"Effects of smoking cessation and vaccination”

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- Impact of smoking cessation on COPD
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  : pharmacologic intervention

  : electronic cigarette
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Therapeutic Options: Smoking Cessation

- Counseling delivered by physicians and other health pr ofessionals significantly increases quit rates over self-in itiated strategies. Even a brief (3-minute) period of co unseling to urge a smoker to quit results in smoking q uit rates of 5-10%.
- Nicotine replacement therapy (nicotinegum, inhaler, na sal spray, transdermal patch, sublingual tablet, or loze nge) as well as pharmacotherapy with varenicline, bup ropion, and nortriptyline reliably increases long-term s moking abstinence rates and are significantly more eff ective than placebo.

Therapeutic Options: Other Pharmacologic Treatments

Influenza vaccines can reduce serious illness.

Pneumococcal polysaccharide vaccine is recommended for COPD patients 65 years and older and for COPD patients younger than age 65 with an FEV_1< 40% predicted.

Tobacco Smoke and Vaccination (GOLD 2014 updated guideline)

- **Smoking cessation is the key intervention for all COPD patients who continue to smoke (Evidence A).**
- **Health care providers are important to the delivery of smoking cessation messages and interventions and should encourage all patients who smoke to quit, even when patients visit a health care provider for reasons unrelated to COPD or breathing problems.**
- **Smoking cessation should be considered the most important intervention for all COPD patients who smoke regardless of the level of disease severity.**
- **Decisions about vaccination in COPD patients depend on local policies, availability and affordability.**

Non-pharmacologic Management of COPD (GOLD 2014 updated guideline)

Patient Group	Essential	Recommended	Depending on local Guidelines
A	**Smoking cessation** (can include pharmacologic treatment)	Physical activity	**Flu vaccination** **Pneumococcal vaccination**
B-D	**Smoking cessation** (can include pharmacologic treatment) Pulmonary Rehabilitation	Physical activity	**Flu vaccination** **Pneumococcal vaccination**

Smoking Prevalence in COPD

TABLE 1 Smoking prevalence among chronic obstructive pulmonary disease patients in large randomised, placebo-controlled trials with inhaled corticosteroids and/or long-acting β_2-agonists and/or long-acting anti-muscarinic drugs

First author [ref.]	Study	Subjects n	Age yrs	FEV1	Smokers %
VESTBO [1]	VESTBO	290	59	2.4 (86)	77
WATSON [2]	EUROSCOP	647	53	2.5 (80)	54
VESTBO [3]	TRISTAN	1465	63	1.4 (45)	51
CALVERLEY [4]	TORCH	5343	65	1.2 (45)	45
BURGE [5]	ISOLDE	751	64	1.4 (50)	38
WEDZICHA [6]	INSPIRE	1323	65	1.3 (39)	38

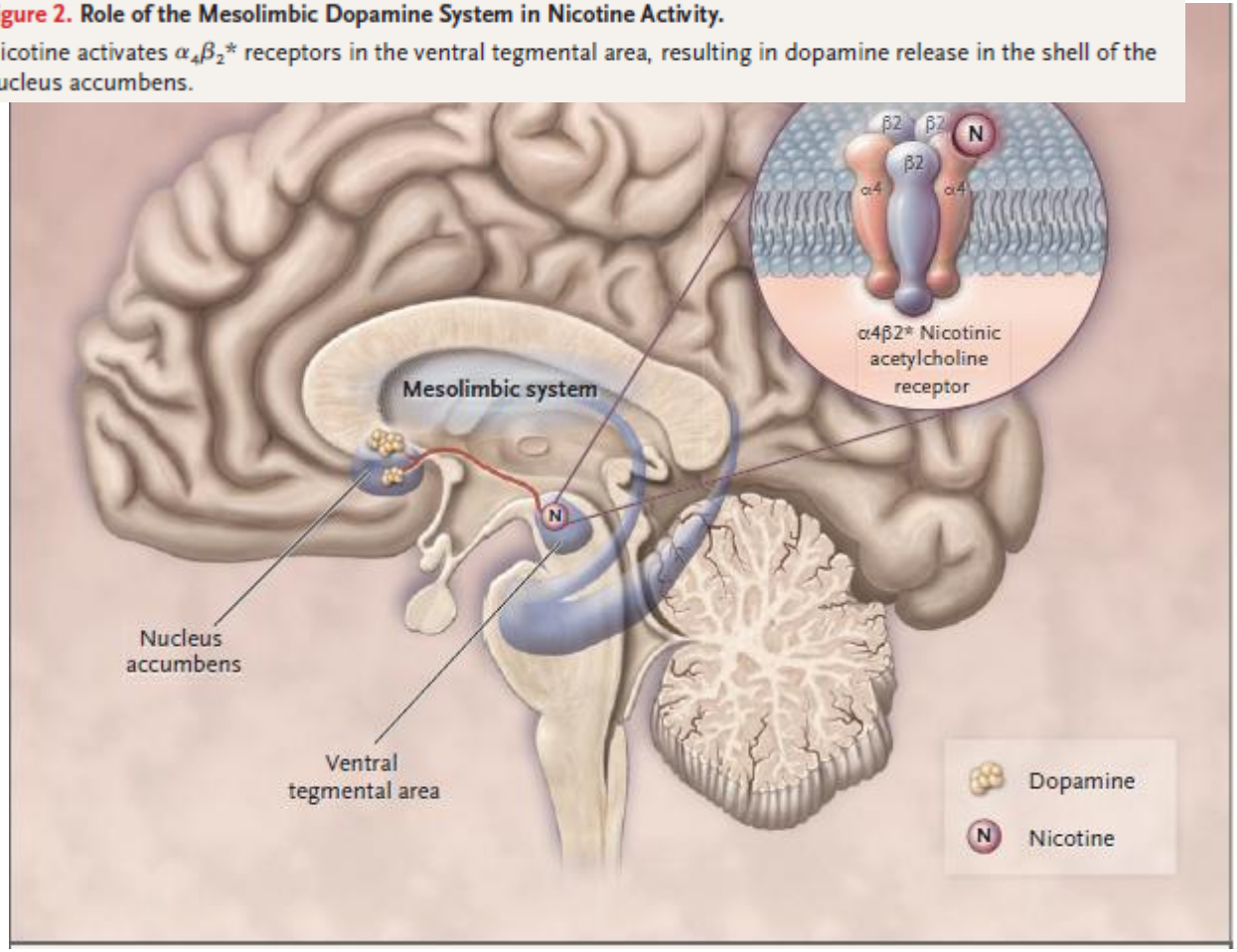
Data for forced expiratory volume in 1 s (FEV1) is presented as L (% predicted).

ERJ 2013;22(127): 37-43.

Role of Mesolimbic Dopamine System in Nicotine Activity

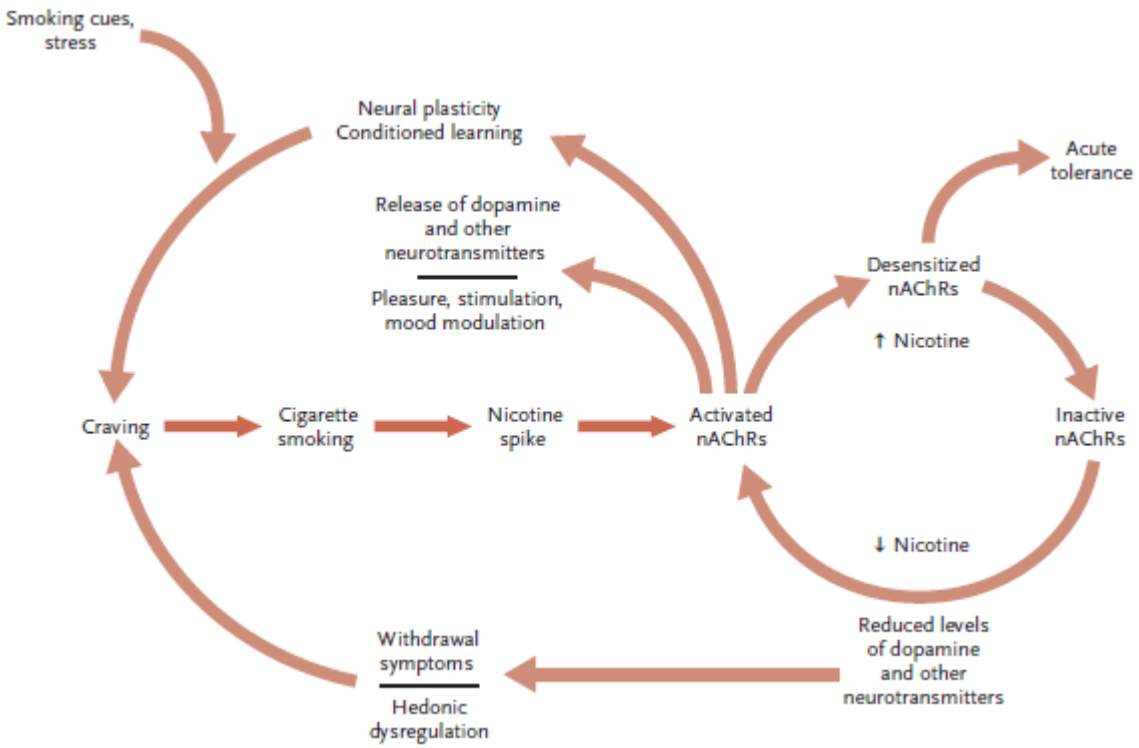
Figure 2. Role of the Mesolimbic Dopamine System in Nicotine Activity.

