

Διακοπή καπνίσματος σε νοσηλευόμενους ασθενείς *(αναπνευστικούς και όχι)*

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30/1/2019

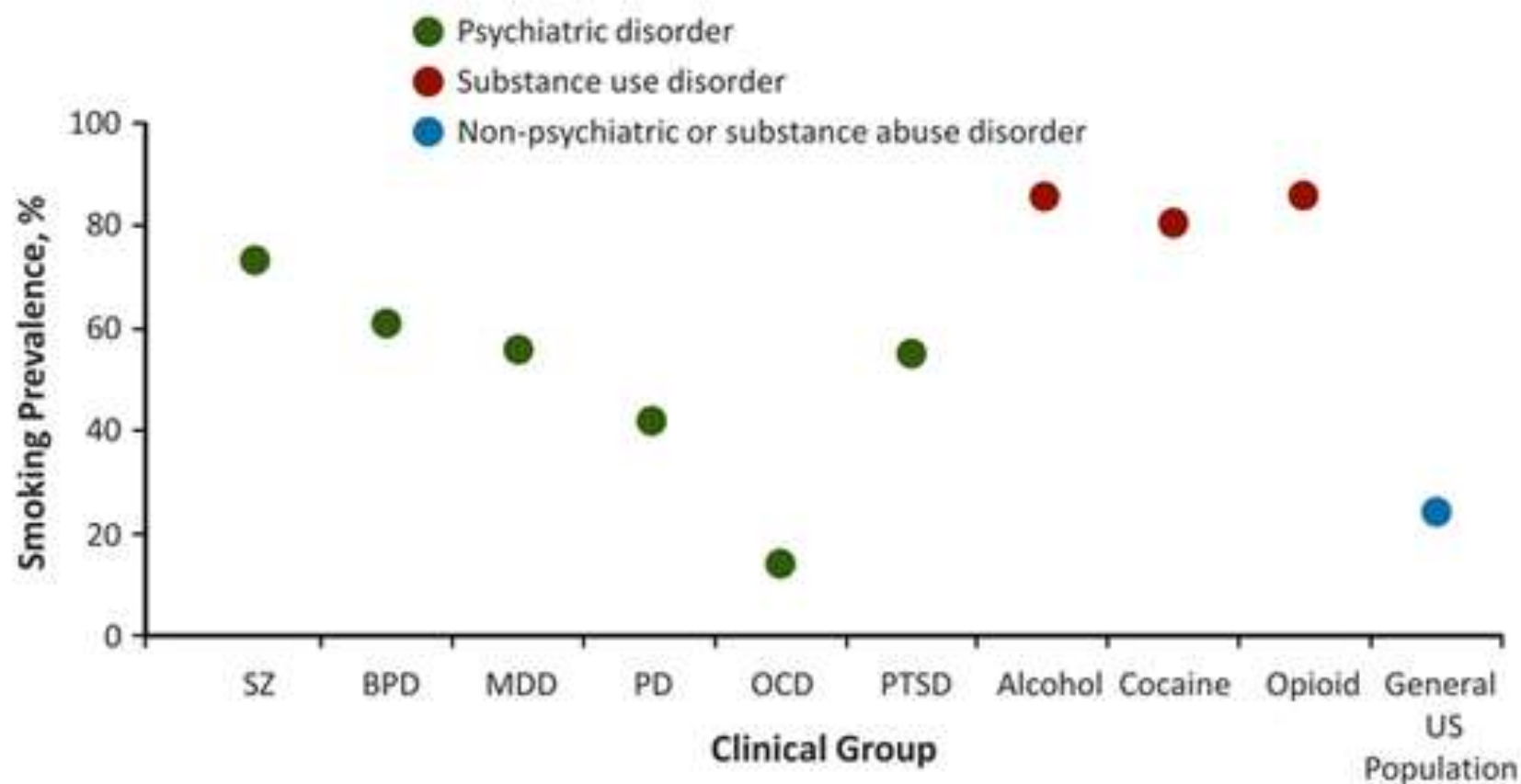
Smoking and Mental Illness — Breaking the Link

Judith J. Prochaska, Ph.D., M.P.H.

“My doctor told me I’m too stressed out to quit smoking,” remarked a woman hospitalized with severe depression. “Well, 43 years later, I’m still stressed and I’m still smoking.”

Now with also
bladder cancer and
Shortness of breath and
coughing

Smoking Rates Among Adults With Mental Illness vs Adults Without Mental Illness

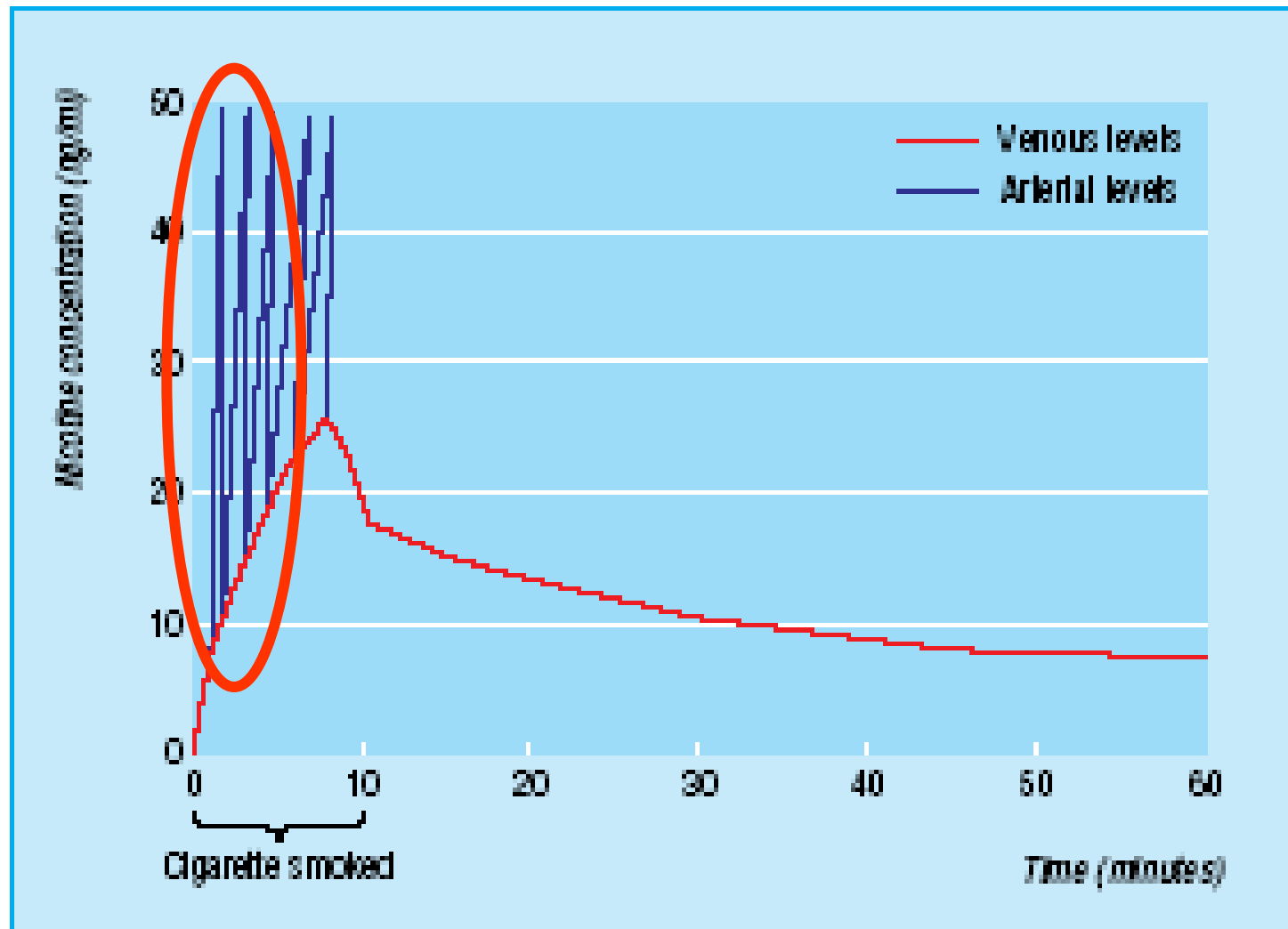


Years 2010-2016

		Total admissions	% Tobacco users
Gender	Female	185 716	24.3
	Male	170 949	31.9
Race	Caucasian	231 601	24.5
	African American	106,780	36.5
	Other	8 438	17.2
	Unknown	9 846	25.2
Age (years)	18–34	56 059	35.7
	35–49	66 320	37.7
	50–64	119 281	32.7
	65–79	85 982	16.1
	≥80	29 023	6.2
Admitting service	Internal medicine	175 456	28.6
	Cardiothoracic surgery	10 625	26.3
	General surgery	62 598	29.8
	Gynecology	12 237	19.7
	Neurology	15 534	29.6
	Neurosurgery	11 282	24.1
	Obstetrics	10 785	20.9
	Ophthalmology	1 900	20.5
	Orthopedic surgery	25 193	17.1
	Otolaryngology	6 587	28.6
	Plastic surgery	3 204	22.0
	Psychiatry	11 577	55.3
	Urology	9 687	24.2
Admission route	Not through ED	213 924	22.2
	Through ED	142 741	36.6
Length of stay	<3 days	167 279	28.3
	≥3 days	189 386	27.6

Tobacco Use Prevalence and Smoking Cessation Pharmacotherapy Prescription Patterns Among Hospitalized Patients by Medical Specialty

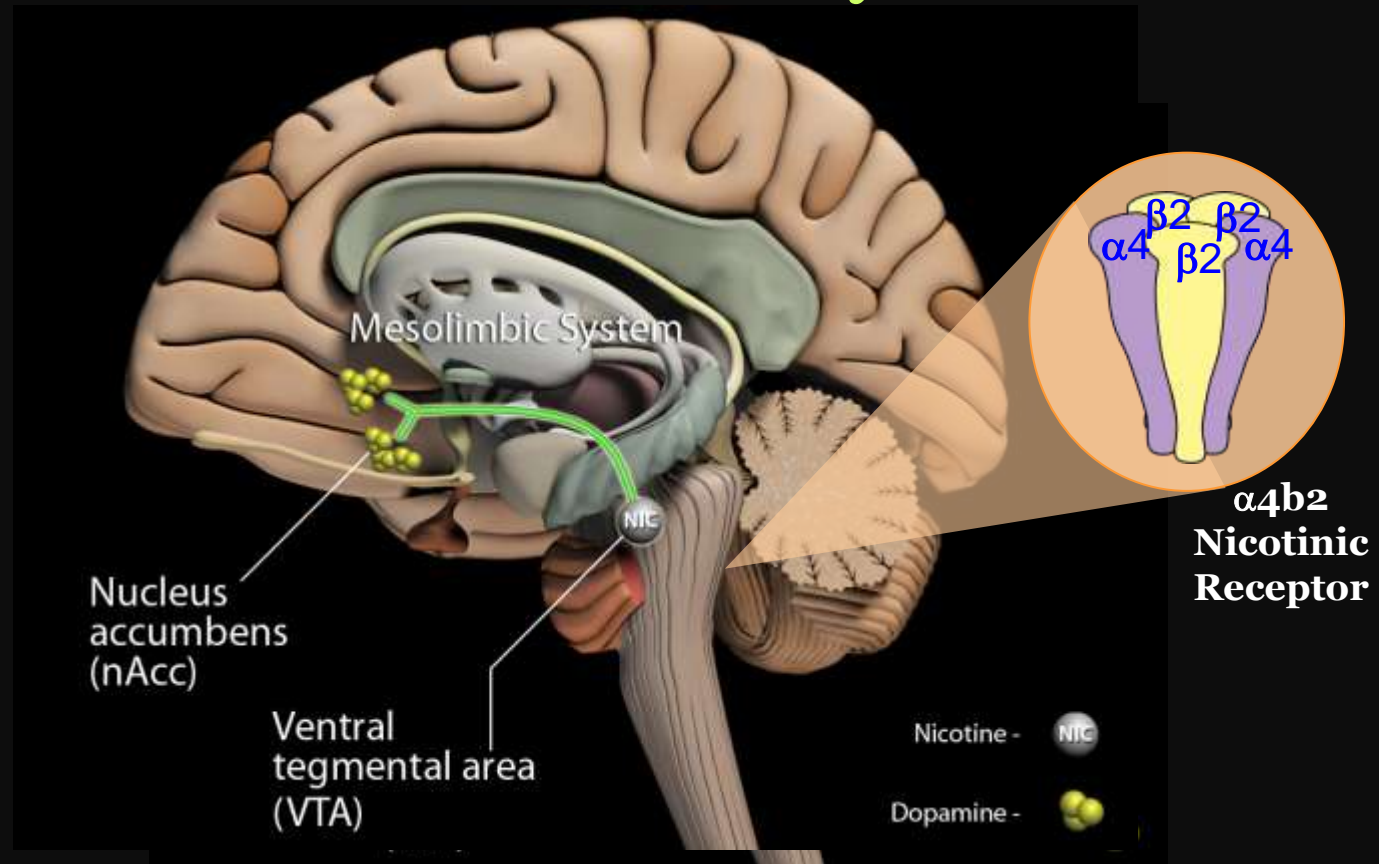
Συγκέντρωση νικοτίνης στο αίμα



Arterial and venous levels of nicotine during cigarette smoking



Mechanism of Action of Nicotine in the Central Nervous System



- Nicotine binds preferentially to nicotinic acetylcholinergic (nACh) receptors in the central nervous system; the primary is the $\alpha 4 \beta 2$ nicotinic receptor in the Ventral Tegmental Area (VTA)
- After nicotine binds to the $\alpha 4 \beta 2$ nicotinic receptor in the VTA, it results in a release of dopamine in the Nucleus Accumbens (nAcc) which is believed to be linked to reward

