 (0.7 to 1.6)	1.0 (0.5 to 1.8)	31/92 (34.8%)	1.44 (0.9 to 2.3)	1.39 (1.2 to 2.5)
Varenicline + placebo	33/84 (39.2%)	1	1	21/87 (24.1%)	1	1
Weeks 2 to 24						
Varenicline + nicotine patch	27/78 (34.6%)	0.99 (0.6 to 1.5)	1.0 (0.7 to 1.6)	29/92 (31.5%)	1.52 (1.0 to 2.5)	1.46 (1.2 to 2.8)
Varenicline + placebo	30/84 (35.7%)	1	1	18/87 (20.6%)	1	1

^aAdjusted by age, gender and therapist. CI, confidence interval; N, number; OR, odds ratio.

Ajustat per edat, sexe i terapeuta

* No diferències significatives en efectes secundaris

Table 4 Adverse events

Adverse event	Varenicline + Nicotine patch	Varenicline + Placebo
	Number = 170 n (%)	Number = 171 n (%)
Insomnia	29 (17.3%)	23 (13.2%)
Nausea	31 (18.3%)	33 (19.1%)
Abnormal dreams	29 (17.4%)	26 (15.1%)
Constipation	15 (8.8%)	13 (7.6%)
Dyspepsia	10 (5.9%)	8 (4.7%)
Headache	7 (4.1%)	4 (2.6%)
Other ^a	9 (5.3%)	11 (6.4%)

^aIrritability, depressive symptoms, fatigue, hypotension.

Original Investigation

Juliol 2014 JAMA

Efficacy of Varenicline Combined With Nicotine Replacement Therapy vs Varenicline Alone for Smoking Cessation
A Randomized Clinical Trial

Coenraad F. N. Koegelenberg, MD, PhD; Firdows Noor, MD; Eric D. Bateman, MD, PhD;
Richard N. van Zyl-Smit, MD, PhD; Axel Bruning, MD; John A. O'Brien, MD; Clifford Smith, MD;
Mohamed S. Abdool-Gaffar, MD; Shaunagh Emanuel, MD; Tonya M. Esterhuizen, MSc; Elvis M. Irušen, MD, PhD

7centres de Sudàfrica

222p V+Pegat Nicot /224p V+Pegat placeb

Fumadors 10cig o + /dia

Varecline dosi estàndar + Pegats 15mg/16h
desde 2 set previ dia D

Seguiment fins 24set

Table 2. Continuous Abstinence and Point Prevalence Abstinence Rates (n=435)

Time Since TQD	Time Period	Per-Protocol Analysis				Multiple Imputation Analysis of Main Outcomes			
		No. (%)		OR (95% CI)	P Value	No. (%) ^a		OR (95% CI)	P Value
		Varenicline and Active Nicotine Patch (n = 216)	Varenicline and Placebo Patch (n = 219)			Varenicline and Active Nicotine Patch (n = 216)	Varenicline and Placebo Patch ^b		
Continuous Abstinence									
8 wk	Weeks 5-8	96 (44.4)	76 (34.7)	1.50 (1.02-2.22)	.04				
12 wk	Weeks 9-12	99 (45.8)	70 (32.0)	1.80 (1.22-2.66)	.003	120 (55.4)	90 (40.9)	1.85 (1.19-2.89)	.007
16 wk	Weeks 9-16	84 (38.9)	56 (25.6)	1.85 (1.23-2.79)	.003				
24 wk	Weeks 9-24	71 (32.9)	42 (19.2)	2.06 (1.33-3.21)	.001	106 (49.0)	71 (32.6)	1.98 (1.25-3.14)	.004
Point Prevalence Abstinence Rates									
1 wk	Week 1	69 (31.9)	61 (27.9)	1.22 (0.81-1.83)	.35				
2 wk	Week 2	98 (45.4)	95 (43.4)	1.08 (0.74-1.58)	.68				
4 wk	Week 4	110 (50.9)	87 (39.7)	1.57 (1.08-2.30)	.02				
8 wk	Week 8	109 (50.5)	96 (43.8)	1.31 (0.90-1.90)	.17				
12 wk	Week 12	116 (53.7)	87 (39.7)	1.76 (1.20-2.58)	.003	138 (63.9)	112 (51.2)	1.68 (1.07-2.66)	.03
16 wk	Week 16	104 (48.1)	81 (37.0)	1.58 (1.08-2.32)	.02				
24 wk	Week 24	94 (43.5)	63 (28.8)	1.91 (1.28-2.84)	.001	141 (65.1)	101 (46.7)	2.13 (1.32-3.43)	.002

