IV Jornada Societat Catalana pel Control i Tractament del Tabaquisme

Actualitzacions/ Revisions en el tractament del tabaquisme

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SCATT
Societat Catalana pel Control i Tractament del Tabaquisme

L'Acadèmia

14 de febrer de 2014

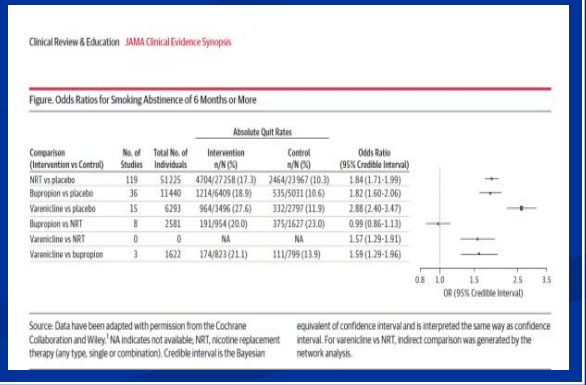
Tractament del tabaquisme

- La majoria dels fumadors deixen per **sí mateixos: consell mínim**
- Enfocament **multidisciplinar** als que necessiten ajuda:
  - Teràpia **psicològica - conductual** + **tractament farmacològic** + **seguiment** (6 mesos – 1 any...):
    - **OR :3,25 (2,05-5,15).** Addiction. 2013 dec 20 . Real –word effectiveness of smoking cessation treatments::a population study
  - Importància **professional expert**: baixes taxes d'èxit sense suport conductual
- L'**objectiu** del tractament farmacològic:
  - Disminuir la síndrome d'abstinència i fer que les primers setmanes els símptomes siguin menys intensos.

Consideracions generals del tractament del tabaquisme

- Els fàrmacs de primera línia son **cost-efectius** i **segurs**
- S'han **d'oferir a totes les persones** que vulguin deixar de fumar.
- Considerar **contraindicacions** abans d'iniciar un tractament.
- Efectes adversos **escassos i reversibles** en 24-48h.
- Poques possibilitats de **sobredosificació**

- Les **combinacions augmenten eficàcia**:
  - **Combinació de TSN**
  - **(Vareniclina + TSN)**
  - **(Bupropion + TSN)**
  - **(Vareniclina +Bupropion: NO)**



Clinical Review & Education JAMA Clinical Evidence Synopsis

Figure. Odds Ratios for Smoking Abstinence of 6 Months or More

Comparison (Intervention vs Control)	No. of Studies	Total No. of Individuals	Absolute Quit Rates: Intervention n/N (%)	Absolute Quit Rates: Control n/N (%)	Odds Ratio (95% Credible Interval)
NRT vs placebo	119	51225	4704/27258 (17.3)	2464/23967 (10.3)	1.84 (1.71-1.99)
Bupropion vs placebo	36	11440	1214/6409 (18.9)	535/5031 (10.6)	1.82 (1.60-2.06)
Vareniciline vs placebo	15	6293	964/3496 (27.6)	332/2797 (11.9)	2.88 (2.40-3.47)
Bupropion vs NRT	8	2581	191/954 (20.0)	375/1627 (23.0)	0.99 (0.86-1.13)
Vareniciline vs NRT	0	0	NA	NA	1.57 (1.29-1.91)
Vareniciline vs bupropion	3	1622	174/823 (21.1)	111/799 (13.9)	1.59 (1.29-1.96)

Source: Data have been adapted with permission from the Cochrane Collaboration and Wiley.[1] NA indicates not available; NRT, nicotine replacement therapy (any type, single or combination). Credible interval is the Bayesian equivalent of confidence interval and is interpreted the same way as confidence interval. For vareniciline vs NRT, indirect comparison was generated by the network analysis.

- Cahill K, Stevens S, Lancaster T. **Farmacological treatments for Smoking Cessation**. JAMA Jan 8, 2014; 311 (2):193-4
- Steinberg M et al . Preventive Medicine 42 (2006) 114-119.