Nicotine Withdrawal

- Avoidance of the negative state produced by nicotine withdrawal represents a motivational component that promotes continued tobacco use and relapse after smoking cessation^[a,b]

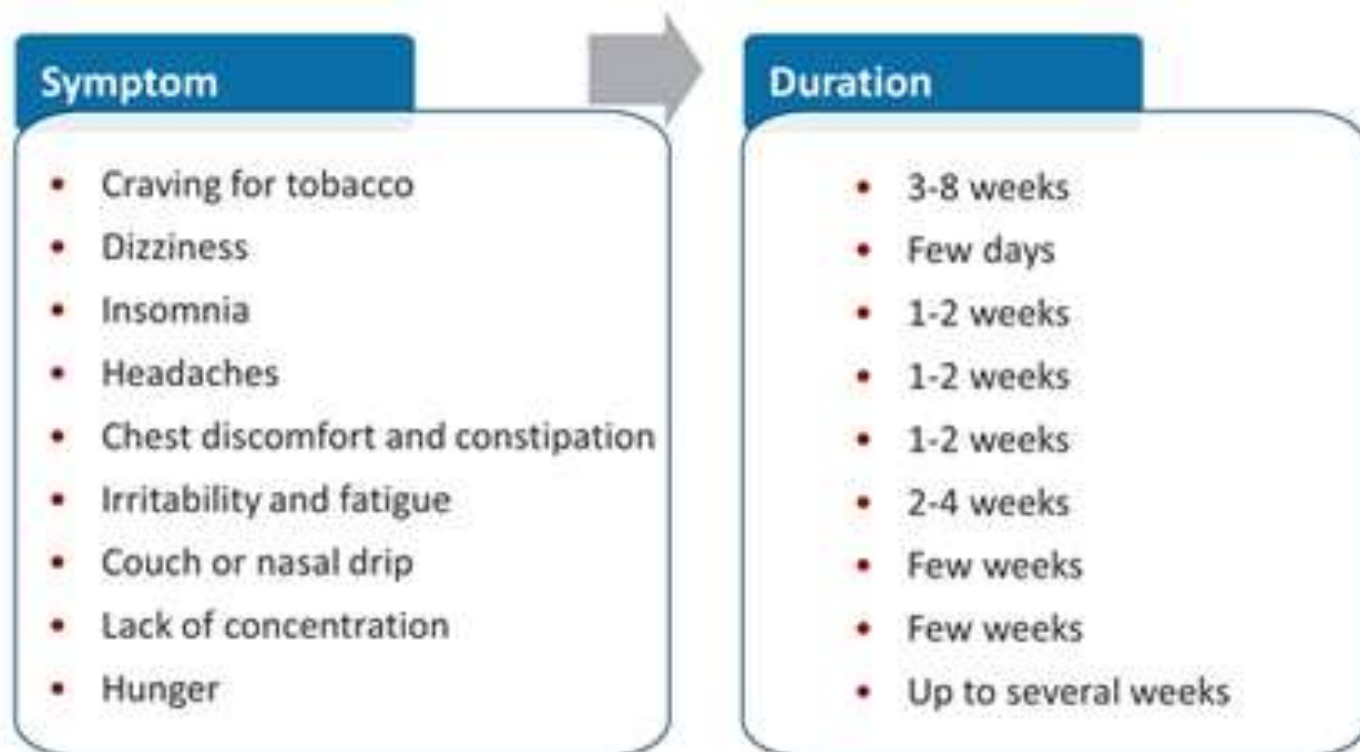


a. Jackson KJ, et al. *Neuropharmacology*. 2015 Sep;96(Pt B):223-234.

b. Hall FS, et al. *Neurosci Biobehav Rev*. 2015;58:168-185.

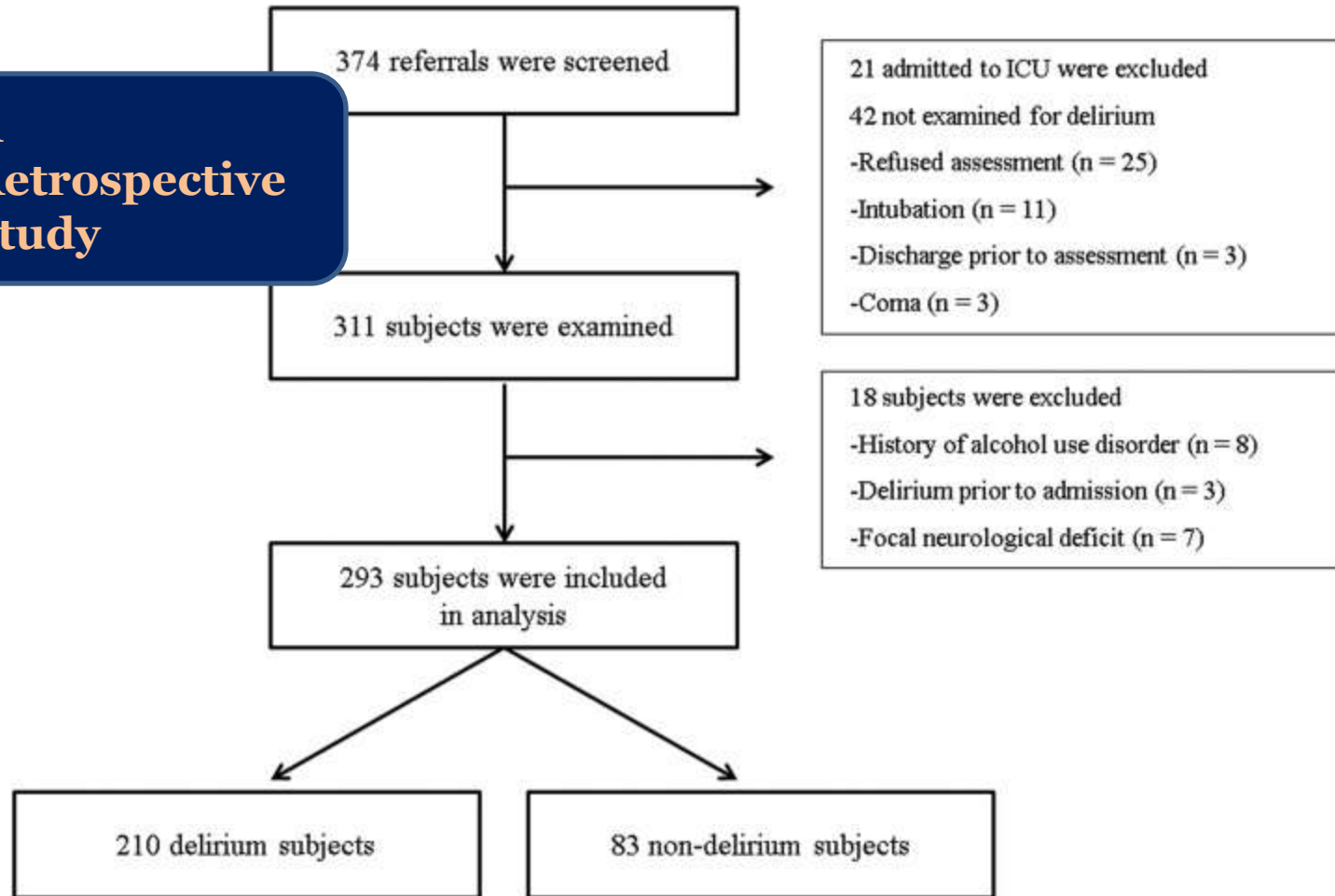
Nicotine Withdrawal Symptoms

Usually worse in the first 24-48 hours, then decline in intensity gradually over time

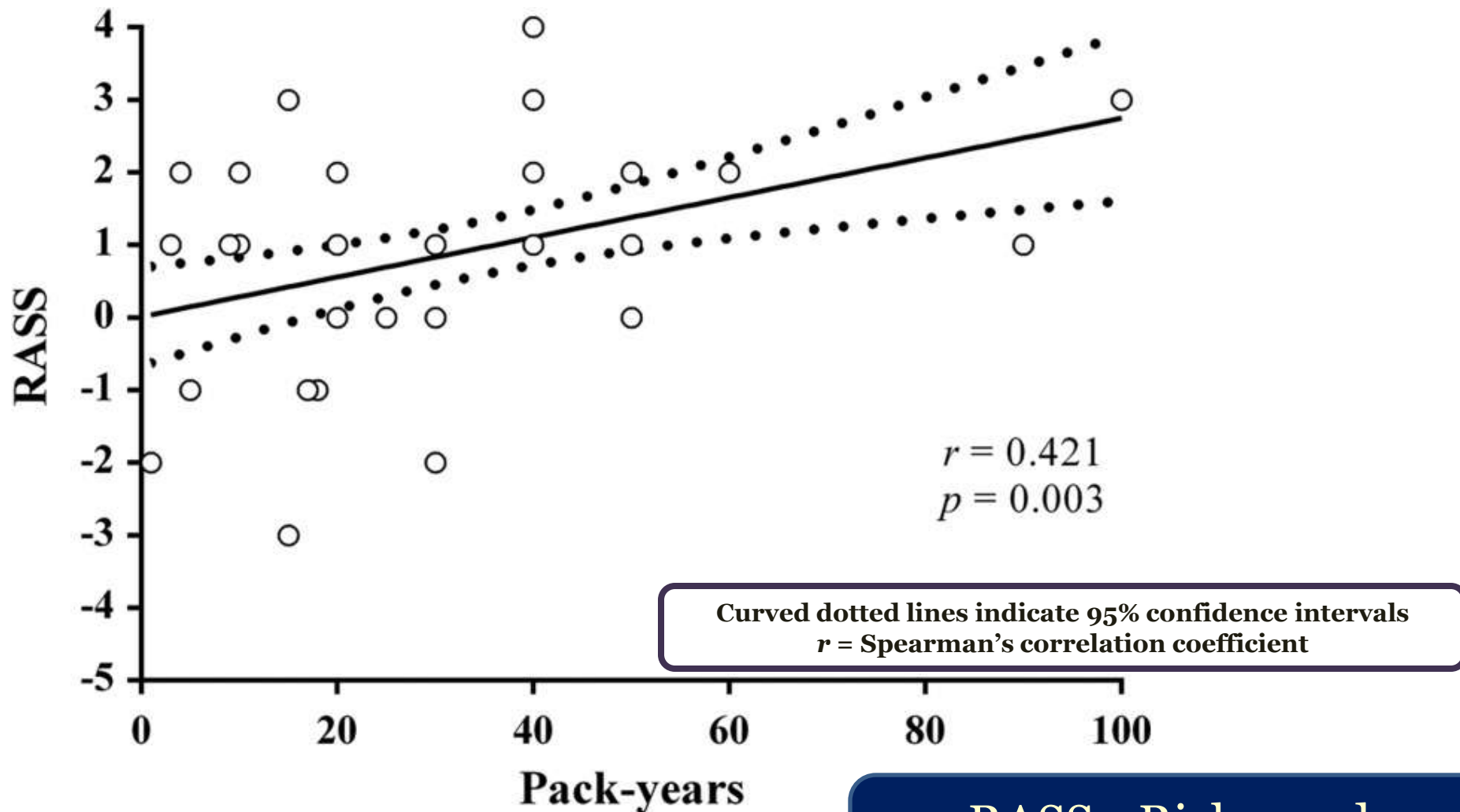


Smoking Cessation and the Risk of Hyperactive Delirium in Hospitalized Patients:

A Retrospective Study



Correlation of scores on the Richmond Agitation Sedation Scale with the amount of smoking in the smoker group



Smoking Cessation and the Risk of Hyperactive Delirium in Hospitalized Patients

- The present findings demonstrated that nicotine withdrawal was associated:

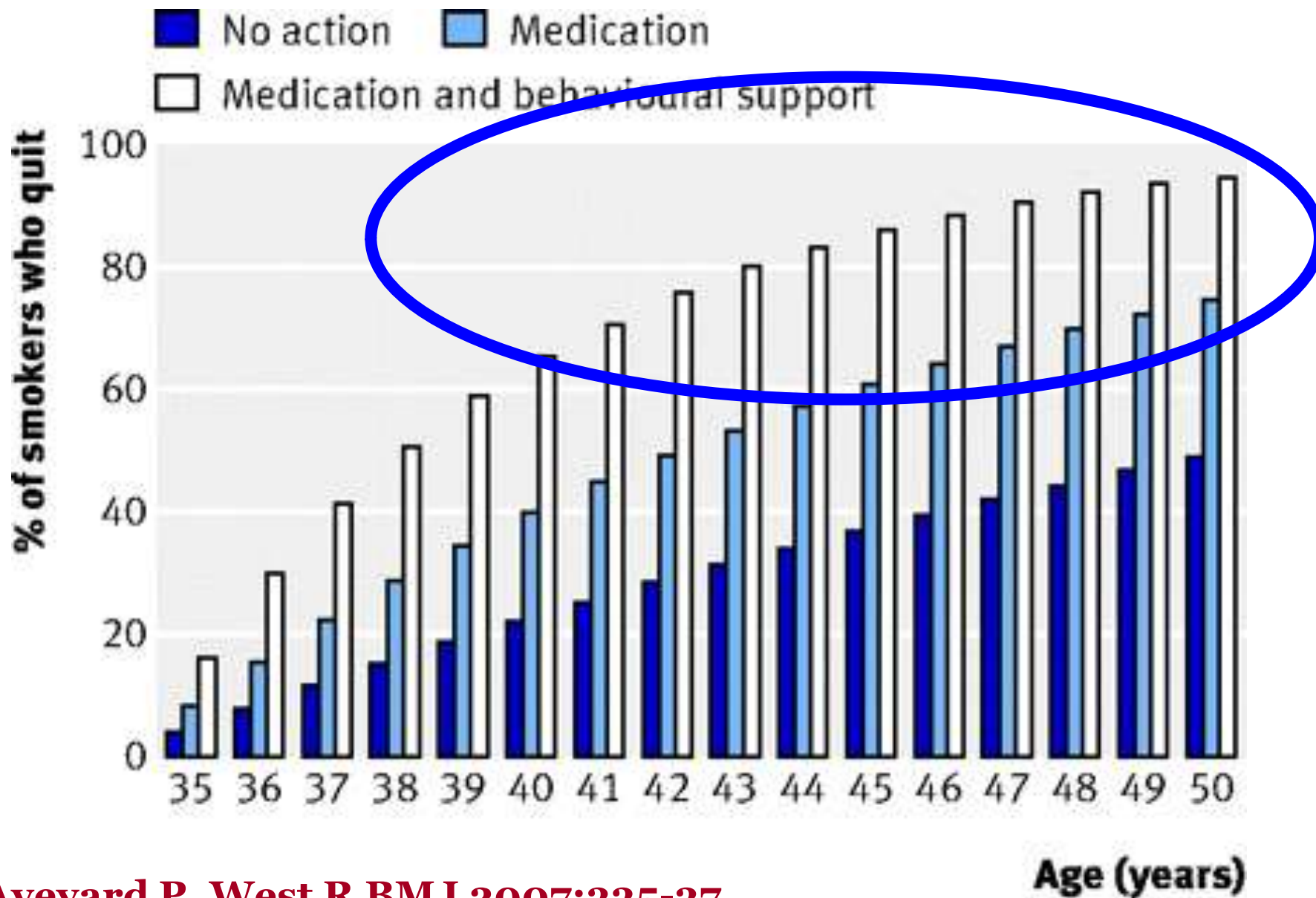
- with hyperactive

- with hypoactive

Delirium

due to drug withdrawal is more likely to be of the hyperactive subtype

whereas metabolic encephalopathy is more likely to be related with the hypoactive subtype



Aveyard P. West R BMJ 2007;335-37

Efficacious approaches for smoking cessation

- Two types of approaches have demonstrated their efficacy for smoking cessation:
 - Counseling
 - Pharmacotherapy
- The best results are obtained by combining the two approaches

Fiore MC. Treating tobacco use and dependence. *Resp Care* 2000;45:1200

West R. Smoking cessation guidelines for health professionals: an update. *Thorax* 2000;55:987

Simon JA. Smoking cessation counseling (intensive vs minimal). *Am J Med* 2003;114(7):555

Εγκεκριμένη Φαρμακοθεραπεία

στη διακοπή του καπνίσματος

- Φάρμακα που μιμούνται τη δράση της νικοτίνης
 - *Υποκατάστατα νικοτίνης*
- Φάρμακα που δρουν στο ΚΝΣ
 - *Καθυστερώντας την αποδόμηση των νευρομεταβιβαστών*
 - *HCL Bupropion*
 - *Ενεργώντας απευθείας στους υποδοχείς $\alpha 4 \beta 2$*
 - *Varenicline*

JAMA 2009

Albert L Siu Ann Internal Med 2015;163:622

Φαρμακοθεραπεία για την Διακοπή του Καπνίσματος

- **Nicotine replacement therapy**
 - Recommended first line therapy
 - Long acting
 - Patch
 - Short acting
 - Gum
 - Inhaler
 - Nasal spray
 - Sublingual tablets/lozenges
- **Bupropion**
- **Varenicline**
 - Recommended first-line therapy (WHO, US, Europe, UK)
- **Nortriptyline**
 - Recommended second-line therapy (WHO, US)
- **Clonidine**
 - Recommended second-line therapy in some countries

↑ ↑ side effects:
dizziness
sedation, ↓ BP



Lung Health Study Results

- 11 year abstinence
 - 22% intervention vs. 6% control ¹
- 11 year FEV1 decline per year

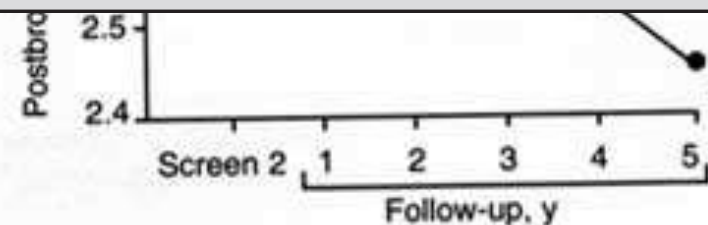
CLINICAL YEAR IN REVIEW

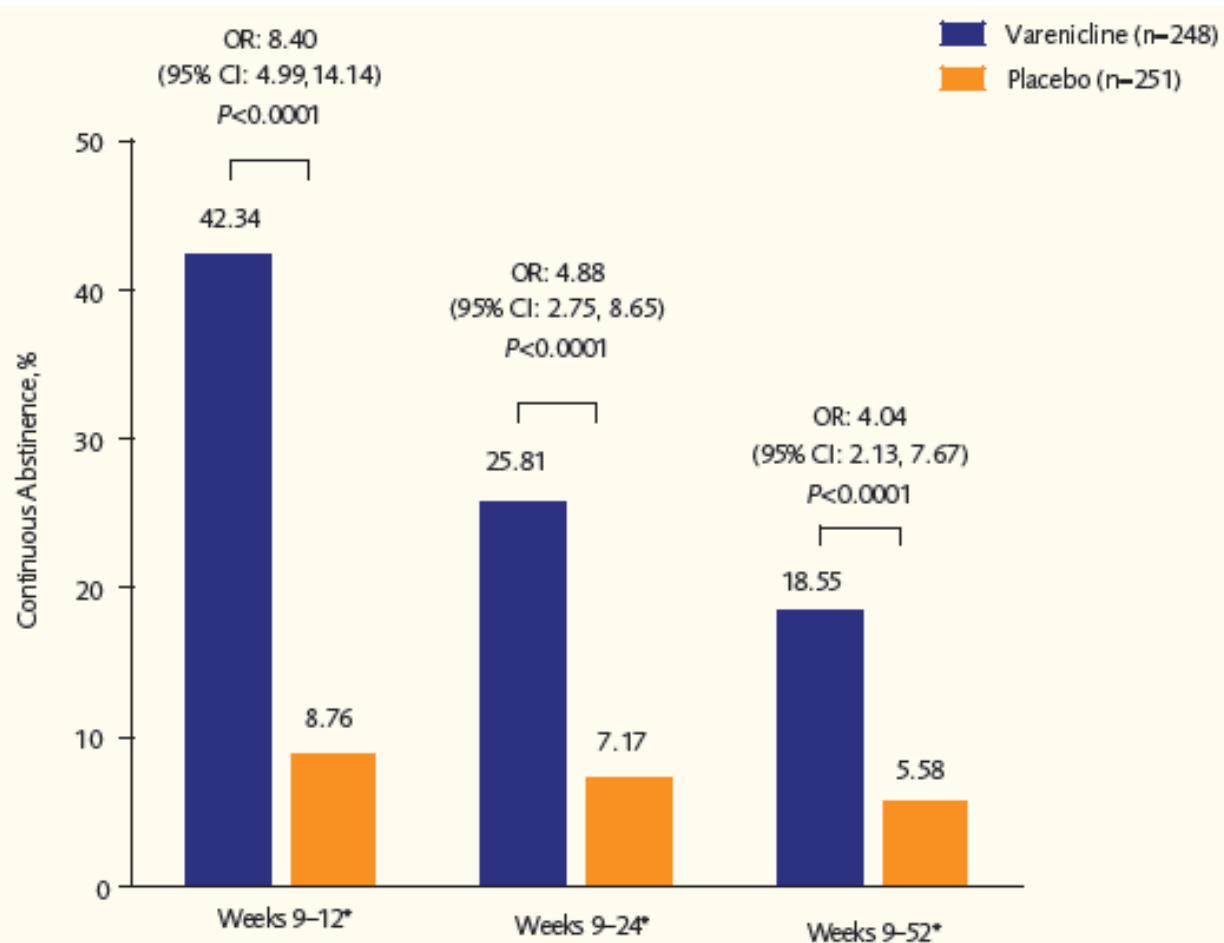
Smoking cessation and COPD

Philip Tønnesen


Sustained Quitters

Medication	Subjects n	FEV1 % pred	12-month sustained quit rates	
			Active	Placebo
Varenicline	505	70	18.6	5.6
Bupropion SR	404	72	10	8
NRT	370	56	14	5





*Primary endpoint

OR, odds ratio; CI, confidence interval

Tashkin DP (27 centers) Chest 2009

A summary of the efficacy of different non-pharmacologic and pharmacologic interventions in patients by COPD status.

Intervention	Reference	Follow-up	Cessation rate (%)	Control (%)	COPD Status	Counseling
Minimal advice from GP	44	None	3.0 ^a	1.0 ^a	General smoking population	None
Being informed of COPD status	26	1 year	16.3	12.0	General smoking population	Brief counseling
Being informed of COPD status	27	3 years	25.0	7.0	General smoking population	Brief counseling/yearly reinforcement by GP
Being informed of "lung age"	28	1 year	13.6	6.4	General smoking population	Brief counseling/referral to smoking cessation services
NRT	18,31					Group intervention
	48					Individual intervention
						Support group
Bupropion						
Varenicline						
	70					Brief counseling
Nortriptyline	64	6 months	21.2	8.5	Mild-moderate	Brief counseling
		6 months	32.1	22.0	At risk of COPD	Brief counseling

Αναπνευστικοί ασθενείς

Όλα τα φάρμακα ασφαλή και αποτελεσματικά

References	N	Participants	Findings
Thomson et al ²⁹	760	BTS Severe Asthma Registry with severe refractory asthma: 69 (9%) current smokers 210 (28%) ex-smokers 461 (62%) never smokers	Compared with never smokers, current smokers had poorer asthma control (ACQ 4.1 vs 2.9, $P<0.001$), more unscheduled health care visits (6 vs 4, $P=0.008$), more rescue oral steroids (6 vs 4 courses, $P=0.04$), higher anxiety (13 vs 8, $P<0.001$), and depression (10 vs 6, $P<0.001$), but no differences in spirometry

To et al²⁸

Review

Smoking cessation strategies for patients with asthma: improving outcome

Perret et al: Journal of Asthma and Allergy 2016;9

Cerveri et al

Boulet et al²⁷

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-smokers), and

eism ($P<0.01$)

Zheng et al ³²	4070	Meta-analysis of ten controlled studies in smokers vs nonsmokers with asthma using inhaled corticosteroids	Compared with nonsmokers with asthma, smoking was associated with an attenuated inhaled corticosteroid response, reduced mean change in FEV ₁ , reduced posttreatment FEV ₁ , and increased use of concomitant medication
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Pharmacotherapies for acute admissions and stable outpatients with cardiovascular disease