Abbreviations: OR, odds ratio; TQD, target quit date.

^a Calculated mean proportional values (numbers rounded) derived from data of participants who completed follow-up to 12 and 24 weeks, respectively, and, to account for missing data, 5 sets of imputed values for the participants who

did not attend their 12- and 24-week follow-up visits (Figure). Data for 2 participants (in the placebo group) were insufficient to perform the multiple imputation analysis at 24 weeks.

^b n = 219 at 12 wk and n = 217 at 24 wk.

Augment èxit amb
la convinació
V+Pegat Nicotina

Efecte

“Precàrrega” ???

* No diferències significatives en efectes secundaris, tret de major reaccions cutànies no greus en la combinació V+Pegat Nicot

Table 3. Adverse Events Reported in at Least 2% of Participants per Study Group

Adverse Event	No. (%)		P Value
	Varenicline and Active Nicotine Patch (n = 216)	Varenicline and Placebo Patch (n = 219)	
Nausea	59 (27.3)	54 (24.7)	.53
Insomnia and disturbed sleep	43 (19.9)	35 (15.1)	.18
Abnormal dreams	10 (4.6)	13 (5.9)	.54
Headaches	17 (7.9)	22 (10.0)	.43
Any skin reactions	31 (14.4)	17 (7.8)	.03
Constipation	9 (4.1)	6 (2.7)	.42
Depression	5 (2.3)	3 (1.4)	.50 ^a

però

Two women became pregnant during the treatment phase (both were randomized to receive the placebo NRT patch). One pregnancy was anembryonic and considered an unrelated serious adverse event (SAE). Another participant gave birth to an infant with Down syndrome (confirmed trisomy 21) with associated congenital heart defects. There was no family history of chromosomal abnormalities, and it was considered a possibly related SAE. Five other unrelated

En grup V+ Pegat placebo 2 embarassades: 1 sense embrió i l'altre neix amb Trisomia 21 amb defectes cardíacs, sense poder confirmar relació.

Varenicline + bupropion nicotina és més efectiu que vareniline sola ?

Original Investigation

Combination Varenicline and Bupropion SR for Tobacco-Dependence Treatment in Cigarette Smokers
A Randomized Trial **JAMA gener 2014**

Jon O. Ebbert, MD, MSc; Dorothy K. Hatsukami, PhD; Ivana T. Croghan, PhD; Darrell R. Schroeder, MS; Sharon S. Allen, MD; J. Taylor Hays, MD; Richard D. Hurt, MD

Minnessota

249p V+B

257p V+placebo

38% perdues

Fumadors 10cig o + /dia

Varenicline i Bupropion dosi estandar (fins a 12set)

Seguiment fins 52set

Efectes adversos: Més aparició d'ansietat i depressió amb la combinació però no estadísticament significatiu