Nicotine activates $\alpha_4\beta_2$* receptors in the ventral tegmental area, resulting in dopamine release in the shell of the nucleus accumbens.



NEJM 2010:262:2295-303

Molecular and Behavioral aspects of Nicotine Addiction



NEJM 2010:262:2295-303

Landmark Studies for the effect of tobacco treatment on cardiopulmonary health outcomes

Table I Seminal studies evaluating the effect of tobacco treatment on cardiopulmonary health outcomes

Study (reference number)	Sample size	Study findings
Enlargement (SAVE) study[**]		cessation reduced mortality, risk of recurrent myocardial infarction, hospitalization from congestive heart failure, and death. The benefit of smoking cessation was greater than that related to the use of an angiotensin converting enzyme inhibitor.

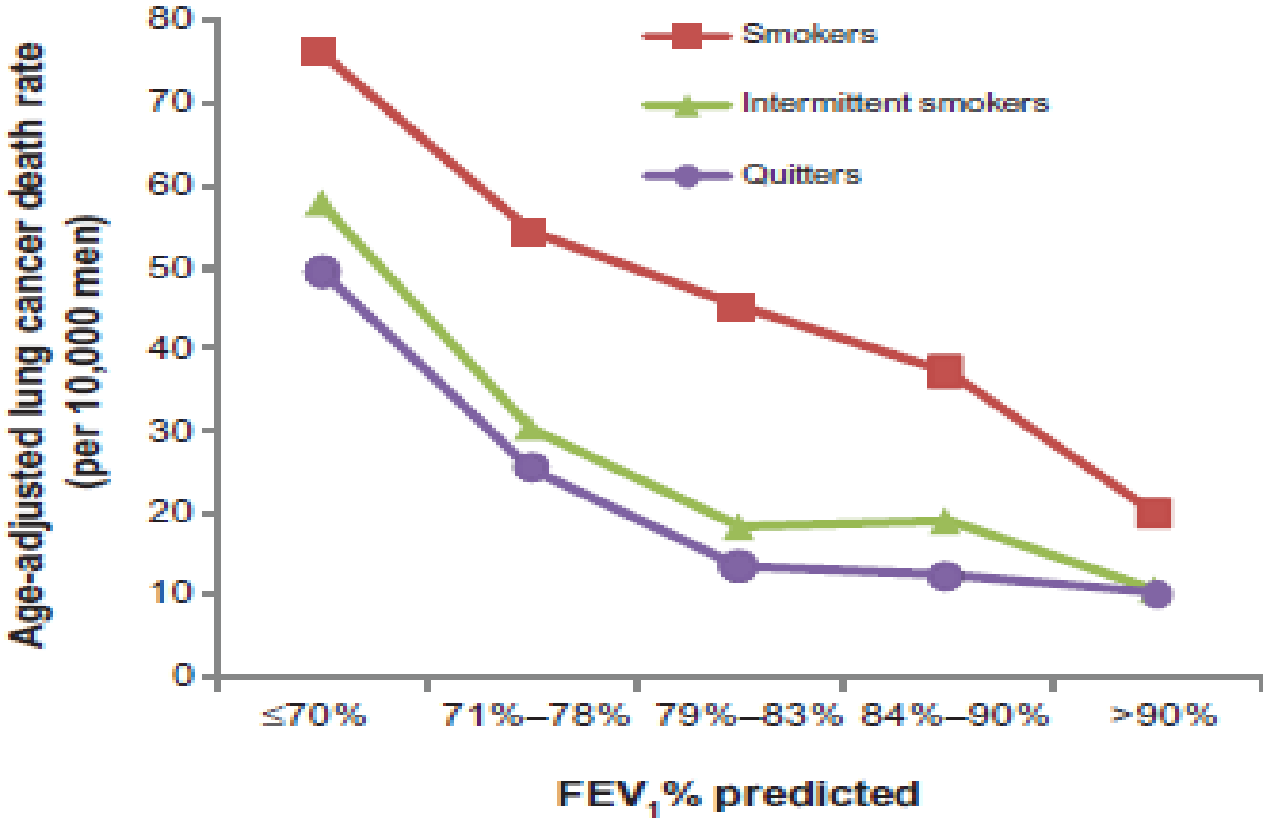
LHS : 35세에서 60세

1. **Smoking intervention + bronchodilator (atrovent 2puff tid)**
2. **Smoking intervention + placebo**
3. **No intervention**

Smoking intervention : intensive 12-session smoking cession program + behavior modification+ nicotine gum+ 5년간 maintenance program

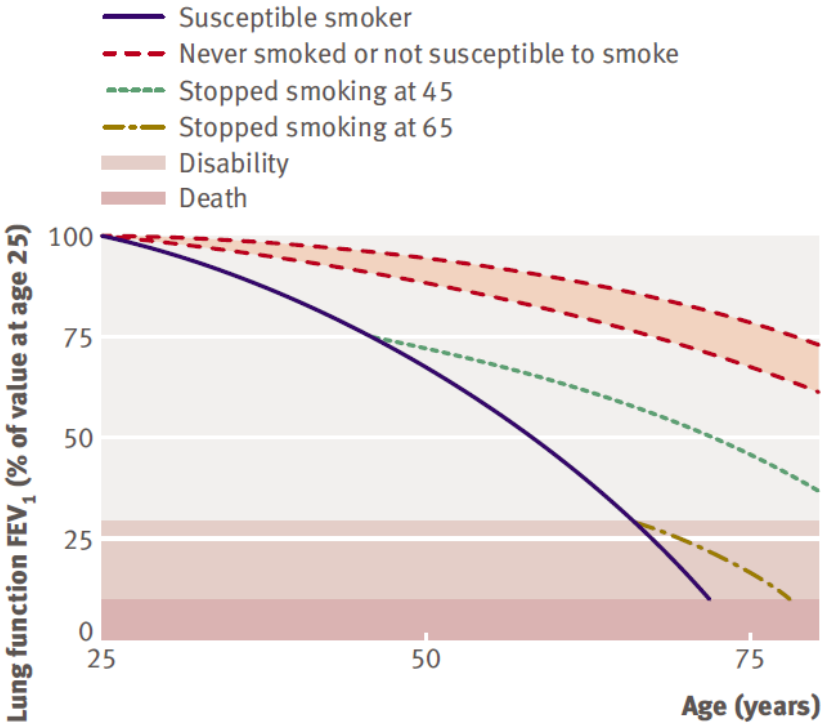
Int J of COPD 2011;6:259-267.

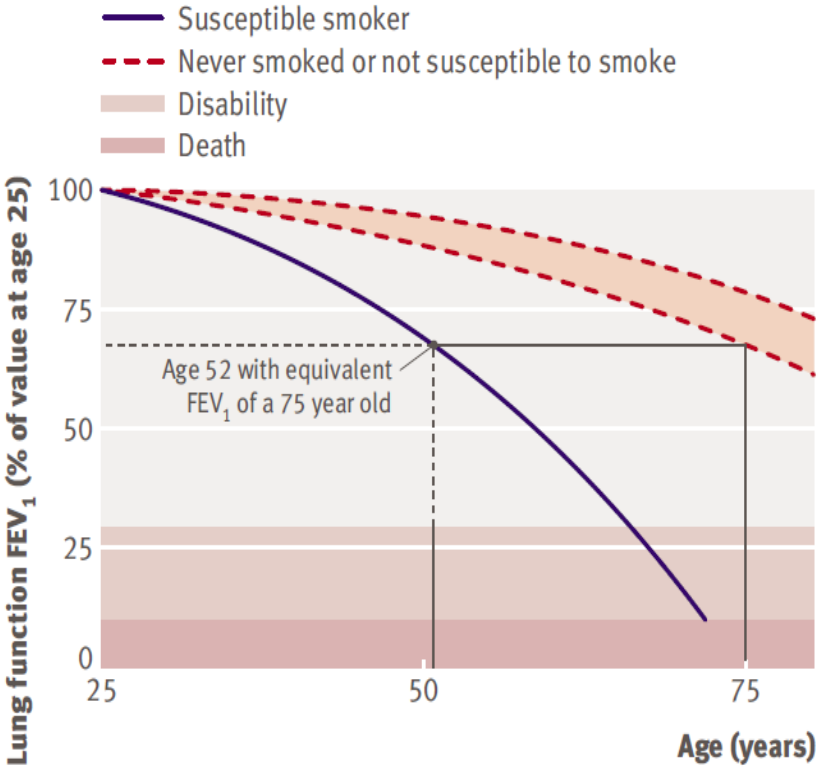
The relation of lung function and lung cancer mortality to smoking status (MRFIT Study)



Int J of COPD 2011;6:259-267.