Nicotine patch

Ad libitum nicotine
inhalator, spray,
microtab)

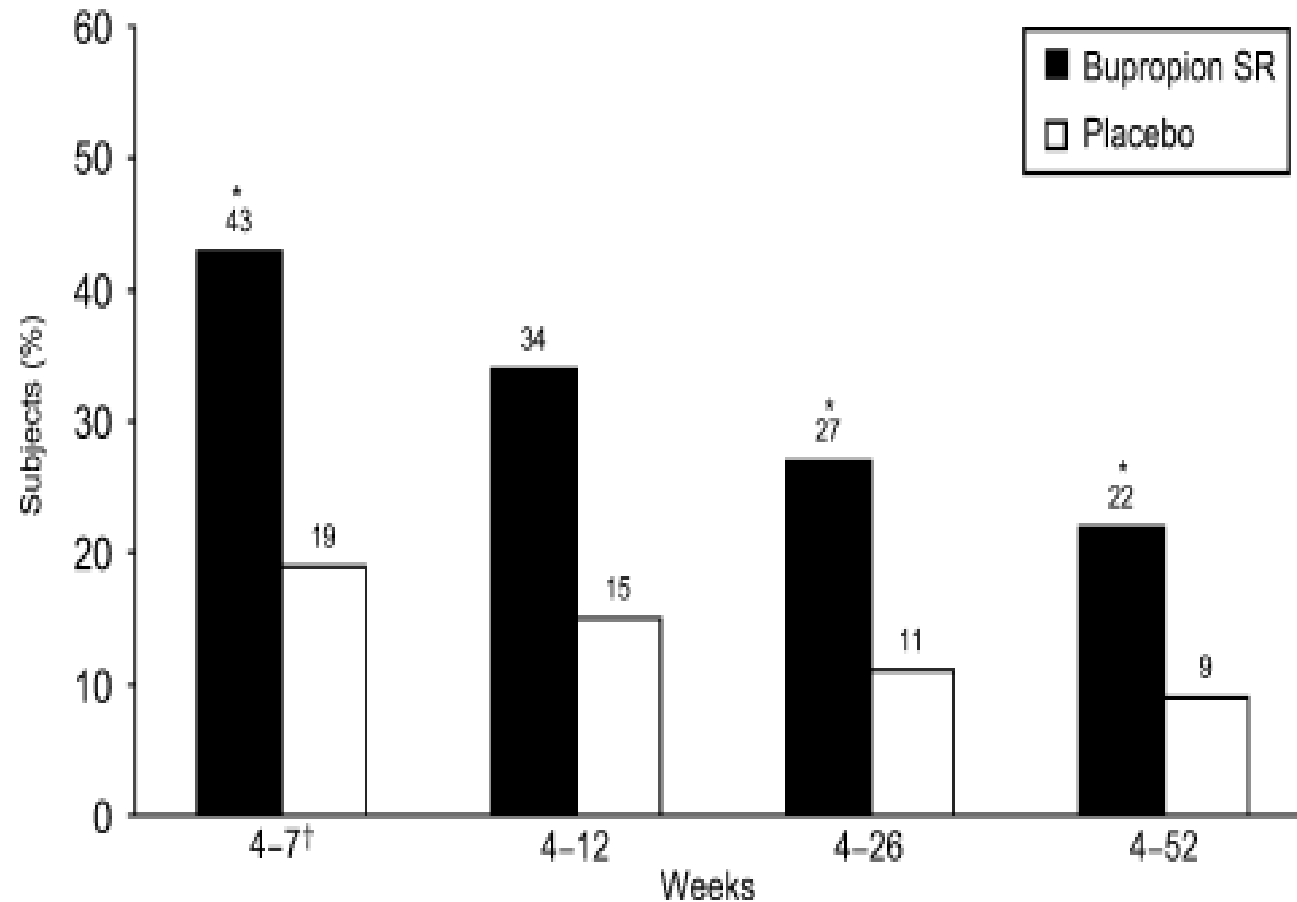
Bupropion

Varenicline

Καρδιοπαθείς:
Όλα τα φάρμακα ασφαλή
και
αποτελεσματικά

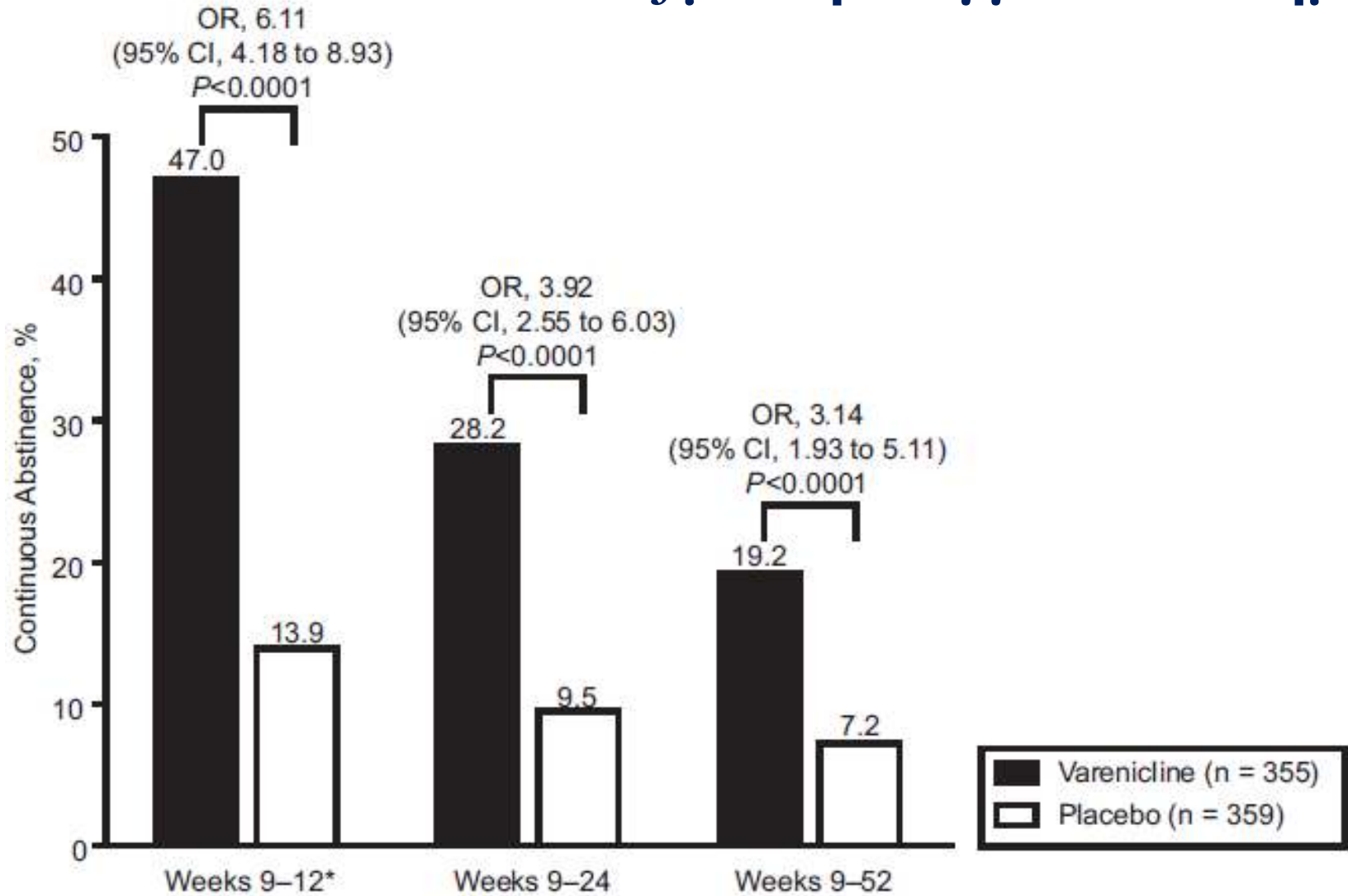
Tonstad S Heart 2009 95: 1635-40

Μελέτη χρήσης HCL Bupropion σε ασθενείς με καρδιαγγειακό νόσημα



Tonstad S et al EHJ 2003 (n=629)

Ασθενείς με καρδιαγγειακό νόσημα



Rigotti N Circulation 2010; 121:221-29

EAGLES Study Results: CARs in Patients With Anxiety Disorder

EAGLES Study: Summary

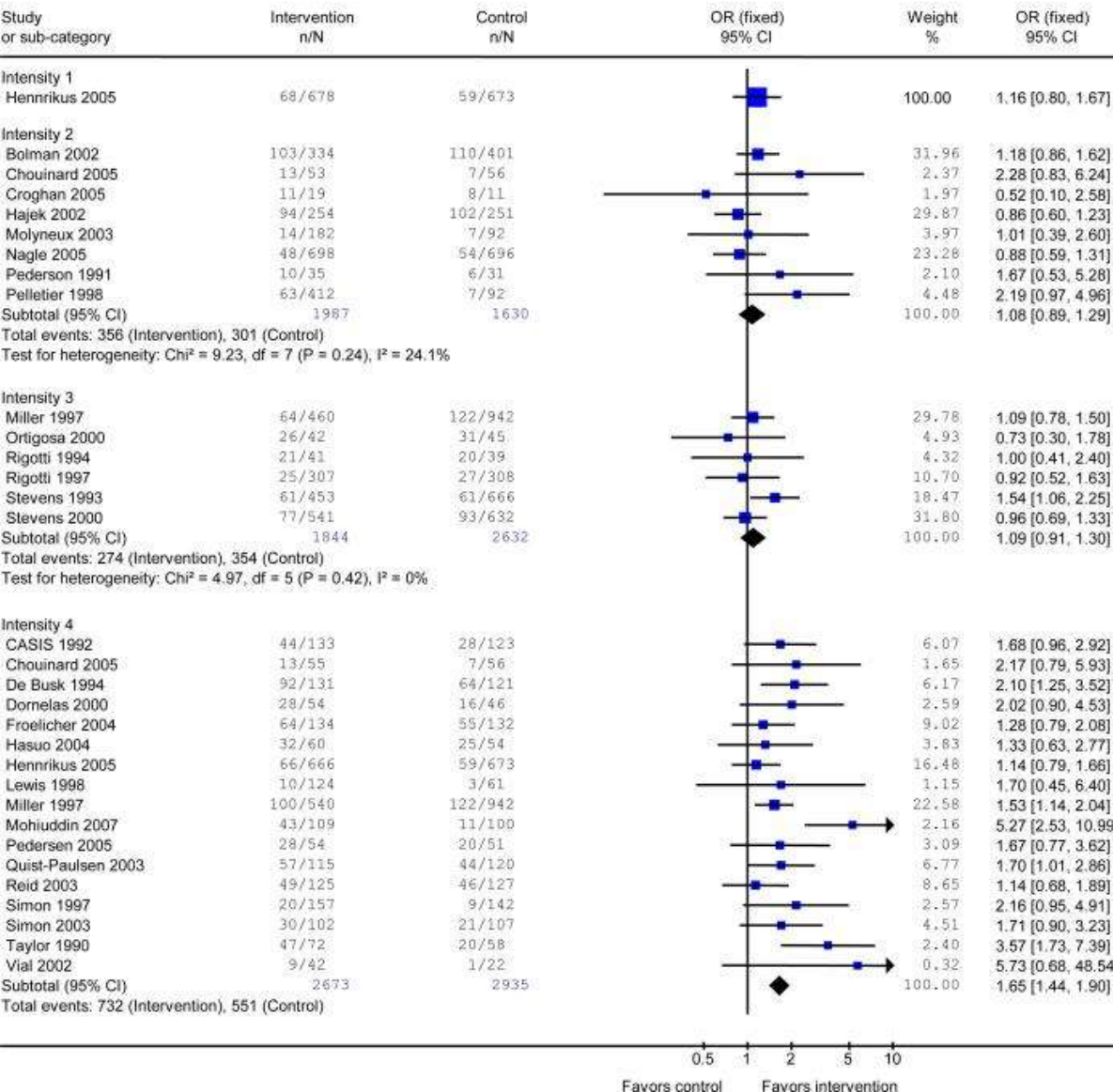
- Varenicline, bupropion, and NRT were more effective than placebo in helping smokers achieve abstinence
 - Varenicline was more effective than bupropion and NRT
- All 3 medications were effective in patients with or without a history of psychiatric illness
 - CARs were lower in patients with a history of psychiatric illness vs those without
- All 3 medications were effective in patients regardless of psychiatric history (ie, psychotic, mood, or anxiety disorder)