Tractaments que han demostrat la seva eficàcia

- **Nicotina (TSN)** (NICOTINELL) – (NICORETTE) (NIQUITIN)
  - **Pegats** : 21 – 14- 7 mgrs/24h i 15 – 10- 5 mgrs / 16 h
  - **Xiclets** 2 mgrs / 4 mgrs
  - **Comprimits** 1 mgrs – 1,5 mgrs/ 2 mgrs/ 4 mgrs
  - **Spray bucal / Spray nasal / Inhalador**
- **Vareniclina** (CHAMPIX)
  - Comprimits 0,5 – 1 mgrs
- **Bupropion** (ZYNTABAC /ELONTRIL)
  - Comprimits 150 mgrs

Eficàcia dels Tractaments

Comparació	N assaijos	Nº Participants	OR combinat (IC 95%)
NTR vs placebo	119	51225	1,84 (1,71–1,99)
Bupropion vs placebo	36	11440	1,82 (1,60– 2,06)
Vareniclina vs placebo	15	6293	2,88 (2,40–3,47)
Bupropion vs NTR	8	2581	0,99 (0,86–1,13)
Vareniclina vs TSN	0	0	1,57 (1,29–1,91)
Vareniclina vs bupropion	3	1622	2,48 (1,24–4,94)
Combinació vs monoteràpia	7	3.202	1,59 (1,29–1,96)

1.- *Cochrane Database Syst Rev*.. 2012; 11 (11): CD000146. doi:10.1002/ 14651858.CD000146.pub4

Contraindicacions

EMBARAS

VARENICLINA

ULCERA GD ACTIVA

TRASTORN DERMATOLOGIC (PEGAT)

TRASTORNS DENTARIS (XICLETS)

ESOFAGITIS ACTIVA (COMPRIMITS)

TSN - PEGAT

XICLET

COMPRIMIT

SPRAY

EMBARAS

TRASTORN BIPOLAR

CRISIS CONVULSIVES

ANOREXIA O BULIMIA

TUMOR SNC

IMAOS

CIRROSIS HEPATICA GREU

BUPROPION

Vareniclina (Champix [R])

- Inici **1 setmana abans** de deixar de fumar.

Dies 1–3:	**0,5 mg 1 vegada al dia**	**(1-0-0)**
Dies 4–7:	**0,5 mg 2 vegades al dia**	**(1-1-0)**
Dia 8– final del tractament	**1 mg dos vegades al dia**	**(1-1-0)**

- Durada del tractament: 12 setmanes.
- Temps màxim: 24 setmanes a 1 mg 2 vegades/dia.
- En I.H., gent gran e I.R. lleu o moderada **no ajustar les dosis**.
- **En I.R. greu**: dosis inicial 0,5 mg/dia durant 3 dies, després 1 mg/dia. **(0,5-0,5-0)**

Vareniclina (Champix [R])

- **Controls dels efectes adversos(EA) a l'inici del tractament:** (7-10 dies després dia D i després als 15 dies de la visita anterior).
- **Prendre després de l'esmorzar i dinar o berenar:**
  - **Per evitar nàusees i vòmits**
  - **Per evitar insomni**
  - **Major efecte durant la tarda**
- Si EA els primers dies : probablement canvi de tractament
- Si apareixen EA s'ha de reduir la dosi i si persisteixen retirar
- En casos de **malalties psiquiàtriques associades**, cardiovasculars s'ha de fer un **seguiment més acurat** per professionals experts en unitats especialitzades.

Vareniclina - Pacients depressius ?

ORIGINAL RESEARCH | Annals of Internal Medicine

Effects of Varenicline on Smoking Cessation in Adults With Stably Treated Current or Past Major Depression

A Randomized Trial

Robert M. Anthenelli, MD; Chad Morris, PhD; Tanya S. Ramey, MD, PhD; Sarah J. Dubrava, MS; Kostas Tsilkos, MD; Cristina Russ, MD; and Carla Yunis, MD, MPH

Background: Depression is overrepresented in smokers.

Objective: To evaluate smoking abstinence and changes in mood and anxiety levels in smokers with depression treated with varenicline versus placebo.