Table 3. Adverse Events*

Adverse Events	No. (%)		P Value ^b
	Varenicline + Bupropion SR (n = 249)	Varenicline + Placebo (n = 257)	
Sleep disturbance	100 (40.2)	91 (35.4)	.27
Nausea	55 (22.1)	54 (21.0)	.83
Constipation	26 (10.4)	19 (7.4)	.28
Headache	21 (8.4)	22 (8.6)	>.99
Irritability	21 (8.4)	12 (4.7)	.11
Anxiety	18 (7.2)	8 (3.1)	.04
Difficulty concentrating	14 (5.6)	10 (3.9)	.41
Mood disturbance	13 (5.2)	7 (2.7)	.18
Dizziness	10 (4.0)	10 (3.9)	>.99
Abnormal dreams	9 (3.6)	19 (7.4)	.08
Restlessness	9 (3.6)	5 (1.9)	.29
Depressive symptoms	9 (3.6)	2 (0.8)	.03
Fatigue	7 (2.8)	17 (6.6)	.06
Dry mouth	7 (2.8)	9 (3.5)	.80
Dyspepsia	5 (2.0)	1 (0.4)	.12
Flatulence	1 (0.4)	9 (3.5)	.02

Table 4. Smoking Abstinence Outcomes According to Baseline Smoking Rate and Level of Nicotine Dependence

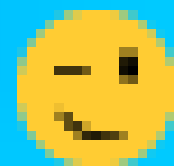
	No. of Participants	7-Day Point-Prevalence Smoking Abstinence ^a			Prolonged Smoking Abstinence ^{a,b}		
		No. (%)	OR (95% CI)	P Value	No. (%)	OR (95% CI)	P Value
Baseline Smoking Rate							
Lighter smokers^c							
Week 12							
Varenicline + bupropion SR	102	61 (59.8)	1.20 (0.68-2.11)	.53	58 (56.9)	1.14 (0.65-2.01)	.65
Varenicline + placebo	105	59 (56.2)			57 (54.3)		
Week 26							
Varenicline + bupropion SR	102	41 (40.2)	0.94 (0.53-1.66)	.82	40 (39.2)	1.01 (0.57-1.80)	.97
Varenicline + placebo	105	45 (42.9)			42 (40.0)		
Week 52							
Varenicline + bupropion SR	102	40 (39.2)	1.10 (0.62-1.96)	.74	30 (29.4)	0.80 (0.43-1.46)	.47
Varenicline + placebo	105	40 (38.1)			37 (35.2)		
Heavier smokers^c							
Week 12							
Varenicline + bupropion SR	147	79 (53.7)	1.52 (0.96-2.40)	.07	74 (50.3)	1.84 (1.16-2.93)	.01
Varenicline + placebo	152	66 (43.4)			54 (35.5)		
Week 26							
Varenicline + bupropion SR	147	54 (36.7)	1.79 (1.09-2.96)	.02	51 (34.7)	2.24 (1.32-3.81)	.003
Varenicline + placebo	152	37 (24.3)			29 (19.1)		
Week 52							
Varenicline + bupropion SR	147	51 (34.7)	1.76 (1.06-2.93)	.03	47 (32.0)	2.26 (1.31-3.92)	.004
Varenicline + placebo	152	35 (23.0)			26 (17.1)		
Level of Nicotine Dependence							
Low/Moderate^c							
Week 12							
Varenicline + bupropion SR	127	77 (60.6)	1.20 (0.72-2.00)	.48	74 (58.3)	1.31 (0.79-2.18)	.30
Varenicline + placebo	133	74 (55.6)			68 (51.1)		
Week 26							
Varenicline + bupropion SR	127	55 (43.3)	1.16 (0.69-1.92)	.58	52 (40.9)	1.10 (0.66-1.84)	.71
Varenicline + placebo	133	54 (40.6)			52 (39.1)		
Week 52							
Varenicline + bupropion SR	127	49 (38.2)	1.11 (0.66-1.86)	.70	40 (31.5)	0.92 (0.53-1.57)	.76
Varenicline + placebo	133	49 (36.8)			45 (33.8)		
High^c							
Week 12							
Varenicline + bupropion SR	120	62 (51.7)	1.55 (0.93-2.58)	.09	57 (47.5)	1.74 (1.04-2.93)	.04
Varenicline + placebo	123	50 (40.6)			42 (34.2)		
Week 26							
Varenicline + bupropion SR	120	39 (32.5)	1.74 (0.98-3.09)	.06	38 (31.7)	2.76 (1.47-5.21)	.002
Varenicline + placebo	123	27 (22.0)			18 (14.6)		
Week 52							
Varenicline + bupropion SR	120	41 (34.2)	2.04 (1.14-3.66)	.02	36 (30.0)	2.77 (1.44-5.30)	.002
Varenicline + placebo	123	25 (20.3)			17 (13.8)		