SMOKING CESSATION INTERVENTIONS FOR HOSPITALIZED SMOKERS: A SYSTEMATIC REVIEW 2015 **NHS**

- Rigoti Arch Intern Med. 2008 Oct 13;
168(18): 1950–1960
- [Nancy A. Rigotti, MD, Marcus R. Munafo, PhD, and Lindsay F. Stead, MSc](#)

Efficacy of smoking cessation counseling by intensity of counseling intervention

Comparison: Intervention v Control, by intensity of counselling intervention
Outcome: Quit at longest follow-up (6+ months)



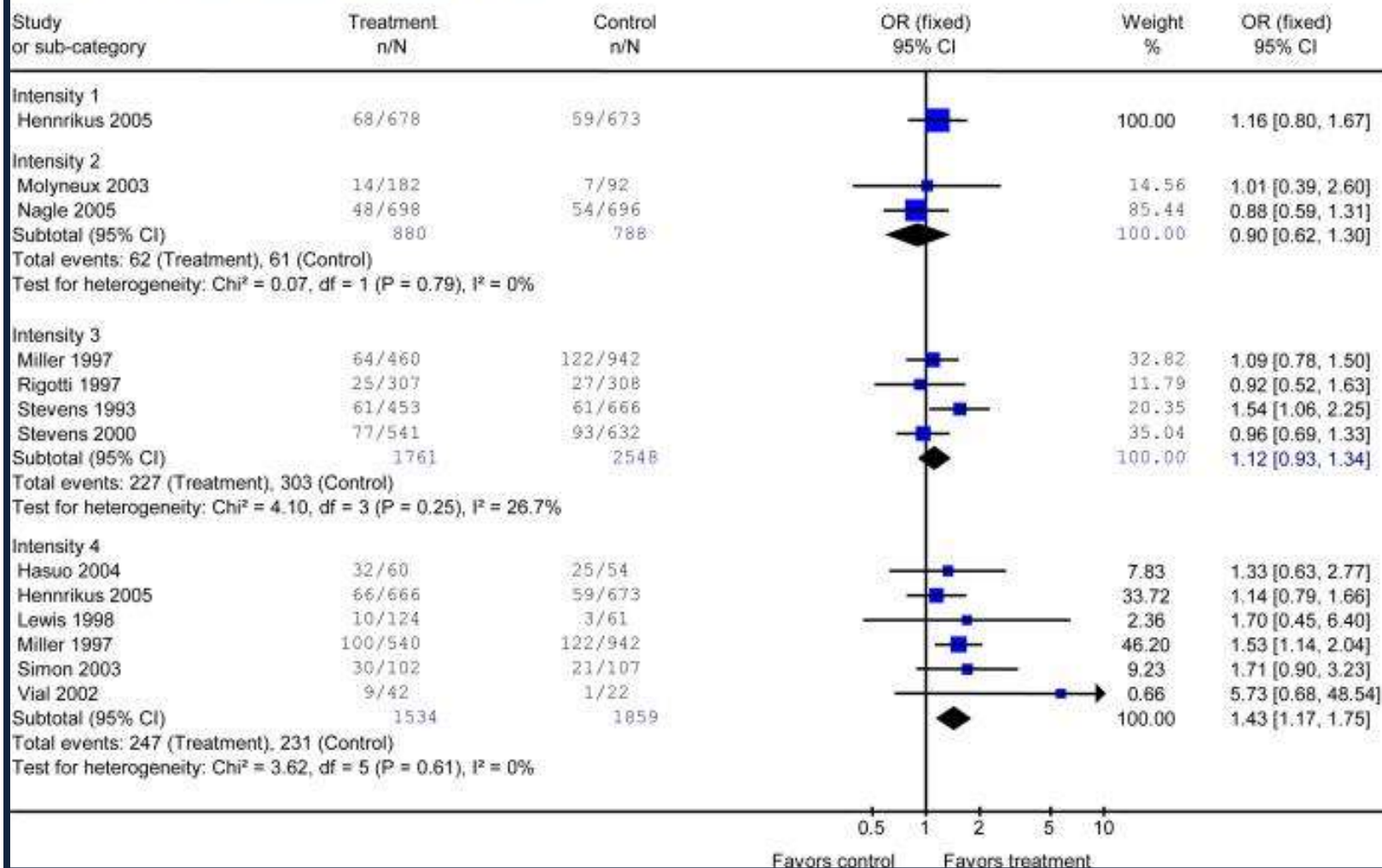
Intensity 1= contact in hospital of ≤ 15 minutes and no post-discharge support

Intensity 2= contact in hospital of >15 minutes and no post-discharge support

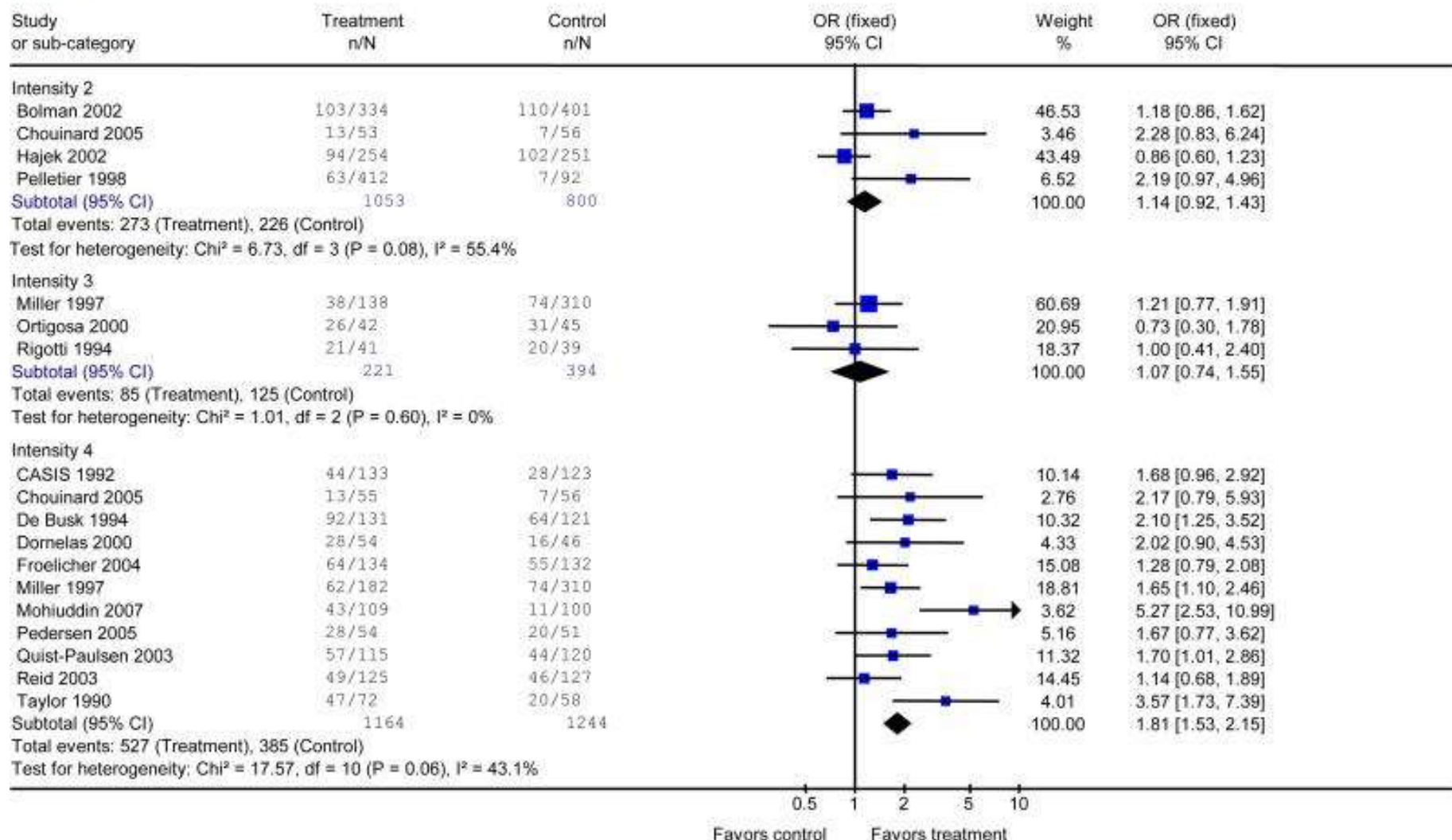
Intensity 3= any hospital contact plus post-discharge support lasting ≤ 1 month

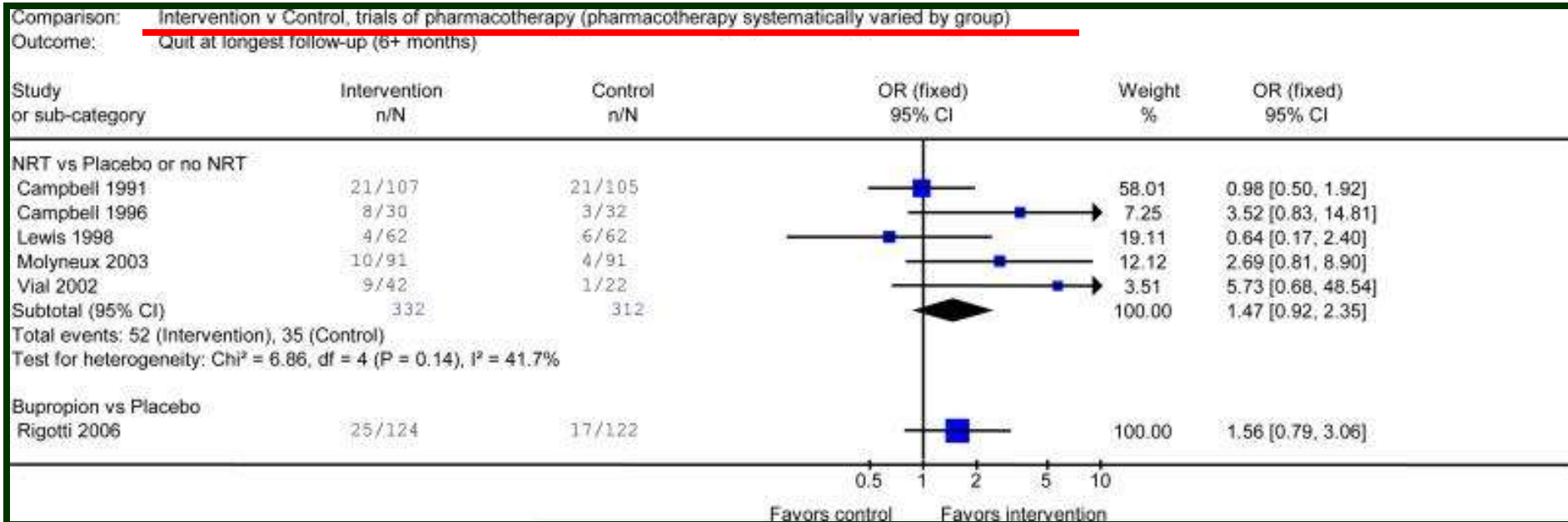
Intensity 4=any hospital contact plus post-discharge support lasting >1 month

Comparison: Intervention v Control, by intervention intensity within diagnostic subgroups
 Outcome: All hospital patients, unselected by diagnosis



Comparison: Intervention v Control, by intervention intensity within diagnostic subgroups
 Outcome: Patients with cardiovascular disease





Rigoti Arch Intern Med. 2008 Oct 13; 168(18): 1950–1960

Sustained Care Intervention and Postdischarge Smoking Cessation Among Hospitalized Adults A Randomized Clinical Trial

Nancy A. Rigotti, MD; Susan Regan, PhD; Douglas E. Levy, PhD; Sandra Japuntich, PhD;
Yuchiao Chang, PhD; Elyse R. Park, PhD, MPH; Joseph C. Viana, BA; Jennifer H. K. Kelley, RN, MA;
Michele Reyen, MPH; Daniel E. Singer, MD