Design: Phase 4, multicenter, parallel, 1:1 allocation, double-blind, randomization trial. Randomization, stratified by antidepressant use

Limitations: Some data were missing, and power to detect differences between groups was low in rare events. Smokers with untreated depression, with co-occurring psychiatric conditions, or receiving mood stabilizers and antipsychotics were not included.

Conclusion: Varenicline increased smoking cessation in smokers with stably treated current or past depression without exacerbating depression or anxiety.

Primary Funding Source: Pfizer.

Ann Intern Med. 2013;159:390-400. www.annals.org

groups, respectively, completed the study. Varenicline-treated par-

ticipants had higher CARs versus placebo at weeks 9 to 12 (35.9% vs. 15.6%; odds ratio [OR], 3.35 [95% CI, 2.16 to 5.21]; $P <$ 0.001), 9 to 24 (25.0% vs. 12.3%; OR, 2.53 [CI, 1.56 to 4.10]; $P <$ 0.001), and 9 to 52 (20.3% vs. 10.4%; OR, 2.36 [CI, 1.40 to 3.98]; $P =$ 0.001). There were no clinically relevant differences between groups in suicidal ideation or behavior and no overall worsening of depression or anxiety in either group. The most frequent adverse event was nausea (varenicline, 27.0%; placebo, 10.4%). Two varenicline-group participants died during the non-treatment phase.

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Conclusion: Varenicline increased smoking cessation in smokers with stably treated current or past depression without exacerbating depression or anxiety.

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For author affiliations, see end of text.

Vareniclina - Altres trastorns psiquiàtrics ?

Original Investigation

Maintenance Treatment With Varenicline for Smoking Cessation in Patients With Schizophrenia and Bipolar Disorder
A Randomized Clinical Trial

A. Eden Evins, MD, MPH; Corinne Cather, PhD; Sarah A. Pratt, PhD; Gladys N. Pachas, MD; Susanne S. Hoeppner, PhD; Donald C. Goff, MD; Eric D. Achtyes, MD, MS; David Ayer, PhD; David A. Schoenfeld, PhD

Supplemental content at jama.com

IMPORTANCE It is estimated that more than half of those with serious mental illness smoke tobacco regularly. Standard courses of pharmacotherapeutic cessation aids improve short-term abstinence, but most who attain abstinence relapse rapidly after discontinuation of pharmacotherapy.

OBJECTIVE To determine whether smokers diagnosed with schizophrenia and bipolar disease have higher rates of prolonged tobacco abstinence with maintenance pharmacotherapy than with standard treatment.

RESULTS Sixty-one participants completed the relapse-prevention phase; 26 discontinued participation (7 varenicline, 19 placebo) and were considered to have relapsed for the analyses; 18 of these had relapsed prior to dropout. At week 52, point-prevalence abstinence rates were 60% in the varenicline group (24 of 40) vs 19% (9 of 47) in the placebo group (odds ratio [OR], 6.2; 95% CI, 2.2-19.2; $P < .001$). From weeks 12 through 64, 45% (18 of 40) among those in the varenicline group vs 15% (7 of 47) in the placebo group were continuously abstinent (OR, 4.6; 95% CI, 1.5-15.7; $P = .004$), and from weeks 12 through 76, 30% (12 of 40) in the varenicline group vs 11% (5 of 47) in the placebo group were continuously abstinent (OR, 3.4; 95% CI, 1.02-13.6; $P = .03$). There were no significant treatment effects on psychiatric symptom ratings or psychiatric adverse events.

CONCLUSIONS AND RELEVANCE Among smokers with serious mental illness who attained initial abstinence with standard treatment, maintenance pharmacotherapy with varenicline and cognitive behavioral therapy improved prolonged tobacco abstinence rates compared with cognitive behavioral therapy alone after 1 year of treatment and at 6 months after treatment discontinuation.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00621777

JAMA. 2014;311(2):145-154. doi:10.1001/jama.2013.285113

Vareniclina - Pacients cardíacs ?