Use of spirometry (“lung age”) in quitting





Lung age calculation formula developed by Morris and Temple[5]

Men

Lung age=2.87×height (in inches)−(31.25×observed FEV_1 (litres)−39.375

Women

Lung age=3.56×height (in inches)−(40 ×observed FEV_1 (litres)−77.28

BMJ 2008;336:598-600

Use of spirometry ("lung age") in quitting

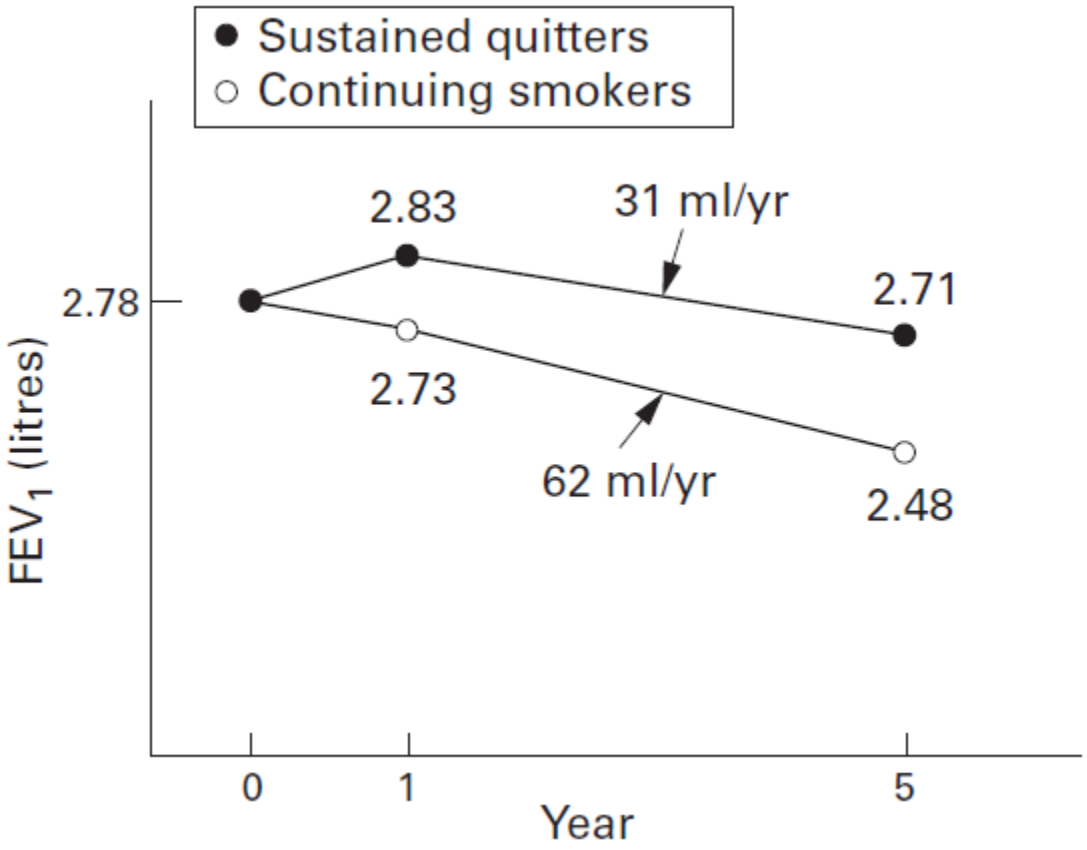
Table 3 | Results at 12 months. Figures are percentages (numbers) unless stated otherwise

	Control (n=281)	Intervention (n=280)	P value
Lost to follow-up	11.4 (32)	11.0 (31)	0.9
Smoking status			
Confirmed cessation*	6.4 (18)	13.6 (38)	0.01
Smoker at 12 months	90.4 (254)	84.6 (237)	
Unknown	3.2 (9)	1.8 (5)	
Mean (SD) daily cigarette consumption	13.7 (10.5)	11.7 (9.7)	0.03
Attended NHS smoking clinics	1.4 (4)	1.7 (5)	
Used smoking cessation help (clinic, NRT, bupropion, acupuncture)	7.8 (22)	10.7 (30)	0.2†

NRT=nicotine replacement therapy.
*Cotinine and CO measurement.
†χ^2 test.

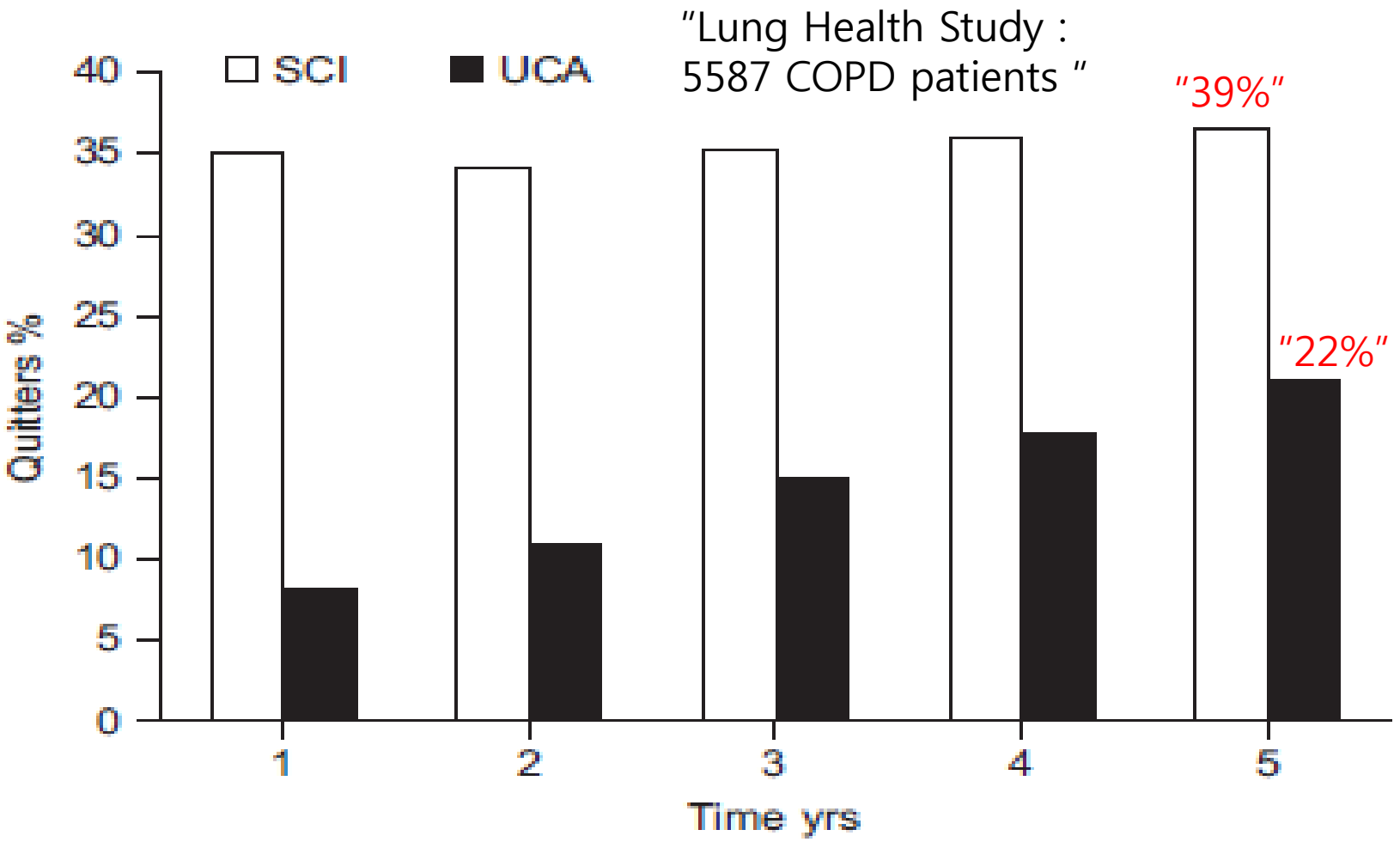
BMJ 2008;336:598-600

FEV1 change in continuing smokers and sustained quitters in the LHS (Lung Health Study)



AJRCCM 2000;161:381-90

Smoking Cessation rate change



ERJ 2013;22(127): 37-43.