6237 Smokers counseled by the
Massachusetts General Hospital
Tobacco Treatment Service

JAMA. 2014;312(7):719-728

Baseline Characteristics of Study participants By Treatment Group

	Sustained Care (n = 198) ^a	Standard Care (n = 199) ^a
Quitting history and predictors		
Prior use		
Nicotine replacement therapy	118 (59.6)	131 (65.8)
Bupropion	25 (12.6)	38 (19.1)
Varenicline	51 (25.8)	54 (27.1)
Smoking counseling	3 (1.5)	12 (6.0)
Live with smoker	79 (39.9)	86 (43.2)
Importance to quit now, mean (SD) ^f	9.4 (1.3)	9.5 (1.1)
Confidence to resist urges in any situation, mean (SD) ^f	7.2 (2.2)	7.4 (2.2)
Tobacco use		
Cigarettes/d, mean (SD)	17.1 (10.0)	16.3 (10.4)
Past 30 d		
Non-cigarette tobacco product	7 (3.5)	5 (2.5)
Electronic cigarette	11 (5.6)	12 (6.0)
Marijuana	27 (13.6)	32 (16.1)
Fagerström Test for Nicotine Dependence, mean (SD) ^c	5.0 (2.2)	4.6 (2.2)
Comorbidities, mean (SD)		
Depression symptoms ^d	9.3 (5.7)	10.3 (5.8)
Alcohol use ^e	3.4 (2.5)	3.6 (2.6)
Used smoking cessation medication in hospital		
Nicotine replacement therapy	130 (65.7)	125 (62.8)
Bupropion	2 (1.0)	3 (1.5)
Varenicline	7 (3.5)	9 (4.5)
Postdischarge medication recommendation by hospital counselor		
Nicotine replacement therapy	191 (96.5)	191 (96.0)
Bupropion	14 (7.1)	12 (6.0)
Varenicline	13 (6.6)	13 (6.5)

Use of Smoking Cessation Treatment After Hospital Discharge by Treatment Group

Outcome Measure	No. (%) of Patients	
	Sustained Care (n = 198)	Standard Care (n = 199)
Smoking cessation treatment use ^b		
1-mo follow-up	164 (82.8)	125 (62.8)
3-mo follow-up (cumulative)	172 (86.9)	152 (76.4)
6-mo follow-up (cumulative)	178 (89.9)	160 (80.4)
Smoking cessation counseling use ^c		
1-mo follow-up	73 (36.9)	45 (22.6)
3-mo follow-up (cumulative)	114 (57.6)	82 (41.2)
6-mo follow-up (cumulative)	136 (68.7)	102 (51.3)
Smoking cessation medication use ^d		
1-mo follow-up	156 (78.8)	117 (58.8)
3-mo follow-up (cumulative)	164 (82.8)	132 (66.3)
6-mo follow-up (cumulative)	170 (85.9)	140 (70.4)
Nicotine replacement therapy use ^e		
1-mo follow-up	147 (74.2)	110 (55.3)
3-mo follow-up (cumulative)	155 (78.3)	123 (61.8)
6-mo follow-up (cumulative)	161 (81.3)	130 (65.3)
Duration of medication use, wk		
≥2	146 (73.7)	103 (51.8)
≥4	137 (69.2)	90 (45.2)
≥8	120 (60.6)	73 (36.7)

Tobacco Abstinence Rates After Discharge by Treatment Group

Outcome Measure	No. (%) of Patients	
	Sustained Care (n = 198)	Standard Care (n = 199)
Biochemically confirmed		
Abstinent for past 7 d ^b		
6-mo follow-up	51 (25.8)	30 (15.1)
Self-report		
Abstinent for past 7 d ^c		
1-mo follow-up	103 (52.0)	78 (39.2)
3-mo follow-up	89 (44.9)	73 (36.7)
6-mo follow-up	81 (40.9)	56 (28.1)
Abstinent since hospital discharge ^c		
1-mo follow-up	91 (46.0)	66 (33.2)
3-mo follow-up	67 (33.8)	47 (23.6)
6-mo follow-up	54 (27.3)	32 (16.1)

Effect of the Intervention in Subgroups

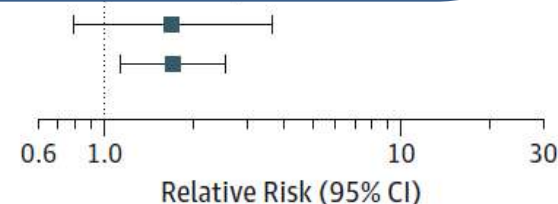
Age, y	No. of Patients				Favors Standard Care	Favors Sustained Care
	Sustained Care		Standard Care			
	7-d		7-d			
	Abstinence	Total	Abstinence	Total		

Among hospitalized adult smokers who wanted to quit smoking, a postdischarge intervention providing automated telephone calls and

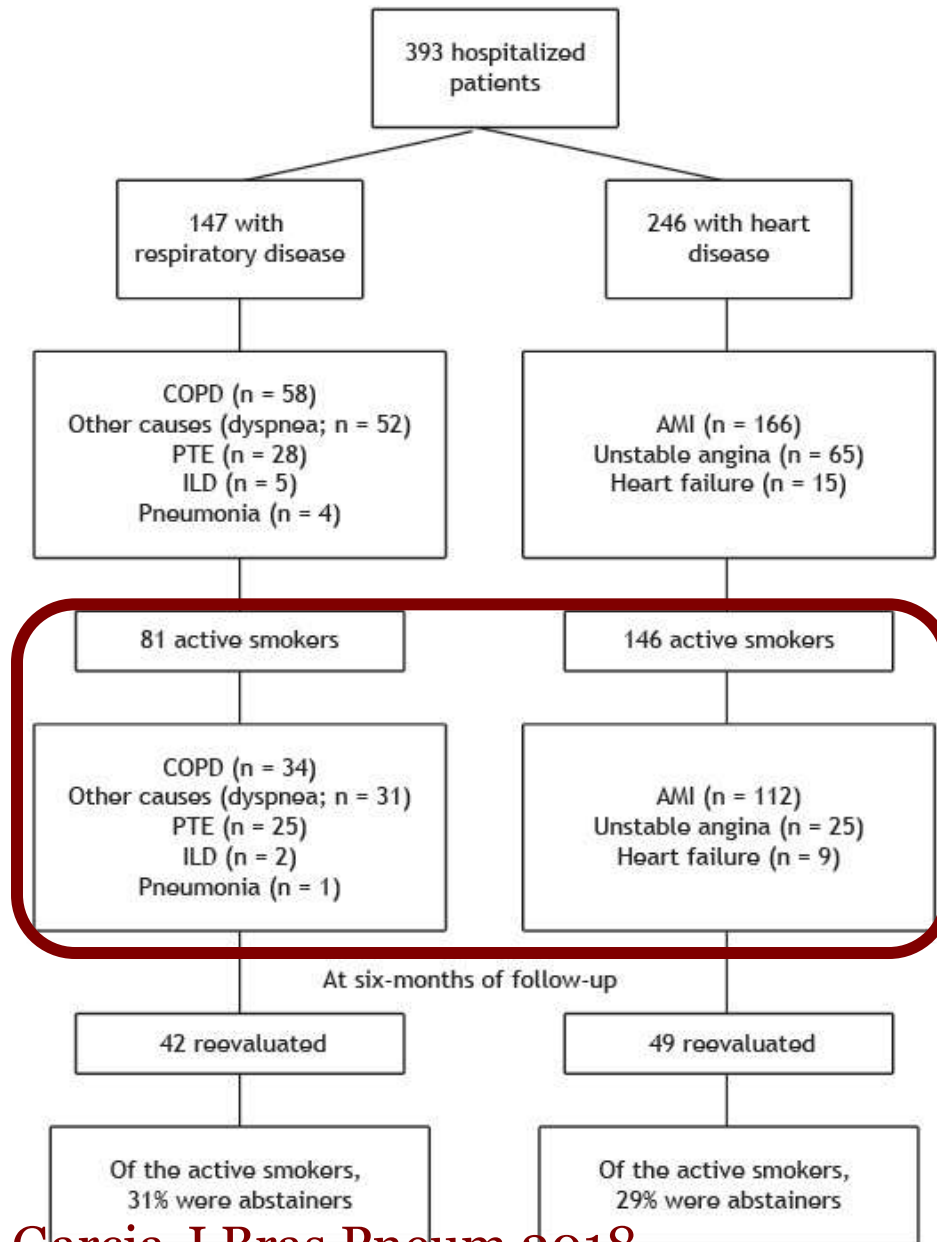
Free medication resulted in higher rates of smoking cessation at 6 months compared with a standard recommendation to use counseling and medication after discharge.

These findings, if replicated, suggest an approach to help achieve sustained smoking cessation after a hospital stay.

No	14	68	9	74
Overall	51	198	30	199



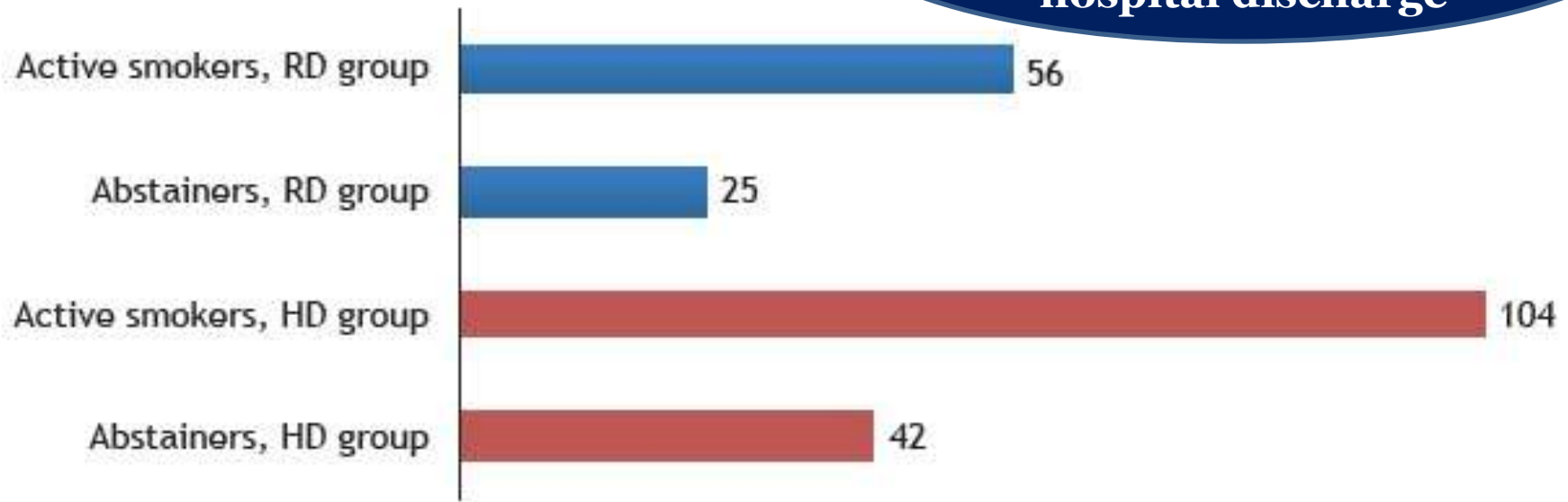
Evaluation of smoking cessation treatment initiated during hospitalization in patients with heart disease or respiratory disease



All participants received smoking cessation treatment during hospitalization and were followed in a cognitive-behavioral smoking cessation program for six months after hospital discharge.

Evaluation of smoking cessation treatment initiated during hospitalization in patients with heart disease or respiratory disease

Number of patients in each group by smoking status at six months after hospital discharge



All patients underwent two 15-min sessions of individual counseling during hospitalization.