BMJ

BMJ 2012;344:e2856 doi: 10.1136/bmj.e2856 (Published 4 May 2012) Page 1 of 11

RESEARCH

Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis

OPEN ACCESS

Judith J Prochaska *associate professor*[1], Joan F Hilton *professor*[2]

[1]Department of Psychiatry and Center for Tobacco Control Research and Education, University of California, San Francisco, CA 94143-0984; [2]Department of Epidemiology and Biostatistics, University of California

What is already known on this topic

There have been drug safety concerns about the use of varenicline for tobacco cessation and the emergence of cardiovascular serious adverse events

However, this association has since been called into question, owing to less than optimal methodology used, and the US FDA has called for further analysis

What this study adds

Our meta-analysis of all published, randomised controlled trials of varenicline use for tobacco cessation included 50% more studies than a previous meta-analysis by Singh and colleagues; used an unbiased summary estimate and compared findings with three other estimates; and examined events that occurred during drug treatment, which is more biologically relevant and obviates problems with differential drop out

All four summary estimates indicated no significant increase in the risk of treatment emergent, cardiovascular serious adverse events attributed to varenicline use

Med Clin (Barc). 2013;**xx(x)**:xxx–xxx

MEDICINA CLINICA

ELSEVIER DOYMA

www.elsevier.es/medicinaclinica

Carta científica

Síndrome coronario agudo: una complicación grave e infrecuente en la deshabituación tabáquica con vareniclina

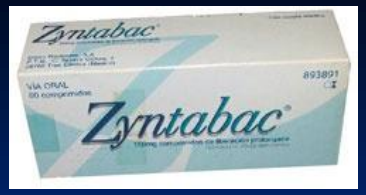
Acute coronary syndrome. An uncommon serious complication of smoking cessation with varenicline

Sr. Editor:

La vareniclina (Champix®) es uno de los fármacos más

como un agonista menor intensidad síntomas de la a (actividad agonist satisfacción asocia antagonista)[2].

Son conocidos tratamiento con v vómitos, cefalea, n



Bupropion (Zyntabac ®)

- Bupropión és un comprimit no nicotínic de liberació retardada para deixar de fumar
- Desenvolupat inicialment como antidepressiu, posteriorment es va veure que era eficaç per a deixar de fumar[1]
- Dos possibles mecanismes d'acció:
  - Bloqueig de la recaptació de dopamina[2,3]
  - Inhibició no competitiva dels receptors nicotínics α3β2 y α4β2[4,5]

1. Prospecto de bupropión SR hidrocloruro [Zyntabac®]. GlaxoSmithKline.
2. Henningfield JE, et al. *CA Cancer J Clin*. 2005;55:281–299.
3. Foulds J, et al. *Expert Opin Emerg Drugs*. 2004;9:39–53.
4. Slemmer JE, et al. *J Pharmacol Exp Ther*. 2000;295:321–327.
5. Roddy E. *Br Med J*. 2004;328:509–511.