	7-Day Point-Prevalence Smoking Abstinence ^a		Prolonged Smoking Abstinence ^{a,b}		
	OR (95% CI)	P Value	No. (%)	OR (95% CI)	P Value
	0.95-1.93)	.09	132 (53.0)	1.49 (1.05-2.12)	.03
			111 (43.2)		
	0.91-1.91)	.14	91 (36.6)	1.52 (1.04-2.22)	.03
			71 (27.6)		
	0.96-2.05)	.08	77 (30.9)	1.39 (0.93-2.07)	.11
			63 (24.5)		

N
d

Però

Major abstinència en fumadors de >20cig i en alta dependència



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Am J Psychiatry. 2014 Jun 17. doi: 10.1176/appi.ajp.2014.13050595. [Epub ahead of print]

Combination Treatment With Varenicline and Bupropion in an Adaptive Smoking Cessation Paradigm.

Rose JE, Behm FM.

Abstract

OBJECTIVE The authors assessed the efficacy and safety of combination treatment with varenicline and sustained-release bupropion for smokers who, based on an assessment of initial smoking reduction prior to the quit date, were deemed unlikely to achieve abstinence using nicotine patch treatment. **METHOD** In a randomized, double-blind, parallel-group adaptive treatment trial, the authors identified 222 cigarette smokers who failed to show a reduction of more than 50% in smoking after 1 week of nicotine patch treatment. Smokers were randomly assigned to receive 12 weeks of varenicline plus bupropion or varenicline plus placebo. The primary outcome measure was continuous smoking abstinence at weeks 8-11 after the target quit date. **RESULTS** Both treatments were well tolerated. Participants who received the combination treatment had a significantly higher abstinence rate than those who received varenicline plus placebo (39.8% compared with 25.9%; odds ratio=1.89; 95% CI=1.07, 3.35). Combination treatment had a significantly greater effect on abstinence rate in male smokers (odds ratio=4.26; 95% CI=1.73, 10.49) than in female smokers (odds ratio=0.94; 95% CI=0.43, 2.05). It also had a significantly greater effect in highly nicotine-dependent smokers (odds ratio=3.51, 95% CI=1.64, 7.51) than in smokers with lower levels of dependence (odds ratio=0.71, 95% CI=0.28, 1.80). **CONCLUSIONS** Among smokers who did not show a sufficient initial response to prequit nicotine patch treatment, combination treatment with varenicline and bupropion proved more efficacious than varenicline alone for male smokers and for smokers with a high degree of nicotine dependence.

PMID: 24934962 [PubMed - as supplied by publisher]



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Combination Treatment With Varenicline and Bupropion in an Adaptive Smoking Ce... PubMed

Smoking cessation in smokers who smoke... PubMed

Diu que V+B més efectiva en especial en fumadors rs molt dependents.... Però n petita i seguiment a 12set només i en pacients que han “fallat” amb TSN

I el pes...?