Smoking and lung function of LHS participants after 11 years (LHS3)

TABLE 1. GENERAL CHARACTERISTICS OF LUNG HEALTH STUDY 3 PARTICIPANTS COMPARED WITH THOSE WHO REFUSED

	LHS 3	Refused	p Value
Number	4,517	896	
SI, %	67.3	64.6	0.119
Age as of LHS 3	61.3 (6.8)	59.7 (6.8)	< 0.001
Sex, % male	61.9	66.0	0.021
Cigarettes/d, baseline LHS 1	30.9 (12.7)	32.7 (13.2)	< 0.001
Smoking status at end of LHS 1			
Sustained quitter, %	18.8	6.6	< 0.001
Intermittent quitter, %	29.0	21.5	< 0.001
Continuing smoker, %	52.2	71.9	< 0.001
Attended last LHS 1 visit, %	99.2	85.6	0.001
Symptoms at end of LHS 1, %			
Cough	32.6	39.7	0.001
Phlegm	33.1	39.2	0.001
Wheeze	59.5	62.9	0.053
Dyspnea	33.6	32.5	0.532
FEV_1 % predicted post-BD, baseline LHS 1	78.4	78.4	0.966
FEV_1 % predicted post-BD, end of LHS 1	75.3	74.9	0.362
BD response (%), baseline LHS 1	4.3	4.3	0.844
Change in FEV_1% predicted/yr in LHS 1	−0.62	−0.81	0.005
Methacholine reactivity			
Reaction to ≤ 5 mg/ml, %	33.6	31.9	0.334
No reaction to 25 mg/ml, %	28.2	30.0	0.414

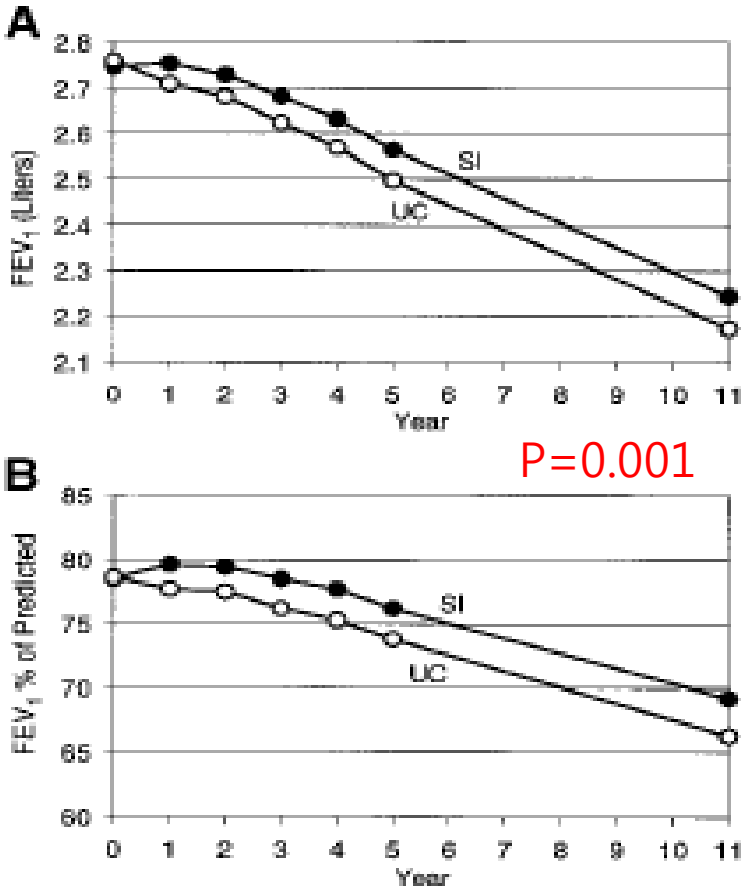
Definition of abbreviation: BD = bronchodilator; LHS = Lung Health Study; SI = smoking intervention.

AJRCCM 2002;166:675-9

Smoking and lung function of LHS participants after 11 years (LHS3)

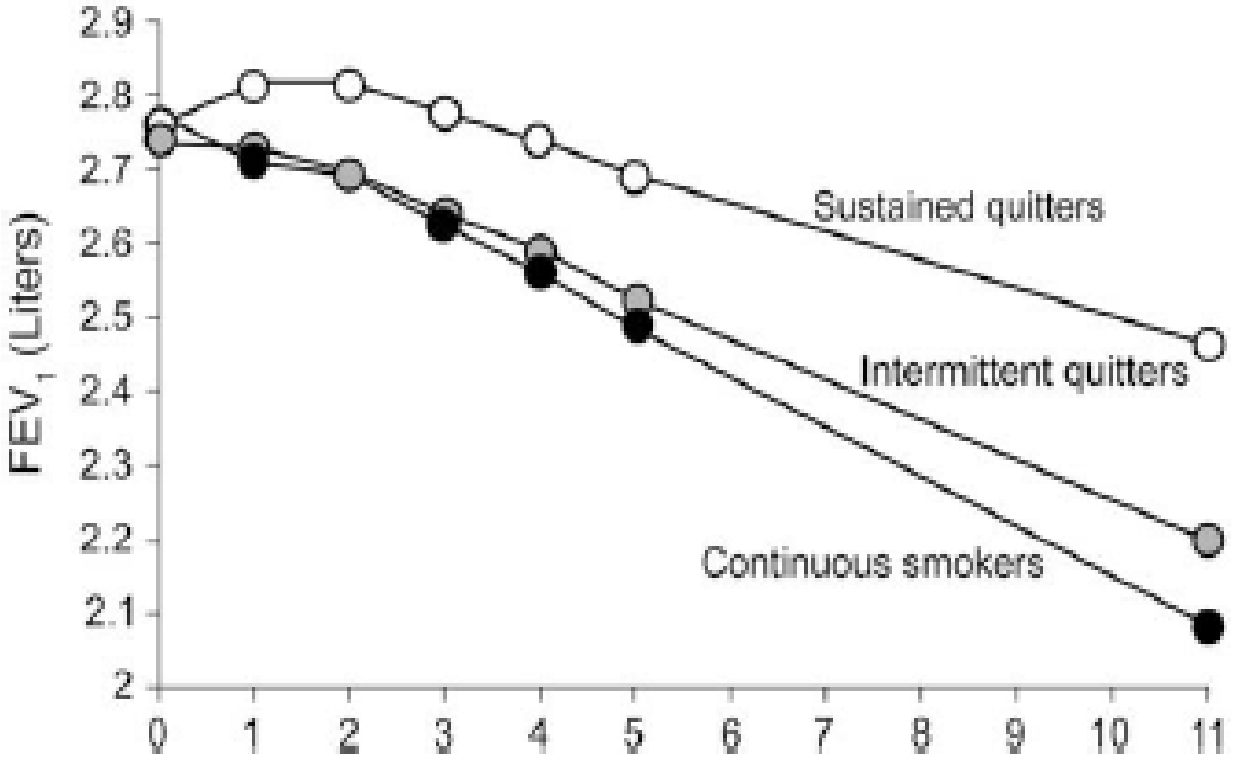
TABLE 2. CHANGE IN SMOKING STATUS BETWEEN END OF LUNG HEALTH STUDY 1 AND LUNG HEALTH STUDY 3

	% Quit (CO Validated) at LHS 3		
Status at End of LHS 1	Total (*n* = 4,517)	SI (*n* = 3,040)	UC (*n* = 1,477)
Sustained quitter	92.9	92.7	94.7
Intermittent quitter			
Not smoking	79.9	76.2	87.3
Smoking	43.3	42.8	45.1
Continuous smoker	24.1	22.4	26.3



AJRCCM 2002;166:675-9

Impact of smoking cessation vs continuing smoking on COPD (Lung Health Study3)