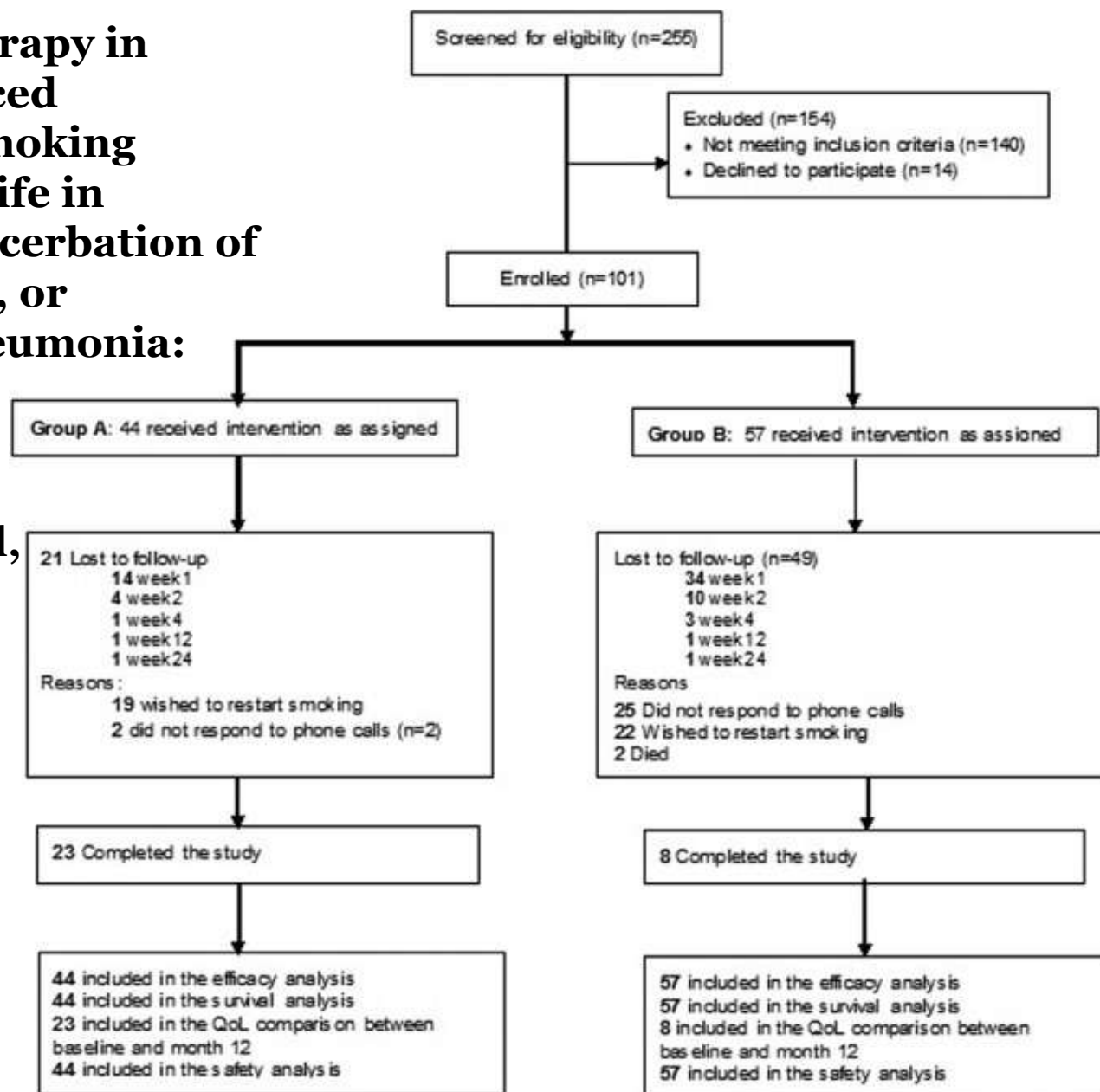
Smoking cessation medications were used at the physician's discretion, in accordance with smoking cessation guidelines

that is, all patients with a dependence score ≥ 5 or who experienced withdrawal symptoms during hospitalization were prescribed smoking cessation medications

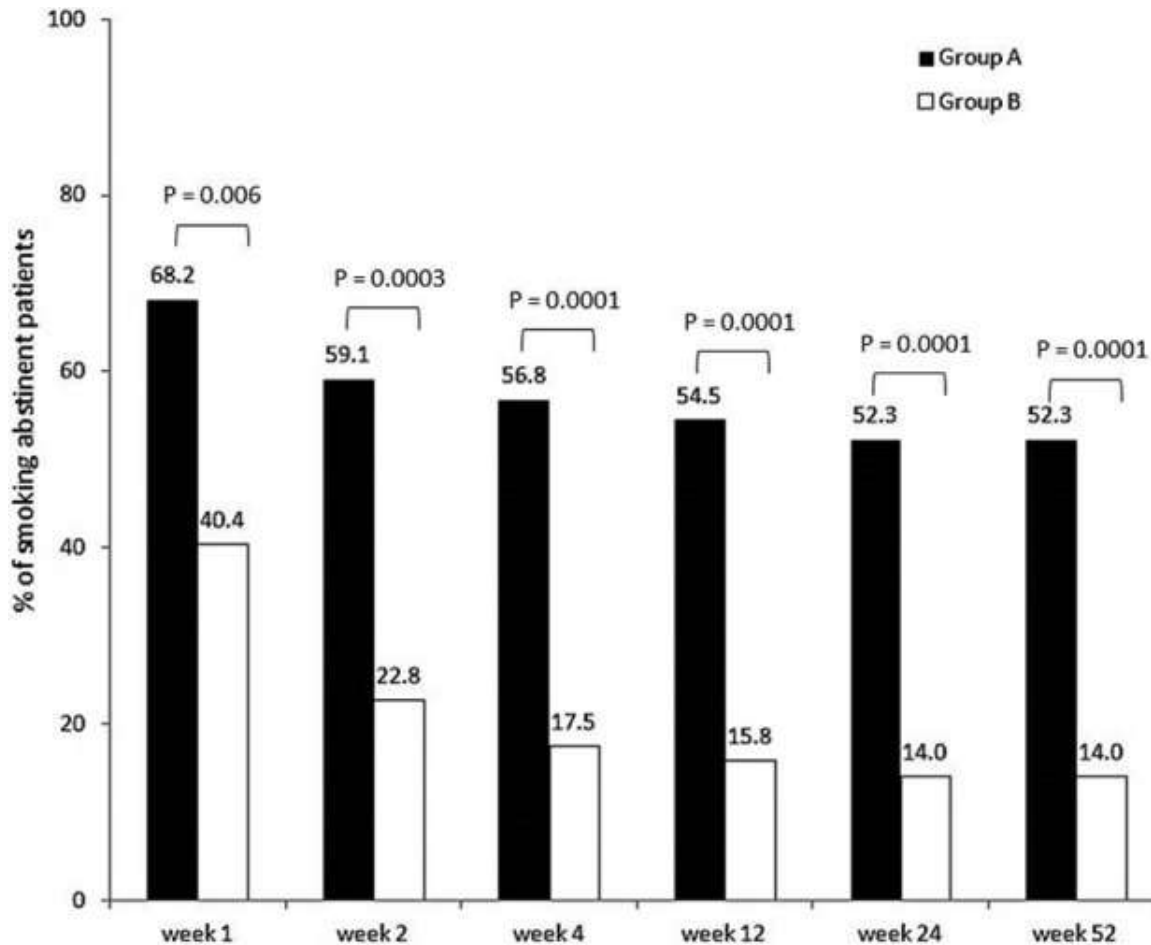
(nicotine replacement therapy, bupropion, or varenicline)

Effects of varenicline therapy in combination with advanced behavioral support on smoking cessation and quality of life in inpatients with acute exacerbation of COPD, bronchial asthma, or community-acquired pneumonia:

A prospective, open-label, preference-based, 52-week, follow-up trial.

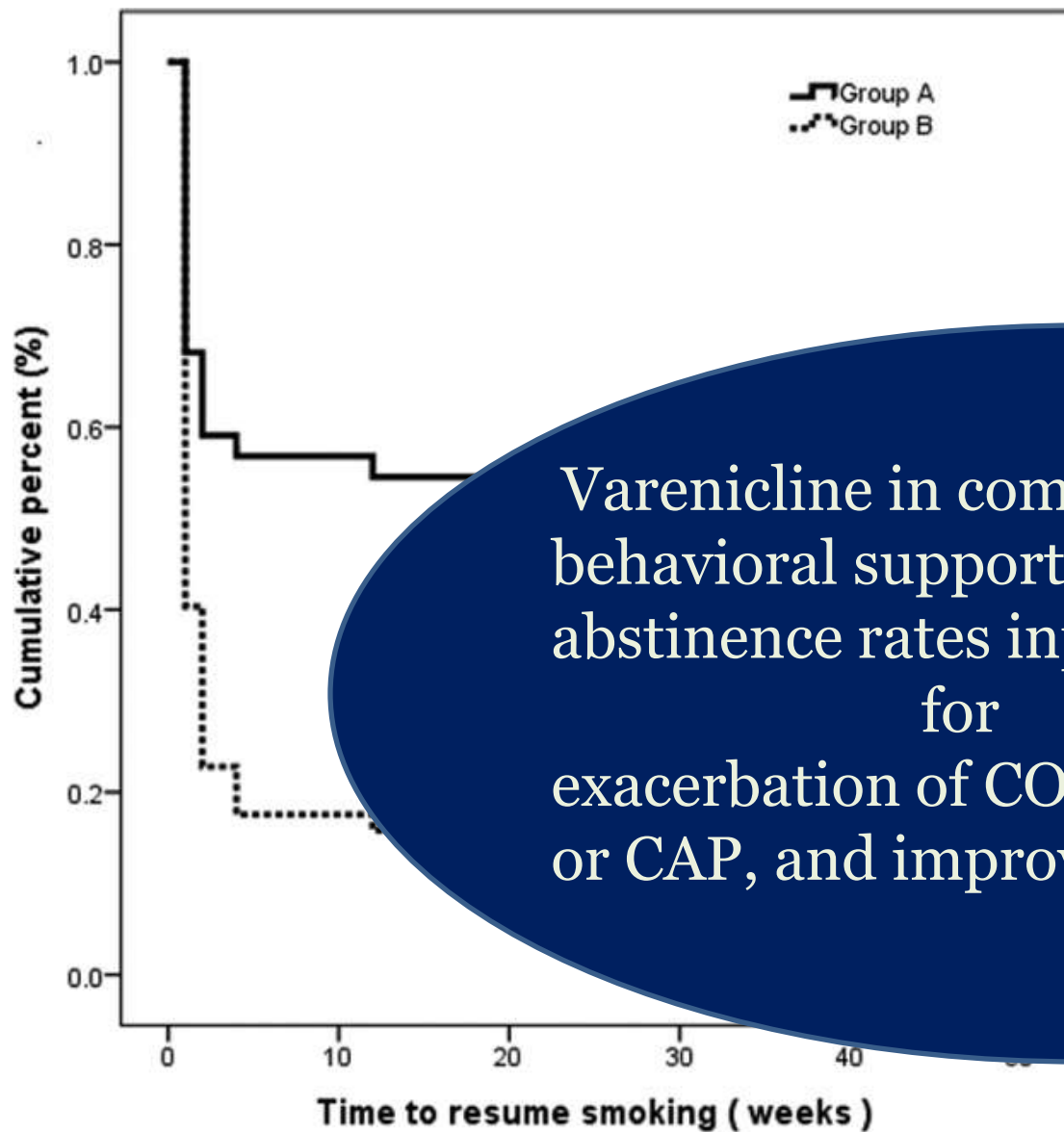


Percentage of smoking abstinent patients *by group*



group A
a standard regimen
of varenicline combined
with post-discharge
advanced behavioral
support

group B
one private consultation
session during
hospitalization



Varenicline in combination with behavioral support resulted in high abstinence rates inpatients hospitalized for exacerbation of COPD, asthma attack, or CAP, and improved QoL.

Kaplan–Meier curves of time to resume smoking for both groups.

Smoking Cessation in Patients with Acute Coronary Syndrome

Franck C: The American Journal of Cardiology

In press

Characteristics of RCT of pharmacotherapy in pts *with acute coronary syndrome*

[illegible]

Efficacy of pharmacological and behavioral treatment in pts *with acute coronary syndrome*

Study (Year)	Therapy	n	Duration of Treatment	PPA		RD (%) 95% CI*	CA	
				6 mo	12 mo		6 mo	12 mo
Pharmacological								
Planer et al. (2011) ²⁶	Bupropion + MS	75	Bupropion SR 150 mg QD x 3 days,	-	-	-	45.0%	31.0%
Rigotti et al. (2006) ²⁵								
Eisenberg et al. (2013) ⁵								
Eisenberg et al. (2016) ⁶								
Behavioral								
Taylor et al. (1990) ³⁷								
Feeney et al. (2001) ³⁸	SF program	96	Self-help manual x2 wks, telephone counseling x4 wk, & at 2, 3, 6, and 12 mo	-	-	-	-	33.7%
	Minimal care	102		-	-	-	-	1.0%
Smith et al. [§] (2009) ³⁹	Intensive intervention	137	Bedside counseling, self-help, 7 tel. counseling sessions at 2, 7, 14, 21, 30, 45, & 60 days	66.7%	62.2%	15.9% (4.2%, 27.5%)	-	54.0%
	Minimal intervention	139		48.9%	46.0%		-	35.0%

Among pharmacological trials
only varenicline increases point prevalence
abstinence at 12 months


Behavioral interventions produced
significantly improved abstinence at 6 and 12
months

Among pharmacological trials
only varenicline increases point prevalence
abstinence at 12 months

Behavioral interventions produced
significantly improved abstinence at 6 and 12
months

Specific populations

Before surgery

- Smoking is a risk factor for both surgery and port-surgery complications
- The use of NRT as partial substitution therapy to reduce tobacco use should be proposed to patients unwilling to stop  Grade B
- Smoking cessation should be proposed at least 6 weeks before surgery

Co

During the inpatient admission

Hospitals are smoke-free environments

Obvious link between the admission and the underlying smoking behavior

Pressing opportunity to prescribe NRT to lessen the withdrawal symptoms

To be followed by motivational interviewing and prescription of other pharmacotherapy

The positive experience of nicotine withdrawal during the admission might facilitate the maintenance of abstinence

These individuals have short- as well as longer-term supportive contacts from health professionals

Minimize the likelihood of relapse

Characteristics Associated With Smoking Cessation Pharmacotherapy Prescriptions for Hospitalized Patients Who Use Tobacco

Tobacco Use Prevalence and Smoking Cessation Pharmacotherapy Prescription Patterns Among Hospitalized Patients by Medical Specialty

Pharmacotherapy prescriptions for hospitalized smokers

		<i>n</i>	Percent
Gender	Female	45 037	21.1
	Male	54 549	21.8
Race	Caucasian	56 641	22.6
	African American	39 009	20.1
	Other	1454	20.6
	Unknown	2482	17.4
Age (years)	18–34	19 996	23.9
	35–49	24 968	25.8
	50–64	39 022	20.8
	65–79	13 808	13.9
Admission year	2010	5168	18.3
	2011	16 449	19.0
	2012	16 304	19.5
	2013	16 010	21.4
	2014	15 243	22.4
	2015	16 128	23.7
	2016	14 284	24.4
	Orthopedic surgery	4315	5.4
	Otolaryngology	1884	10.8
	Plastic surgery	706	4.7
	Psychiatry	6402	71.8
	Urology	2341	10.9
Admission route	Not through ED	47 381	17.2
	Through ED	52 205	25.3
Length of stay	<3 days	47 369	15.9
	≥3 days	52 217	26.6

Srivastava A.B:
Nicotine & Tobacco
Research, 2018

Tobacco Use Prevalence and Smoking Cessation Pharmacotherapy Prescription Patterns Among Hospitalized Patients by Medical Specialty

Ideally, all hospitalized patients who use tobacco **should receive cessation pharmacotherapy** to reduce withdrawal symptoms and encourage smoking cessation.