Weight Gain

Among participants meeting criteria for prolonged smoking abstinence at the end of treatment (week 12), the mean weight change from baseline to week 12 was significantly less in the combination therapy group compared with the varenicline monotherapy group (1.1 kg [95% CI, 0.5-1.7] vs 2.5 kg [95% CI, 2.0-3.0]; $P < .001$). At 26 weeks, differences in weight gain were not observed and participants in the combination therapy group gained 3.4 kg (95% CI, 2.5-4.3), and participants in the varenicline monotherapy group gained 3.8 kg (95% CI, 2.9-4.8) ($P = .48$). At week 52, weight gain from baseline for the combination therapy group was 4.9 kg (95% CI, 3.6-6.2), and for the monotherapy group it was 6.1 kg (95% CI, 4.6-7.6) ($P = .23$).

Al seguiment al finalitzar el tractament (12set):

1,1 kg Vareni+Bupo vs 2,5 Kg Vareni ($p < 0,01$) 😊

Però...a la set 26 i a la set 52 No diferències significatives 😞

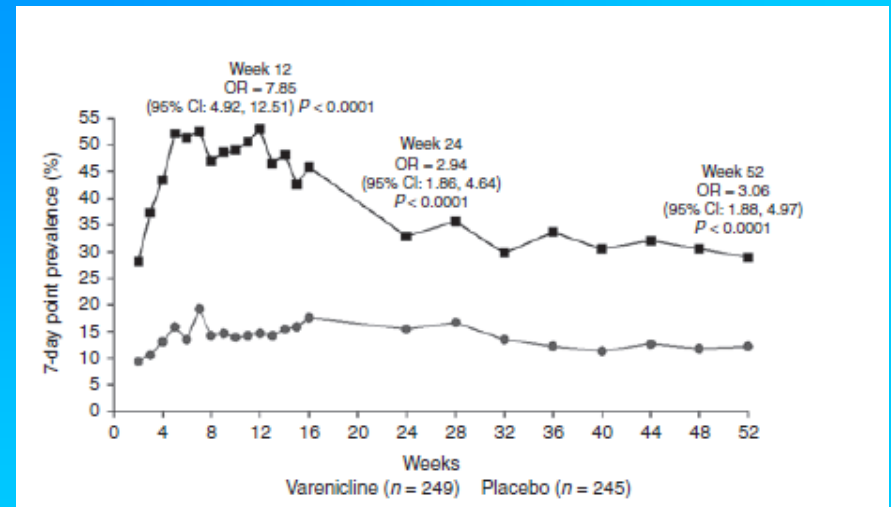
Retreatment With Varenicline for Smoking Cessation in Smokers Who Have Previously Taken Varenicline: A Randomized, Placebo-Controlled Trial

N: V 249, Placebo 245

D Gonzales¹, P Hajek², L Pliamm³, K Nackaerts⁴, L-J Tseng⁵, TD McRae⁵ and J Treadow⁵

En pacients tractats previament* amb Varenicline, el tractar-los de nou amb V segueix sent eficaç

Sense variació significativa en els efectes adversos*



I en breu.... O no tant breu...

HEALTH TECHNOLOGY ASSESSMENT

VOLUME 18 ISSUE 33 MAY 2014
ISSN 1366-5278

23 estudis amb 10610 pacients

(21 varenicline vs 2 citisina amb 937 pacients)

What is the clinical effectiveness and cost-effectiveness of cytisine compared with varenicline for smoking cessation? A systematic review and economic evaluation

Joanna Leaviss, William Sullivan, Shijie Ren, Emma Everson-Hock, Matt Stevenson, John W Stevens, Mark Strong and Anna Cantrell

Citisina i Vareniclina efectius en front a placebo, i probablement Citisina més efectiu i més cost efectiu que Varenicline (*més barat, menys efectes secundaris*)

Cal però estudi Varenicline vs Citisina directe.

Inconvenient posodologia Citisina i no disponible aquí

“Vacunes antinicotina”

“diciendo que la vacuna antinicotina podría estar disponible en humanos en el año 2006”

Edit. Arch Bronconeumol.