AJRCCM 2002;166:675-9

Smoking and lung function of LHS 3 participants after 11 years

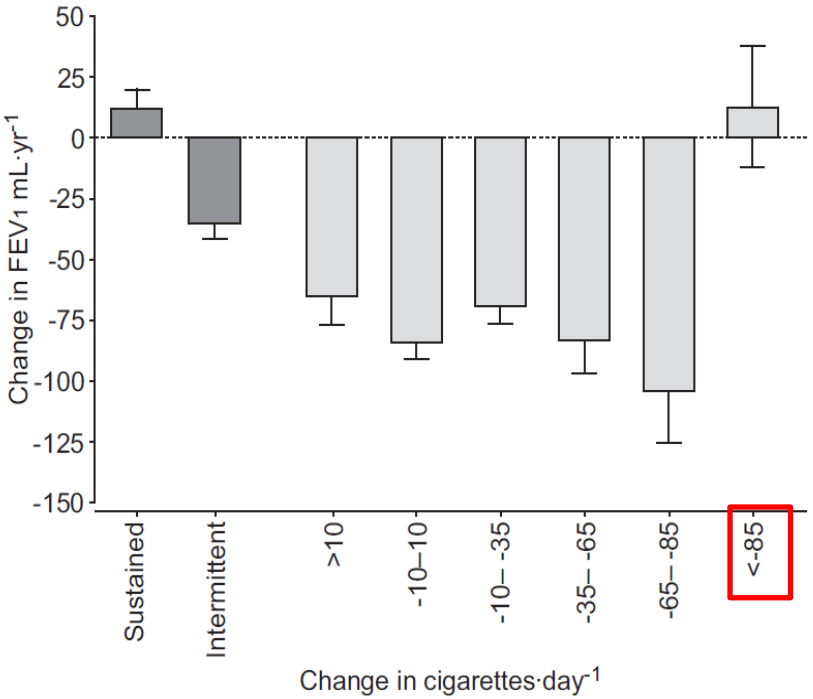
TABLE 3. ANNUAL CHANGE IN FEV_1 AND FEV_1 % PREDICTED-BASELINE LUNG HEALTH STUDY 1 TO LUNG HEALTH STUDY 3 ACCORDING TO LUNG HEALTH STUDY 3 SMOKING HISTORY (CARBON MONOXIDE VALIDATED)

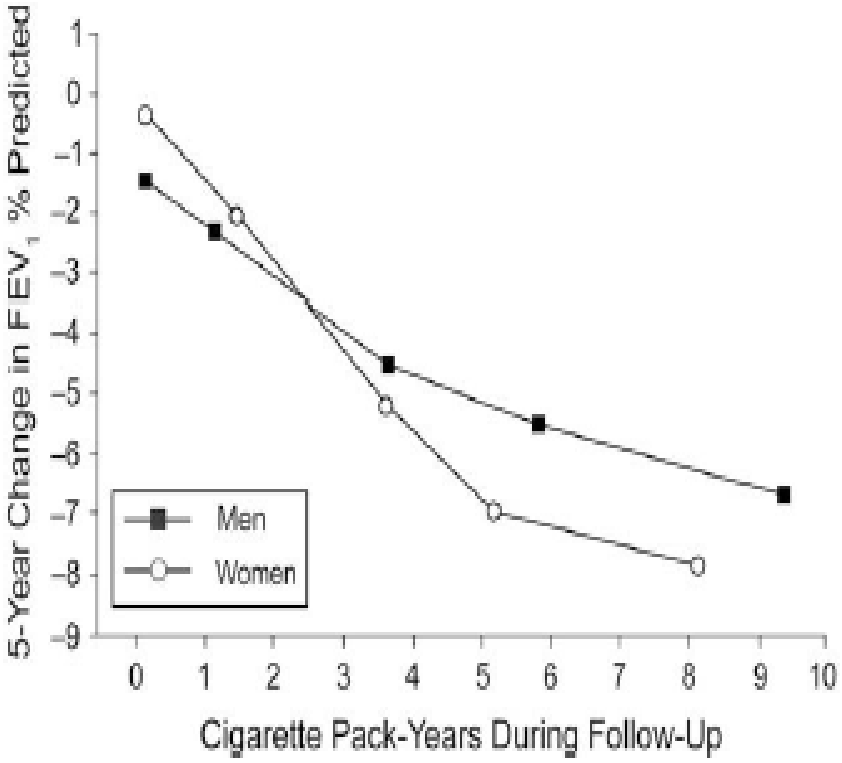
	SI Participants		UC Participants		
Status at LHS 3	n	FEV_1/ml/yr	n	FEV_1/ml/yr	p Value
Sustained quitter	637	−26.7 (26.5)	85	−30.3 (26.5)	0.250
Intermittent quitter	1,521	−47.5 (31.7)	848	−50.0 (34.5)	0.079
Continuing smoker	630	−60.0 (33.7)	424	−63.8 (32.2)	0.070
		FEV_1 % pred/yr		FEV_1 % pred/yr	
Sustained quitter	637	−0.23 (1.03)	85	−0.40 (1.11)	0.109
Intermittent quitter	1,521	−0.91 (1.21)	848	−1.02 (1.28)	0.041
Continuing smoker	630	−1.29 (1.16)	424	−1.44 (1.26)	0.043

Definition of abbreviations: SI = special intervention; UC = usual care.

AJRCCM 2002;166:675-9

Progression of COPD in LHS(Lung Health Study)





Resp Med 2009;103:963-974

Smoking cessation and the risk of hospitalization for pneumonia

Table 2 Risk of hospitalization for pneumonia by smoking status and duration of abstinence.

Tobacco exposure	Total (*N*)	Admissions (*N*)	Person-years	Rate (per 1000 person-years)	Adjusted hazard ratio (95% CI)
Smoking status					
Current	6720	89	6557	13.6	1.00[a]
Former	13,625	232	13,241	17.5	0.83 (0.63–1.09)
Never	4890	38	4825	7.9	**0.48 (0.31–0.74)**
Duration of smoking cessation					
Current	6720	89	6557	13.6	1.00[b]
Quit <1 year	1053	15	1020	14.7	0.93 (0.52–1.66)
Quit 1–5 years	1998	38	1938	19.6	0.95 (0.63–1.42)
Quit 6–10 years	1814	31	1763	17.6	0.79 (0.50–1.26)
Quit >10 years	8760	148	8520	17.4	0.77 (0.57–1.04)

Resp Med 2012;106:1055-1062

Smoking cessation and the risk of hospitalization for pneumonia

Table 3 Risk of hospitalization for pneumonia by smoking status and duration of abstinence, stratified by self-reported physician diagnosis of chronic obstructive pulmonary disease (COPD).

Tobacco exposure	Total (*N*)	Admissions (*N*)	Person-years	Rate (per 1000 person-years)	Adjusted hazard ratio (95% CI)
No self-reported diagnosis of COPD[a]					
Smoking status					
Current	4785	49	4694	10.4	Referent[a]
Former	10,481	113	10,247	11.0	**0.65 (0.45, 0.95)**
Duration of smoking cessation					
Current	4785	49	4694	10.4	Referent[a,b]
Quit <1 year	743	5	727	6.9	0.64 (0.25, 1.64)
Quit 1–5 years	1381	14	1350	10.4	0.71 (0.38, 1.35)
Quit 6–10 years	1347	16	1315	12.2	0.77 (0.41, 1.47)
Quit >10 years	7010	78	6855	11.4	**0.62 (0.41, 0.93)**
Self-reported diagnosis of COPD[a]					
Smoking status					
Current	1935	40	1863	21.5	Referent[c]
Former	3139	118	2990	39.5	1.04 (0.70–1.54)
Duration of smoking cessation					
Current	1935	40	1863	21.5	Referent[c,d]
Quit <1 year	310	10	292	34.2	1.24 (0.59–2.58)
Quit 1–5 years	616	24	587	40.9	1.23 (0.72–2.10)
Quit 6–10 years	466	15	448	33.5	0.83 (0.42–1.61)
Quit >10 years	1747	69	1663	41.5	0.99 (0.64–1.53)

Values in bold indicate *p*-value <0.05.

[a] Adjusted for age, race, marital status, education level, alcohol use, previous myocardial infarction, diabetes mellitus, history of cerebrovascular accident, congestive heart failure, malignancy, prior pneumonia, use of ICS, and average cigarettes per day.

