

Utilizamos correctamente las dosis de los diferentes tipos de tratamientos del tabaquismo

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# Assumptions in nicotine intake

1 cigarette	1,5 mg
2 mg gum	1,2
4 mg gum	2,8
2 mg lozenge	1,5
4 mg lozenge	3,4
Inhaler	13 microgram/puff

# Dosing required for full replacement

# Cigs	Nic int mg	# 2 mg gum	# 4 mg gum	# 2 mg loz	# 4 mg loz	21 mg pat	16 mg pat	# In-hal puffs
10	15	13	5	10	4	1	1	1500
20	30	25	10	20	8	1,5	1,5	3000
30	45	39	15	30	12	2	2	4500

# Is higher dose contributing to better success rates?

For gum 4mg is more effective than 2 mg in more dependent smokers, e.g. Tonnesen et al 1988, Herrera et al 1995.

Probably the same is true for the lozenges, Shiffman et al 2002.

Some evidence with patches e.g. Huges et al 1999

## Animal work

In order to substantially reduce self-administration of nicotine in rats infusions of nicotine (patch) needed to give nicotine concentrations around five times higher than the self administration concentrations.

## Combinations of different NRT preparations.

There is evidence that combining a nicotine patch with a rapid delivery form of NRT is more effective than a single NRT.

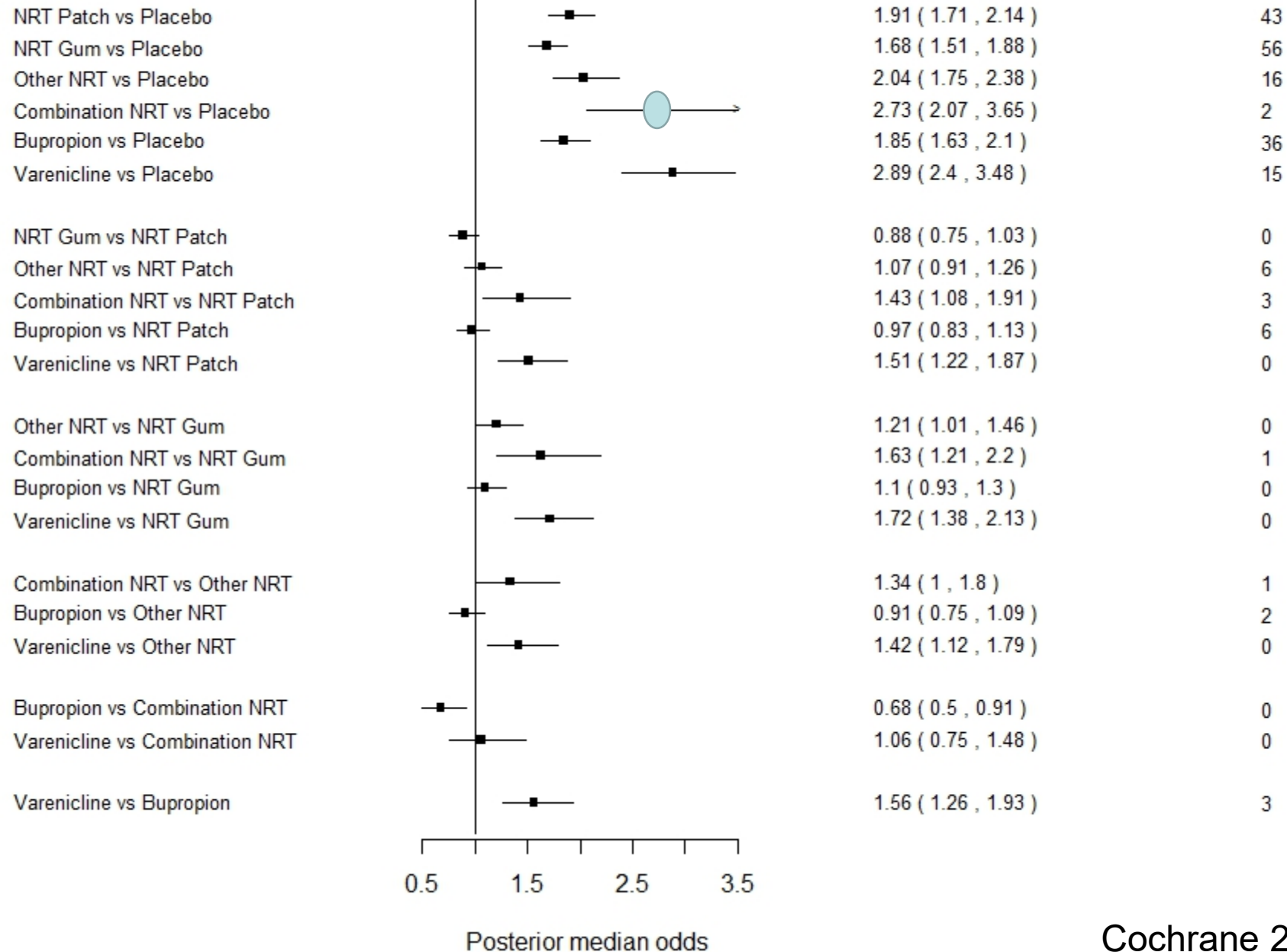
Nine trials compared the use of two types of NRT with the use of a single type only.