2005;41(1):2-4

Vacuna NicVAX: Estudis fase III si resposta anticossos però no canvis cerebrals, ni augment d'eficàcia amb Varenicline o suport conductual *

Vacuna NIC002 i Vacuna TA-NIC: no publicats fase III

Noves investigacions fent servir: nano-lipoplex, a trivalent nicotine vaccine formulated with alum... encara inicial

En estudi... Potser pel futur tractament...?

→ Psilocibina (al·lucinògen)

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J. Psychoactive Drugs. 2014 Sep 11. pii: 62069114546296. [Epub ahead of print]
Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction.
Johnson MW¹, Garcia-Romeu A², Cosman MP³, Griffiths RR¹.

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³Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

Abstract
Despite suggestive early findings on the therapeutic use of hallucinogens in the treatment of substance use disorders, rigorous follow-up has not been conducted. To determine the safety and feasibility of psilocybin as an adjunct to tobacco smoking cessation treatment we conducted an open-label pilot study administering moderate (20 mg/70 kg) and high (30 mg/70 kg) doses of psilocybin within a structured 15-week smoking cessation treatment protocol. Participants were 15 psychiatrically healthy nicotine-dependent smokers (10 males, mean age of 51 years), with a mean of six previous lifetime quit attempts, and smoking a mean of 19 cigarettes per day for a mean of 31 years of intake. Biomarkers assessing smoking status, and self-report measures of smoking behavior demonstrated that 12 of 15 participants (80%) showed seven-day point prevalence abstinence at 6-month follow-up. The observed smoking cessation rate substantially exceeds rates commonly reported for other behavioral and/or pharmacological therapies (typically <35%). Although the open-label design does not allow for definitive conclusions regarding the efficacy of psilocybin, these findings suggest psilocybin may be a potentially efficacious adjunct to current smoking cessation treatment models. The present study illustrates a framework for future research on the efficacy and mechanisms of hallucinogen-facilitated treatment of addiction.
© The Author(s) 2014.

KEYWORDS: Hallucinogen, addiction, nicotine, psilocybin, psychedelic, smoking cessation, tobacco

PMID: 25213996 [PubMed - as supplied by publisher]

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Clin Pharmacol Ther. 2014 Aug 9(62):256-65. doi: 10.1038/cpt.2014.08. Epub 2014 Apr 14
Association of CHRNA5-A3-B4 SNP rs2036527 with smoking cessation therapy response in African-American smokers.
Zhu AQ¹, Zhou Q¹, Cox LS², Davis SP³, Ahluwalia JS⁴, Benowitz NL⁴, Tyndale RF⁵.

Author information

Abstract
Associations between CHRNA5-A3-B4 variants and smoking behaviors exist, however, the association with smoking abstinence is less understood, particularly that among African Americans. In 1,295 African Americans enrolled in two clinical trials, we investigated the association between CHRNA5-A3-B4 and smoking abstinence. The rs2036527(A) allele was associated with lower abstinence with active pharmacotherapy (during treatment odds ratio (OR) = 0.42, P < 0.001), and of treatment (EOT) OR = 0.55, P = 0.004), or with nicotine gum alone (during treatment: OR = 0.31, P = 0.001; EOT: OR = 0.51, P = 0.02), but not significantly with bupropion, although similar directions and magnitudes were observed (during treatment: OR = 0.54, P = 0.05, EOT: OR = 0.59, P = 0.08). In addition, the rs588765(T) allele was associated with abstinence with gum during treatment (OR = 2.31, P < 0.01). The SNP rs16969968 occurred at a low frequency and was not consistently associated with abstinence. CHRNA5-A3-B4 variants were not associated with tobacco consumption, and adjustments for smoking behaviors did not alter the associations with smoking abstinence. Together, our data suggest that among African Americans, CHRNA5-A3-B4 variants are not associated with baseline smoking but can influence smoking abstinence during active pharmacotherapy.
PMID: 24730978 [PubMed - indexed for MEDLINE] FMCID: FMC4111775 [Available on 2015/01/]

Subtipus de receptors de

Acetilcolina

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Ann N Y Acad Sci. 2014 Apr 14. doi: 10.1111/nyas.12421. [Epub ahead of print]
Diverse strategies targeting $\alpha 7$ homomeric and $\alpha 6\beta 2$ heteromeric nicotinic acetylcholine receptors for smoking cessation.
Brunzell DJ¹, McIntosh JM, Pappas RL.