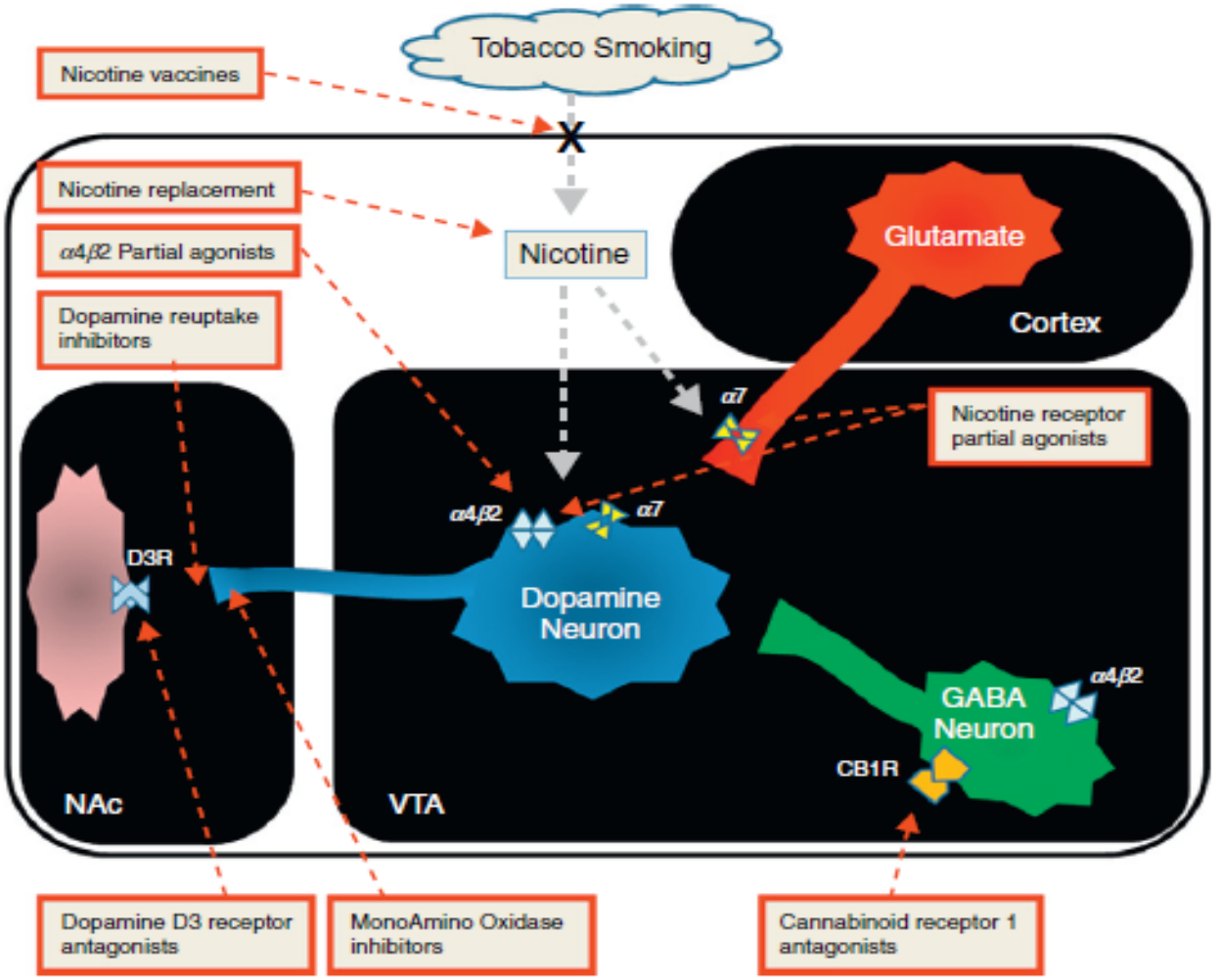
[b] *p*-value for linear trend = 0.03.

[c] Adjusted for same covariates listed above, with the exception of myocardial infarction, which was omitted from the model due to violation of proportional hazard assumptions.

[d] *p*-value for linear trend = 0.75.

Resp Med 2012:106:1055-1062

Classical neural pathways involed in nicotine addiction and related mechanism-based pharmacological rationale



Curr Opi in Pharmacol 2012;12:229-237

The effect of nonpharmacologic and pharmacologic interventions in smoking cessation with COPD

Table 1 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	1 & 5 years	35.0	9.0	Mild-moderate	Group intervention
	48	11 years	21.9	6.0	Mild-moderate	Group intervention
	59	6 months	23.0	10.0	All stages	Low vs. high support
		1 year[b]	17.0	10.0	All stages	Low vs. high support
Bupropion SR	50	6 months	16.0	9.0	Mild-moderate	Individual
		1 year	10.0	8.0	Mild-moderate	Individual
	53	1 year	19.0	9.0	Moderate-severe	Minimal vs. intensive
	64	6 months	27.3	8.3	Mild-moderate	Brief counseling
		6 months	28.6	22.0	At risk of COPD	Brief counseling
	69	1 year	16.1	8.4	General smoking population[c]	Brief counseling
	70	1 year	14.6	10.3	General smoking population[c]	Brief counseling
Varenicline	69	1 year	21.9	8.4	General smoking population[c]	Brief counseling
	70	1 year	23.0	10.3	General smoking population[c]	Brief counseling
Nortriptyline	64	6 months	21.2	8.3	Mild-moderate	Brief counseling
		6 months	32.1	22.0	At risk of COPD	Brief counseling

Resp Med 2009;103:963-974

Smoking Cessation in COPD

TABLE 6 Meta-analysis of smoking cessation trials in chronic obstructive pulmonary disease patients

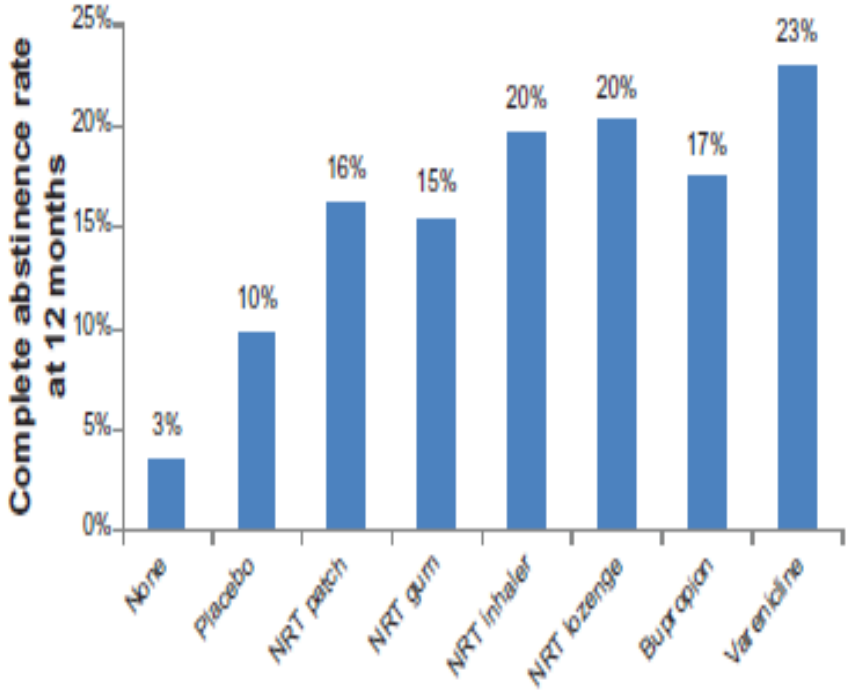
Study	Subjects n	Prolonged abstinence rate
Lung Health Study [36]	5887	12 months: 34% *versus* 9% (NRT)
Hilberink [37]	392	6 months: 16% *versus* 9% (NRT)
Tønnesen [20]	370	12 months: 14% *versus* 5% (NRT)
Tashkin [21]	404	6 months: 16% *versus* 9% (BUP)
Wagena [38]	255	6 months: 30% *versus* 19% (BUP)
Pederson [39]	64	6 months 27% *versus* 16%
Crowley [40]	49	6 months: 14% *versus* 14%
Brandt [41]	56	12 months: 32% *versus* 16%
Tashkin [22]	499	12 months: 19% *versus* 6% (VAR)

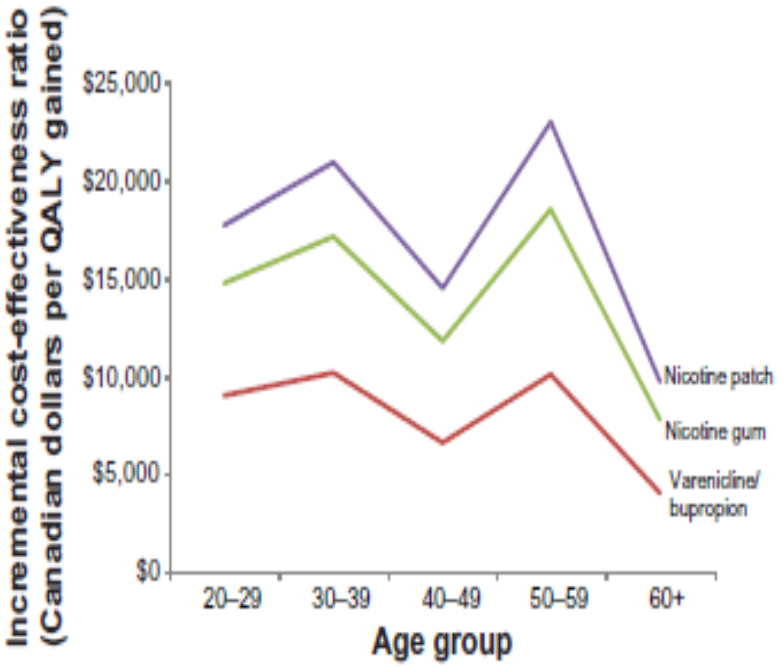
TABLE 7 Efficacy of smoking cessation after 6–12 months from meta-analysis of eight smoking cessation trials in chronic obstructive pulmonary disease patients

Treatment	OR (95% CI)	p-value
Nothing/usual care	1	
Counselling alone	1.82 (0.96–3.34)	0.07
Counselling + antidepressants	3.32 (1.53–7.21)	0.002
Counselling + NRT	5.08 (4.32–5.97)	<0.001
Counselling + varenicline	4.04 (2.13–7.67)	<0.001

ERJ 2013;22(127): 37-43.