Bupropion: tractament

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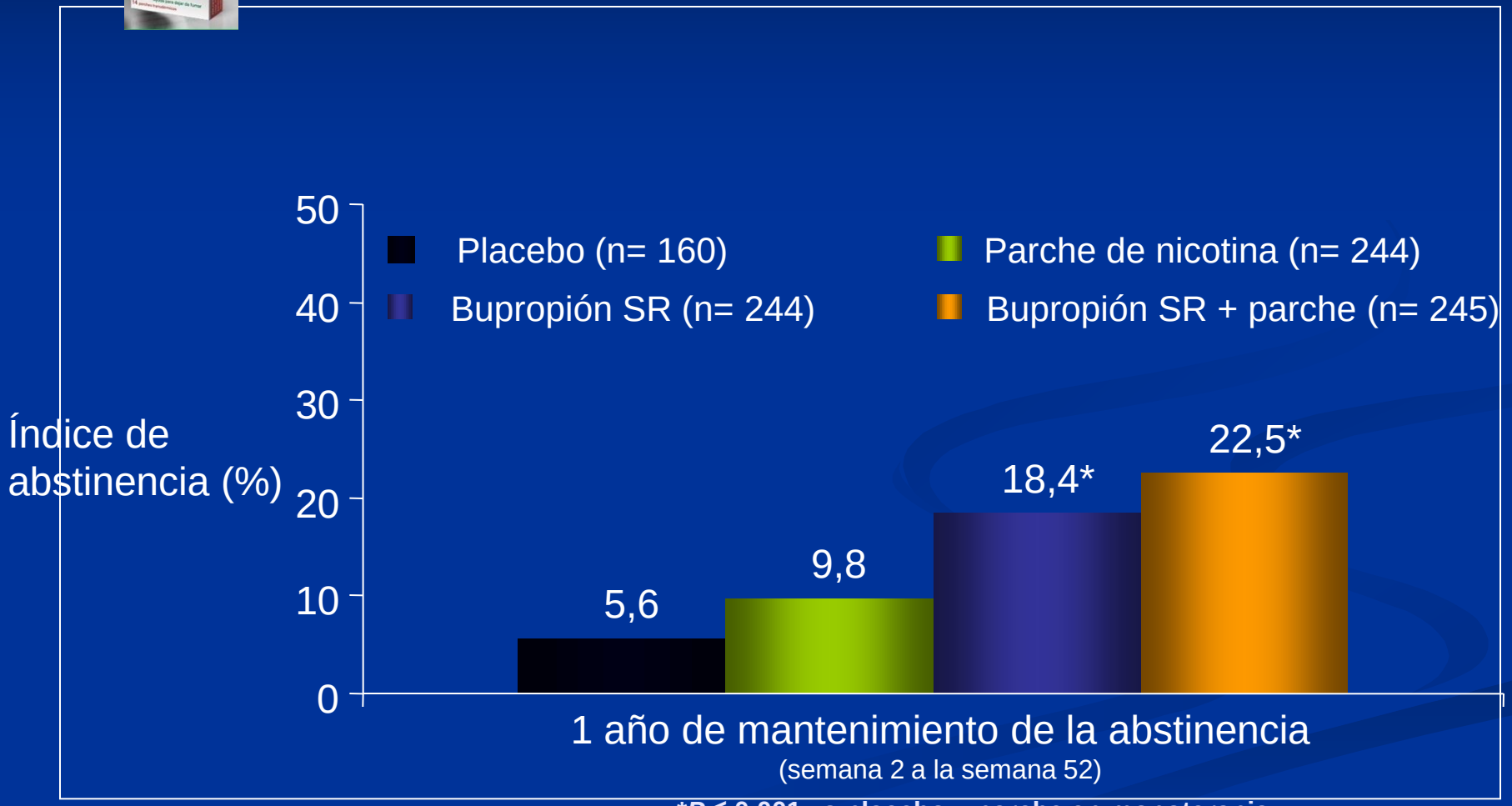
Dies 1–6:	**150 mg 1 vegada al dia**	**(1-0-0)**
Dies 7-60:	**150 mg 2 vegades al dia**	**(1-1-0)**

- En pacients **FUMADORS +DEPRESSIÓ** que no estan en tractament amb altre antidepressiu.
- Té un efecte anorexígen molt positiu
- En cas de malalties psiquiàtriques associades, fer un seguiment més acurat
- En IH, IR, DM,: 150 mgrs/dia

TSN + BUPROPION



***P* ≤ 0,001 vs placebo y parche en monoterapia.**

1. **Jorenby DE, et al. *N Engl J Med*. 1999;340:685–691.**
2. **Talwar A et al. *Med Clin North Am*. 2004;88:1517–1534.**

VARENICLINA + BUPROPION

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Research

Original Investigation

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

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

Table 2. Smoking Abstinence[a,b]

		Overall				OR (95% CI)	P Value
Week 12							
Varenicline + bupropion SR						9 (1.05-2.12)	.03
Varenicline + placebo							
Week 26							
Varenicline + bupropion SR	249	95 (38.2)	1.32 (0.91-1.91)	.14	91 (36.6)	1.52 (1.04-2.22)	.03
Varenicline + placebo	257	82 (31.9)			71 (27.6)		
Week 52							
Varenicline + bupropion SR	249	91 (36.6)	1.40 (0.96-2.05)	.08	77 (30.9)	1.39 (0.93-2.07)	.11
Varenicline + placebo	257	75 (29.2)			63 (24.5)		

Abbreviations: OR, odds ratio; SR, sustained release.