Author information
¹Department of Pharmacology and Toxicology, Interdisciplinary Neuroscience Program and Institute for Drug and Alcohol Studies, Virginia Commonwealth University School of Medicine, Richmond, Virginia.

Abstract
Preclinical studies suggest that a diversity of nicotinic acetylcholine receptors (nAChRs) with different sensitivities to nicotine may contribute to tobacco addiction. Using rodent intravenous self-administration as a preclinical model with good predictive validity for therapeutic efficacy for tobacco cessation, investigators have identified heteromeric $\alpha 6\beta 2$ and homomeric $\alpha 7$ nAChRs as promising novel therapeutic targets to promote smoking abstinence ("denotes possible assembly with other subunits). The data suggest that diverse strategies that target these subclasses of nAChRs, namely inhibition of $\alpha 6\beta 2$ nAChRs and stimulation of $\alpha 7$ nAChRs, will support tobacco cessation. $\alpha 6\beta 2$ nAChRs, members of the high-affinity family of $\beta 2$ nAChRs, function similarly to $\alpha 4\beta 2$ nAChRs, the primary target of the FDA-approved drug varenicline, but have a much more selective neuroanatomical pattern of expression in catecholaminergic nuclei. Although activation of $\beta 2$ nAChRs facilitates nicotine self-administration, stimulation of $\alpha 7$ nAChRs appears to negatively modulate both nicotine reinforcement and $\beta 2$ nAChR function in the mesolimbic dopamine system. Although challenges and caveats must be considered in the development of therapeutics that target these nAChR subpopulations, an accumulation of data suggests that $\alpha 7$ nAChR agonists, partial agonists, or positive allosteric modulators and $\alpha 6\beta 2$ nAChR antagonists, partial agonists, or negative allosteric modulators may prove to be effective therapeutics for tobacco cessation.
© 2014 New York Academy of Sciences.

KEYWORDS: drug development, nicotine dependence, nicotinic, smoking cessation, $\alpha 6$, $\alpha 7$

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Etc...

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[Ann Pharmacother](#). 2014 Nov;48(11):1445-1455. Epub 2014 Aug 5.

Varenicline in the Treatment of Alcohol Use Disorders.

Erwin BL¹, Slaton RM².

Author information

Abstract

OBJECTIVE: To summarize the efficacy and safety data for the use of varenicline in the treatment of alcohol use disorders.

DATA SOURCES: A literature search was conducted in PubMed, International Pharmaceutical Abstracts, and Cochrane Library (through May 2014). Key search terms included varenicline, alcohol, alcohol dependence, alcoholism, ethanol, and nicotinic acetylcholine receptor. Additional references were identified from literature citations.

STUDY SELECTION AND DATA EXTRACTION: Results were limited to clinical trials and case reports that discussed either the use of varenicline in alcohol drinking patients or adverse effects experienced with its use. Only English language studies in humans were reviewed.

DATA SYNTHESIS: In all, 7 randomized, placebo-controlled clinical trials and 1 open-label study were identified that evaluated the impact of varenicline on various drinking-related end points. The studies were conducted in patients dependent on alcohol (n = 4), non-alcohol-dependent patients (n = 3), and patients with a history of alcohol dependence but who had been abstinent for at least 6 months (n = 1). The majority of the studies classified their participants as heavy drinkers; however, this definition varied across studies. Most studies included smokers, but 2 trials included both smokers and nonsmokers.