Pharmacotherapy to effect tobacco treatment





Int J of COPD 2011;6:259-267.

Smoking Cessation in COPD patients (Bupropion)

Week	Continuous abstinence*			Point-prevalence abstinence†		
	Bupropion SR (n=204)	Placebo (n=200)	p	Bupropion SR (n=204)	Placebp (n=200)	p
5	63 (31%)	35 (18%)	0·001	68 (33%)	36 (18%)	<0·001
6	60 (29%)	33 (17%)	0·002	62 (30%)	39 (20%)	0·010
7	57 (28%)	32 (16%)	0·003	66 (32%)	39 (20%)	0·003
10	48 (24%)	28 (14%)	0·013	57 (28%)	32 (16%)	0·003
12	36 (18%)	20 (10%)	0·021	59 (29%)	33 (17%)	0·002
26	32 (16%)	18 (9%)	0·040	47 (23%)	32 (16%)	0·070

*No cigarettes from week 4 onwards. †Participants abstinent from smoking during previous 7 days.

Table 2: **Abstinence rates during treatment and follow-up phases**

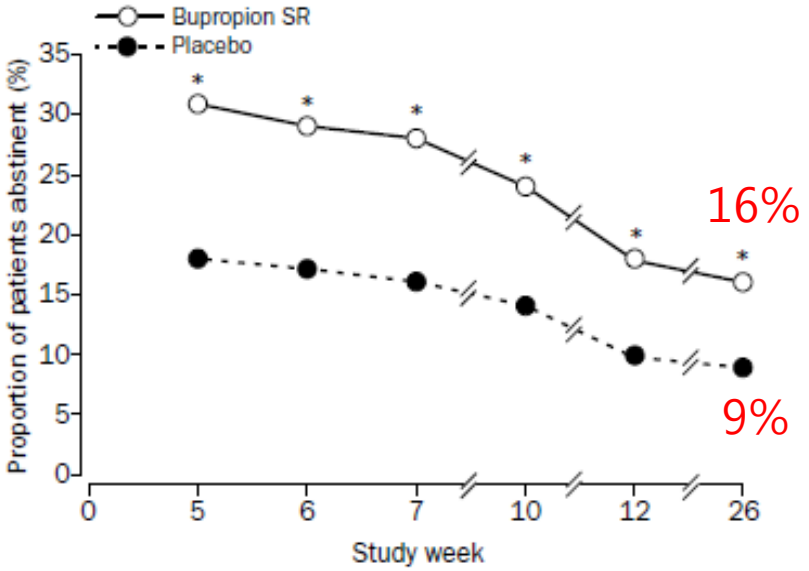
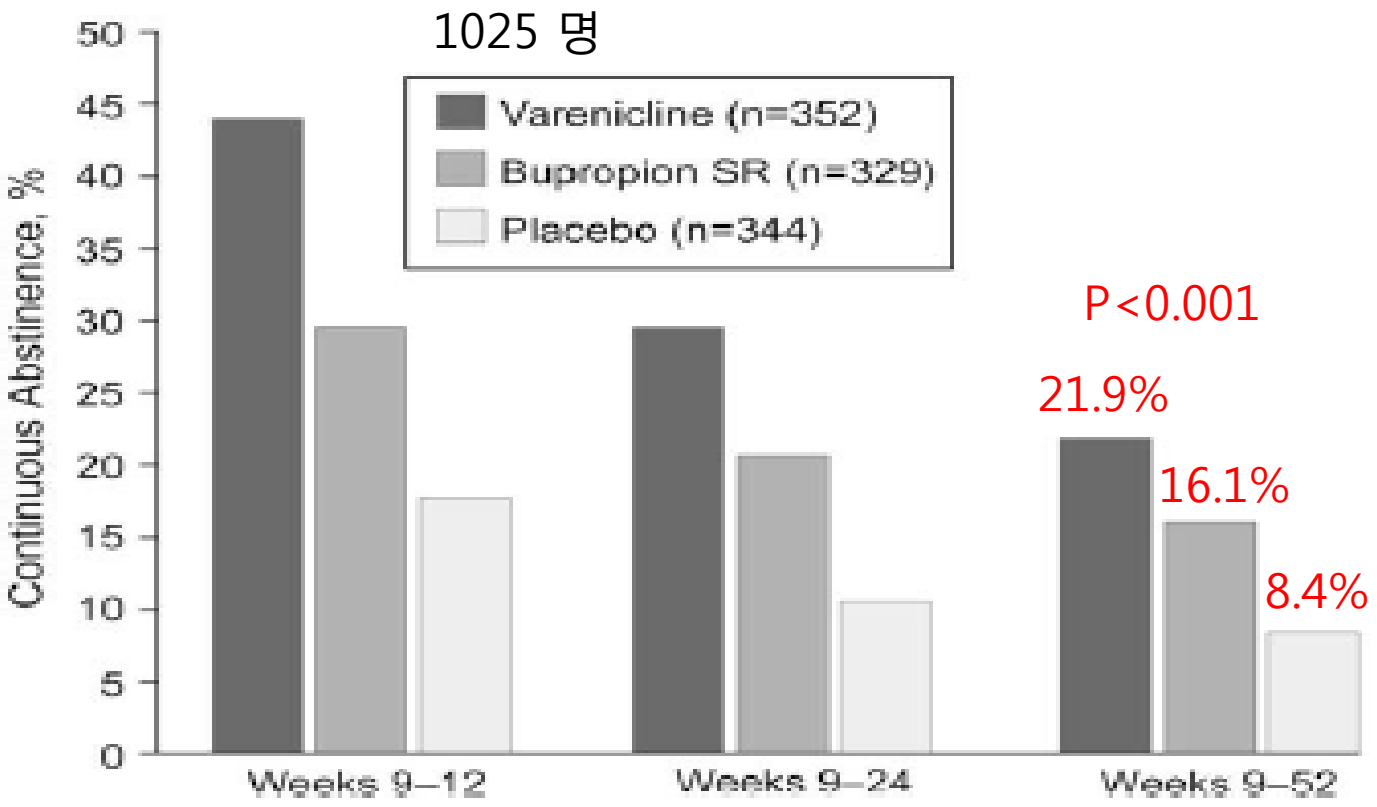


Figure 2: **Rates of continuous abstinence for weeks 4–12 and 4–26**

*p<0·05.

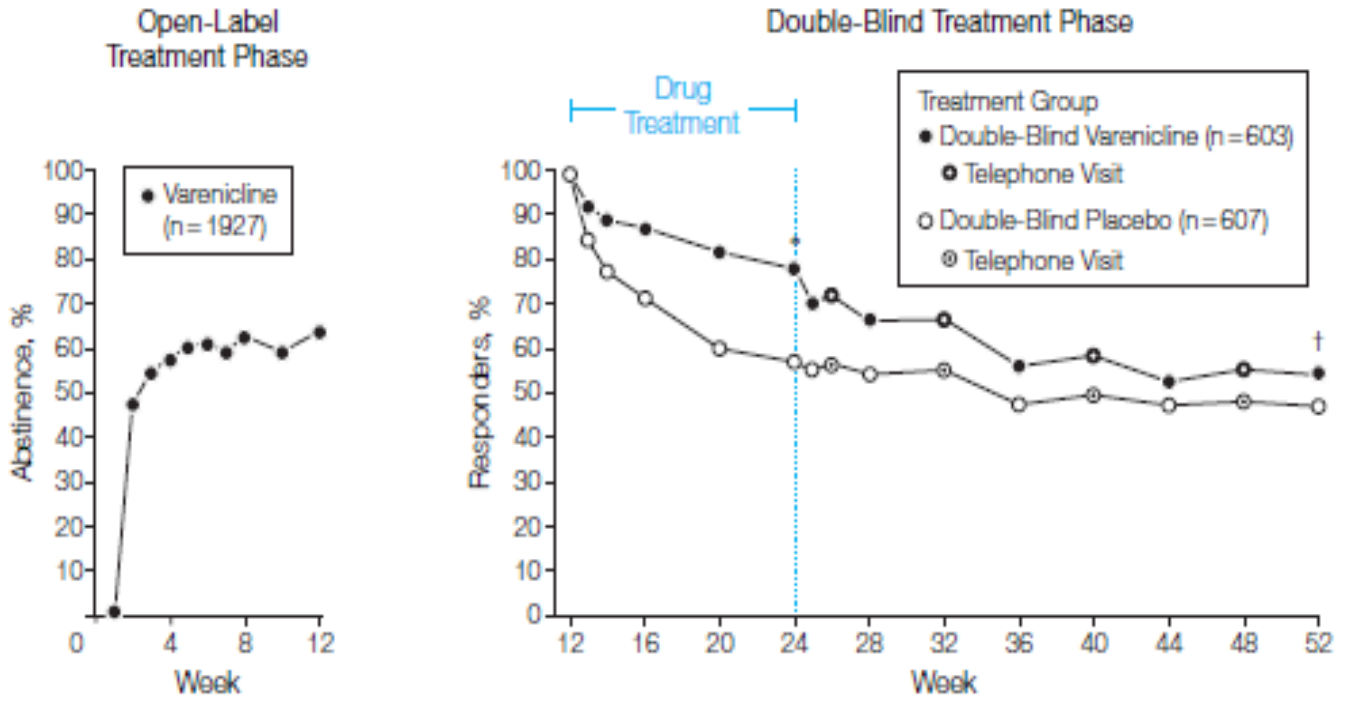
Lancet 2001;357:1571-75.