[a] Analyses were performed using logistic regression. In addition to treatment, the logistic regression analysis included a covariate for study site. ORs greater than 1.0 indicate an increased likelihood of abstinence for varenicline + bupropion SR compared with varenicline + placebo.

[b] Prolonged smoking abstinence indicates no smoking from 2 weeks after the

visit. There were 203 participants (93 varenicline + bupropion SR; 110 varenicline + placebo) who had missing abstinence data at the week 26 visit of whom 118 (56 varenicline + bupropion SR; 62 varenicline + placebo) reported smoking at the last visit or had already failed prolonged abstinence criteria. There were 198 participants (93 varenicline + bupropion SR; 105 varenicline + placebo) who had missing abstinence data at the week 52 visit of

CONCLUSIONS AND RELEVANCE Among cigarette smokers, combined use of varenicline and bupropion, compared with varenicline alone, increased prolonged abstinence but not 7-day point prevalence at 12 and 26 weeks. Neither outcome was significantly different at 52 weeks. Further research is required to determine the role of combination therapy in smoking cessation.

TSN

- Nicotina : NICOTINELL – NICORETTE - NIQUITIN)
  - Pegats : 21 – 14- 7 mgrs/24h i 15 – 10- 5 mgrs / 16 h
  - Xiclets : 2 mgrs / 4 mgrs
  - Comprimits 1 mgrs / 1,5 mgrs/ 2 mgrs/ 4 mgrs
  - Spray bucal
  - Spray nasal
  - Inhalador

TSN

- **Cost-efectiu**
- **Augmenta eficàcia:**
  - Al combinar diferents **vies d'administració** + **dosi adequada + temps necessari**
  - **Combinació** de diferents TSN i amb VARENICLINA I BUPROPION
- **Deixar de fumar del tot** el dia assenyalat
- **Reducció** progressiva : **pactada en menys motivats**
- **Recaiguda**: nou intent i nou tractament
- **Individualitzar la dosi** segons el grau de dependència:
  - 1mg de nicotina en pegat equival a 1 cigarreta.
  - 2mg de nicotina en xiclet o comprimit equival a 1 cigarreta.

Eficàcia de la TSN

Comparació	N assaijos	Nº Participants	OR combinat (IC 95%)
Xiclet	53	17.783	1,43 (1,50–1,66)
Pegat	41	16.691	1,66 (1,53–1,81)
Aerosol nasal	4	887	2,02 (1,49–3,73)
Inhalador	4	976	1,90 (1,36–2,67)
Comprimits/tablets	6	2.739	2,00 (1,63–2,45)
Spray bucal	1	479	2,48 (1,24–4,94)
Combinació vs monoteràpia	7	3.202	3,6 (2,5--5,2)
Qualsevol TSN vs control	**119**	**51.225**	**1,84(1,71–1,99)**

1.- *Cochrane Database Syst Rev.*.

Nicotina i embaràs

- Utilització: únic tractament que es pot donar a l'embaràs.
- Començar sempre a dosis mínimes i retirar-lo el més aviat possible
- Valorar eficàcia: retirar-lo si la embarassada no deixa de fumar després d'un període de 15-30 dies.
- Considerar sempre que fumar es molt pitjor que rebre qualsevol tractament

Conclusions

- Aprofitar **qualsevol moment** : hospitalització, CCEE, visita mèdica o infermera : consell mínim
- **Pactar amb el fumador el que ell es vegi capaç** d'aconseguir: sobretot en els que presenten comorbiditats
- **Sempre utilitzar suport psicològic + fàrmacs i seguiment per professional expert**
- La **teràpia combinada augmenta eficàcia** i no augmenta els EA

Moltes Gràcies

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