CONCLUSIONS: Evidence supports the use of varenicline for the reduction of alcohol craving as well as for the reduction of overall alcohol consumption in patients with alcohol use disorders. However, it is not likely to improve abstinence rates. Although most of the data were derived from patients with concurrent nicotine dependence, the effects of varenicline appear to occur independent of baseline smoking status.

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KEYWORDS: alcohol; alcohol dependence; alcoholism; ethanol; nicotinic acetylcholine receptor; varenicline

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Varenicline reduces alcohol self-administration in heavy-drinking smokers. ... [Biol Psychiatry. 2009]

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Varenicline in the Treatment of Alcohol Use

I potser aviat veurem Varenicline també en tractament del craving en deshabituació alcohòlica...

Νομα διεχτιπα ευροπεα σοβρε “παθυετατγε” δελ ταβαχ normativa europea sobre “paquetatge” del tabac

- Prohíbe los cigarrillos y el tabaco de liar con **aromas característicos**. (*incluido el mentol*)
- Obliga a la industria tabacalera a **informar en detalle a los Estados miembros sobre los ingredientes que utiliza en sus productos** (en particular, los cigarrillos y el tabaco de liar)
- Exige que se incluyan **advertencias sanitarias** en los envases de los productos del tabaco y los productos relacionados. Las advertencias combinadas (imágenes y texto) deben cubrir el **65% de las caras anterior y posterior en el caso de los cigarrillos y el tabaco de liar**.
- Elimina los **envases pequeños** para determinados productos del tabaco. (*no <20cigarrillos o 30gr tabac liar, no “slim”,no envases con otras formas*)
- Excluye todo tipo de **elementos promocionales o engañosos** sobre los productos del tabaco.
- Prevé un **sistema de seguimiento y rastreo a nivel de la UE** para combatir el comercio ilícito de los productos del tabaco.

- Permite que los Estados miembros **prohíban las ventas por internet** de los productos del tabaco y los productos relacionados.
- Establece requisitos de calidad y seguridad para los **cigarrillos electrónicos**.
- Obliga a los fabricantes a **notificar los productos del tabaco novedosos**, antes de introducirlos en el mercado de la UE.



Marca nivells màxims de quitrà (10), nicotina (1) i CO (10) x cigarreta (però sense figurar en el paquet de tabac els gr d'ells per evitar “pensar en el menys dolent el que menys té”)

No incorpora obligació “etiquetat genèric” com a Austràlia

No afecta a normativa del cultiu del tabac

Inici aplicació maig 2014 però 2 anys de moratòria i fins a 4 per alguns aspectes com les cigarretes mentolades

En resum, i pel dia a dia de la consulta:

- *Cal supervisar el pes durant el deixar de fumar i fer especial atenció als/les que augmenten $>1\text{kg}$ al mes en els primers mesos
- *Probablement la TSN es menys eficaç en dones molt fumadores i en joves tots els tractaments tenen menys eficàcia
- *Han aparegut noves dosis de comprimits nicotina i formulació en spray bucal però encara no podem valorar en el nostre medi la seva utilitat, respecte a les fórmules prèvies.
- *Ús molt prudent dels pegats de nicotina en embarassades i amb control de la TA.
- *Combinació de diverses formes de TSN tenen eficàcia similar a Varenicline

En resum, i pel dia a dia de la consulta (II):

*No hi ha evidència clara d'augment d'events CV ni psiquiàtrics amb Varenicline i Bupropion

*La combinació de varenicline + pegats nicotina, si be és segura no sembla augmentar l'efecicàcia encara que cal confirmar-ho en grans fumadors

*La combinació de varenicline i bupropion podria augmentar l'efecicàcia a l'any en fumadors de elevada dependència i consum, però cal confirmació

Moltes Gràcies

Agraïments a la DUI M^a Angeles Santos i als Companys/es del Grapat per la seva col·laboració en aquesta ponència

FELICITATS ÒSCAR