When pooled, the trials suggest a statistically significant benefit  
RR 1.34, 95% CI 1.18 to 1.51, 9 trials.

## Comparison

Odds ratio  
(95% credible interval)

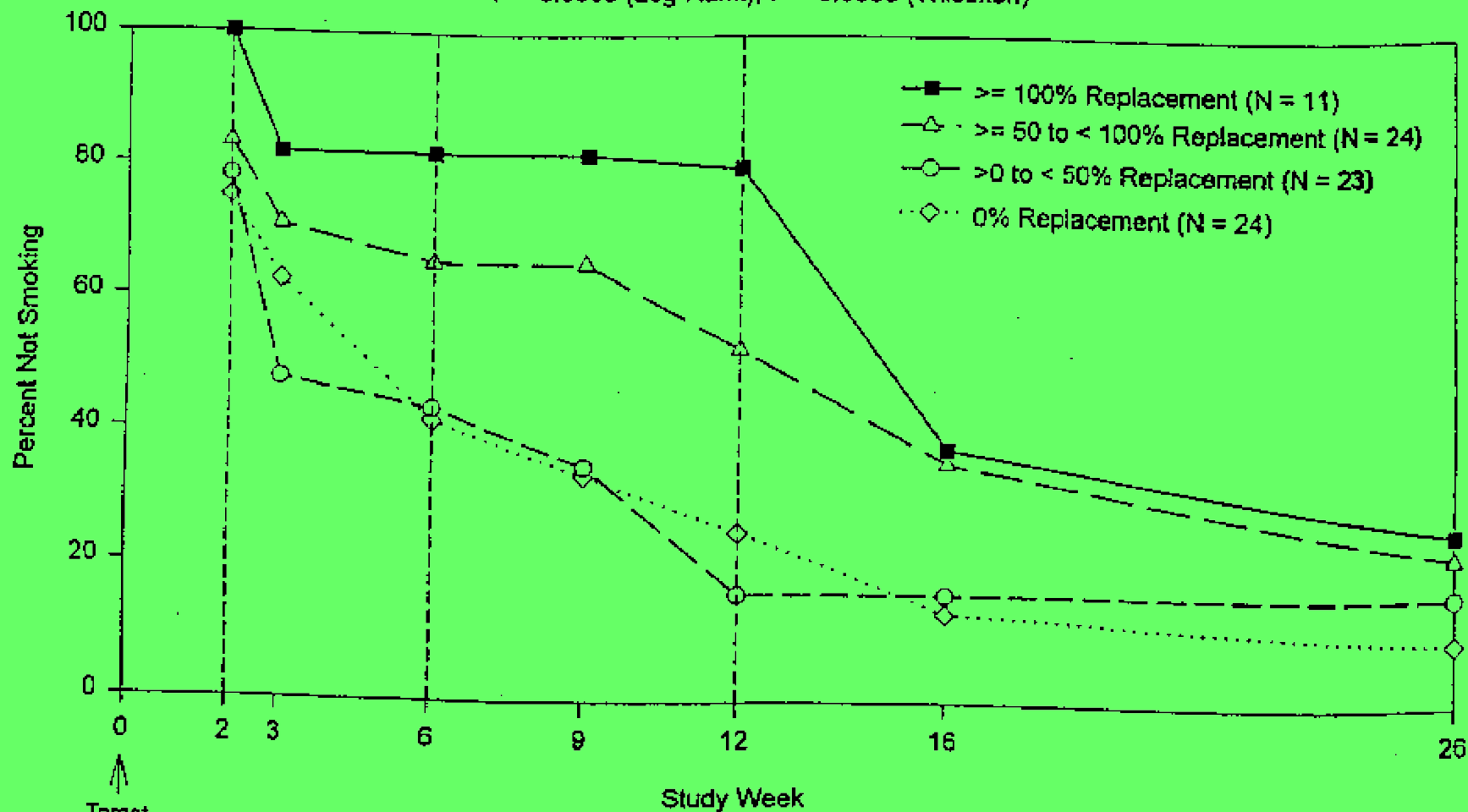
No. of studies  
(direct comparisons)