Several hospital-based strategies may increase the delivery of evidence-based smoking treatment during hospitalization.

Hospitals may benefit from implementing policies and practices that standardize and automate the offer **of smoking cessation pharmacotherapy** for all hospitalized patients who smoke.

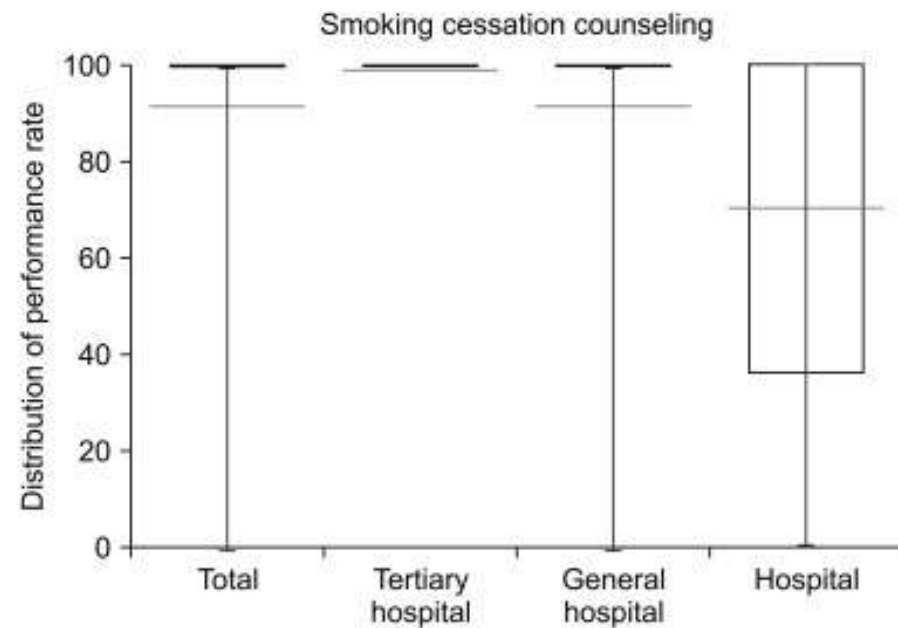
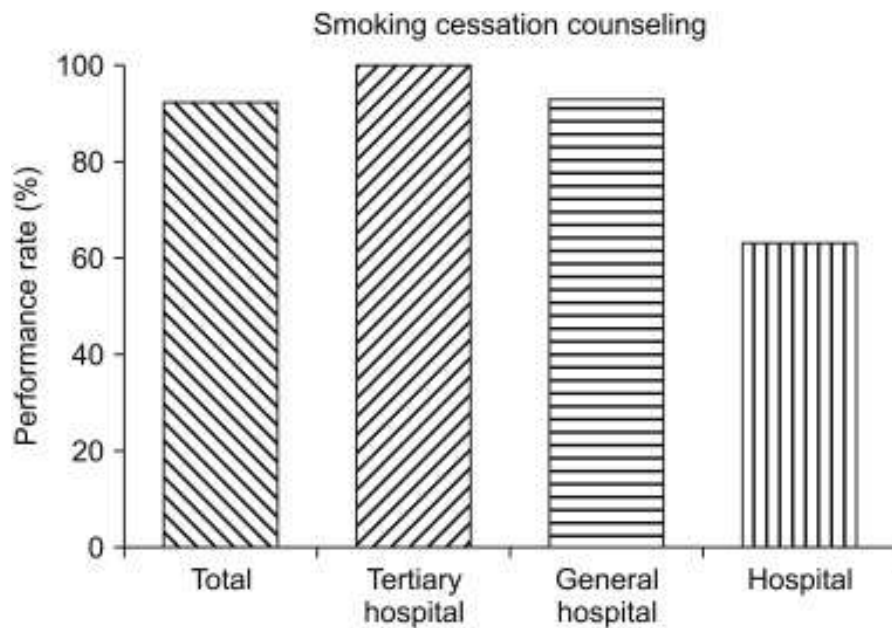
Additionally, **training nurses in bedside delivery of pharmacotherapy** may improve utilization.

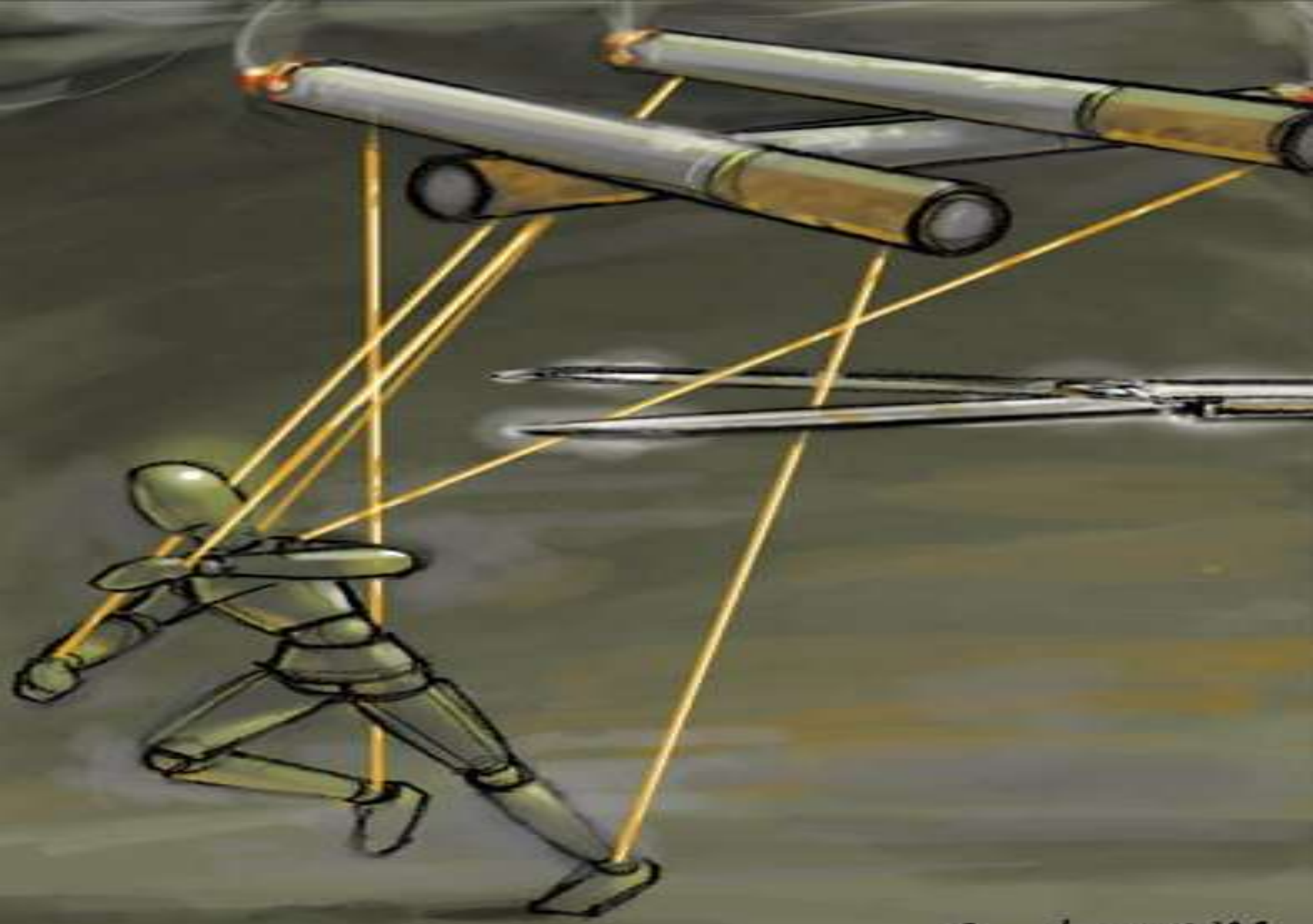
Srivastava A.B: Nicotine & Tobacco Research, 2018

Evaluation of the Quality of Care among Hospitalized Adult Patients with Community-Acquired Pneumonia in Korea

- **Performance rates of oxygenation assessment according to institution**
- **Performance rates of pneumonia severity assessment according to institution**
- **Performance rates of sputum smears within 24 hours of hospital arrival according to institution**
- **The performance rates of sputum cultures performed within 24 hours of hospital arrival according to institution**
- **Performance rates of blood cultures taken prior to the initial administration of antibiotics according to institution**
- **Performance rates of the administration of the first dose of antibiotics within 8 hours of the time of hospital arrival according to institution**
- **Performance rates of smoking cessation counseling according to institution.**
- **Performance rates of screening for pneumococcal vaccination according to institution.**

Evaluation of the Quality of Care among Hospitalized Adult Patients with Community-Acquired Pneumonia in Korea





C. Lynn



Changing Behavior: 3 Main Levers for Helping Patients Quit Smoking

**Is also suggested that:
when smoking cessation
pharmacotherapy is protocolized in the
EHR, as on the psychiatric service,
patients who use tobacco are much more
likely to receive smoking cessation
pharmacotherapy**

Recommended Treatments for Tobacco Dependence and the Evidence Base for Use in Smokers with Mental Illness.*

Treatment Strategy	Findings in Smokers with Mental Illness
Clinician advice to quit and referral	In one trial in clinically depressed smokers, yielded abstinence rate of 19% at 18 months of follow-up. ¹
Individual cessation counseling	At 18 months of follow-up, individual counseling with access to cessation pharmacotherapy achieved abstinence in 18% of smokers with PTSD ³ and 25% of those with depression. ¹
Group cessation counseling	Group counseling plus nicotine replacement achieved 19 to 21% abstinence at 12 months of follow-up in outpatients with serious mental illness; tailoring content for smokers with schizophrenia was equally effective.
Quit-lines	The nearly 25% of callers to the California quit-line who had major depression were significantly less likely than nondepressed callers to have quit smoking at 2 months of follow-up.
Nicotine replacement: patch, gum, lozenge, inhaler, nasal spray	One trial found nicotine gum particularly helpful among depressed (as compared with nondepressed) smokers (36% abstinence at 3 months). In acute care settings, nicotine replacement reduced agitation in smokers with schizophrenia and was associated with lower rates of leaving inpatient psychiatric settings against medical advice. Extended use of a nicotine patch reduced relapse risk among smokers with schizophrenia. A case series documented that nicotine nasal spray was used appropriately by smokers with schizophrenia and supported cessation.
Bupropion	An effective cessation aid in smokers with or without current or past depression. A meta-analysis of 7 trials in 260 smokers with schizophrenia showed significant effects at 6 months of follow-up. ⁴ According to a case study, two smokers with bipolar disorder quit smoking with no adverse effects on mood.
Varenicline	Three case series involving medically stable outpatients with schizophrenia reported significant smoking reduction, 8-to-75% quit rates, improvements on some cognitive tests, and no serious adverse effects; individual case reports reveal mixed effects in smokers with schizophrenia or bipolar disorder. Three randomized, controlled trials in smokers with schizophrenia or depression are in process.
Nortriptyline	Demonstrated efficacy in the general population and among smokers with a history of depression; no data on smokers with current mental illness.
Clonidine	Demonstrated efficacy in the general population; no data on smokers with mental illness.