# -- Optimum Dosing Study -- Nicotine Patch --

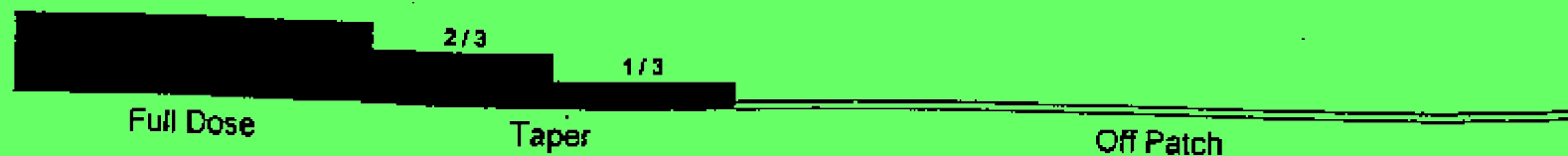
## Six Month Continuous Nonsmoking by Percent Cotinine Replacement Attained from Patch

P = 0.0385 (Log-Rank), P = 0.0336 (Wilcoxon)



Sachs et al 1995

Nicotine Patch Dose





## Adjusting NR dose according to baseline cotinine level.

Design: Randomized multicenter in France N=310 with comorbidities

Standard care group. Nicotine patch with possibility of acute NR

Dose adaptation group. Aim to reach 100% nicotine substitution

determined by saliva cotinine

Abstinence

Standard care

Dose adaptation

8%

12%

# Concurrent Use of Cigarettes and Nicotine Patches

Percent change in blood nicotine concentration, no of cigarettes and carbon monoxide.

	Patch Dose		No of cig.	CO
	14-22mg Nicot.conc.	42-63mg Nicot.conc.		
Carpenter et al 2001	14		-55	-36
Zevin et al 1998	55	170	NA	NA
Mahmarian et al 1997	69		-70	-44
Pickworth et al 1994	105		-15	-18
Pickworth et al 1994		231	-26	-27
Foulds	22		-16	-10
<b>Average</b>	<b>53</b>	<b>200</b>	<b>-36</b>	<b>-27</b>

## Higher dose with varenicline

### Sample.

Those reporting no strong nausea, no clear reduction in enjoyment of smoking, and <50% reduction of their baseline smoking on day 12 received additional tablets of either varenicline (N=100) or placebo (N=100) up to maximum 5 mg/day).

### Results.

Abstinence	High dose	Standard dose	
1 week after quit	48%	37%	
4 “	59%	51%	
12 “	26%	23%	n.s.

**AEs.** Significantly more nausea and vomiting in higher dose group.

# Higher dose with varenicline

## Sample.

After 8 weeks of treatment, the dose was increased to 3 mg/d if patients tolerated varenicline well and continued smoking or experienced severe withdrawal symptoms. N=73 patients.

## Results

CO validated continuous abstinence rates from week 9 to week 24 were 42%.

## AEs.

Higher dose was associated with adverse events in 22 patients (30%). These were mostly mild and included nausea, vomiting, abnormal dreams, and insomnia. Only 2 patients discontinued treatment (both because of nausea and vomiting).

# Higher dose with varenicline

Sample. Tolerated varenicline, reduced smoking >50% but not able to abstain at 6 weeks

Design. These patients were offered dose increase to 3 mg. A control group was created by propensity score matching among those remaining on 2 mg.

Abstinence.	3 mg	2 mg	
3 months after dose adjustment	26%	11%	p<.01

The difference remained significant at 9 months

Adverse Events.	3 mg	2 mg
Proportion with AEs	31%	34%
No serious AEs.		

## Conclusions

- 4 mg gum and lozenges more effective than 2mg, particularly for highly dependent smokers
- Weak evidence that higher dose patch is more effective
- Combining patch with an acute form of NR more effective than single form of NR.
- More research needed on higher dose of varenicline

# HOW TO ASSIGN SMOKERS TO DIFFERENT DOSES OF NR

- NUMBER OF CIGARETTES
- GENERAL DEPENDENCE
- FAGERSTROM TEST FOR NICOTINE DEPENDENCE
- WHEN A LOW DOSE IS NOT ENOUGH

Gracias



Combining NR products has usually yielded higher success rates.

Because of

A. Higher dose

B. A tool to deal with break-through cravings

# Combining medications within NRT

Usually a patch with a more rapid delivery form

- increases the dose
- gives something to do with acute desires to smoke

[www.cochrane.org/reviews/en/ab000146.html](http://www.cochrane.org/reviews/en/ab000146.html)

US Dept of Health and Human Services 2008

# Dose

With Varenicline and Bupropion no choice.

## NRT

Patch, Gum and Lozenges in different doses.

Dependence and earlier experience can be markers for selecting dose

Underdosing common with NRT

# DEATH RATES (PER 100,000) ATTRIBUTABLE TO TOBACCO, 2004

	Sweden	European Union Member States other than Sweden		
		Min	Median	Max
<b>MEN (age 60-69)</b>				
Lung cancer	87	91	220	399
Other cancer	36	41	105	217
All cardiovascular	72	107	170	618
All causes	222	378	550	1388
<b>WOMEN (age 60-69)</b>				
Lung cancer	61	5	39	127
Other cancer	17	1	10	39
All cardiovascular	63	5	50	222
All causes	173	14	115	690

WHO Global Report Mortality Attributable to Tobacco 2012. Adapted by Lars Ramström