CO-confirmed continuous abstinence rates for varenicline vs. bupropion vs. placebo



JAMA 2006;296:47-55

Maintenance Tx with Varenicline on Smoking Cessation



*$P<.001$.
†$P=.01$.

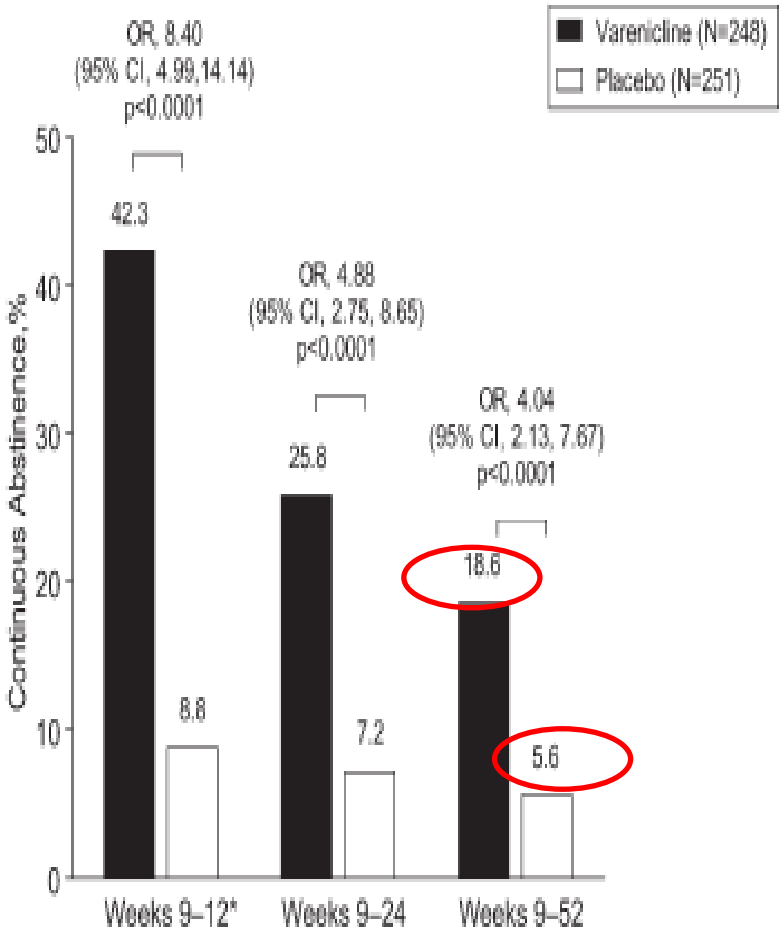
JAMA 2006;296;64-71

Effects of Varenicline on smoking cessation in mild to moderate COPD

27 centers

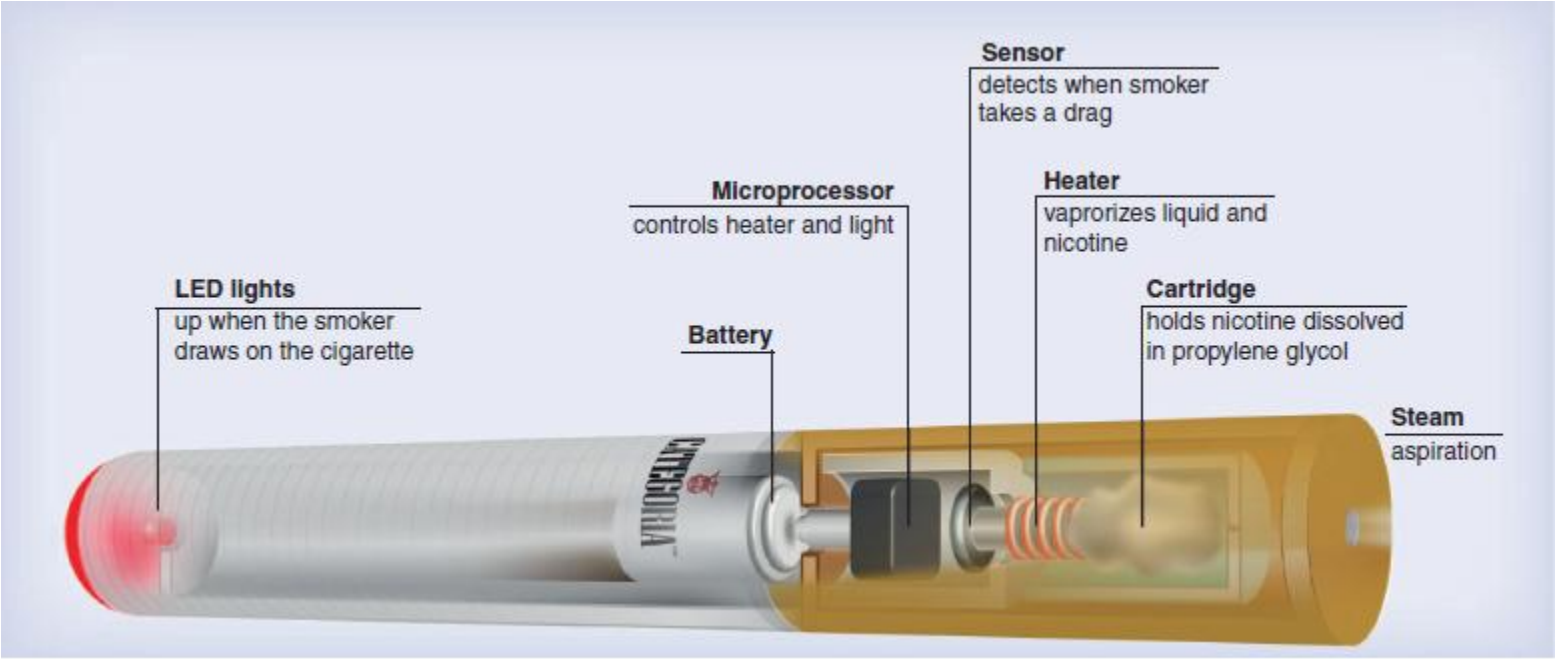
Table 1—*Demographic Characteristics and Smoking History*

Characteristic	Varenicline (n = 248)	Placebo[a] (n = 251)
Age, y	57.2 ± 9.1	57.1 ± 9.0
Height, cm	170.0 ± 9.4	170.4 ± 9.7
Weight, kg	77.9 ± 19.4	77.1 ± 17.6
BMI, kg/m²	26.8 ± 5.7	26.5 ± 5.2
Male sex	155 (62.5)	156 (62.2)
Race		
White	203 (81.9)	211 (84.1)
Black	15 (6.0)	10 (4.0)
Other	30 (12.1)	30 (12.0)
Years smoked	40.4 (11.0-67.0)	40.6 (18.0-64.0)
Cigarettes/d (past mo)	25.3 (10-99)	23.6 (10-60)
One or more previous serious quit attempts	205 (82.7)	200 (79.7)
Previous attempts with nicotine patch	120 (48.4)	115 (45.8)
Previous attempts with bupropion SR	68 (27.4)	68 (27.1)
FTND score[b]	6.2 ± 2.2	5.9 ± 2.1
Postbronchodilator FEV_1, L	2.29 ± 0.64	2.27 ± 0.69
Postbronchodilator FEV_1, % predicted	70.8 ± 17.0	69.1 ± 16.9
GOLD stage, No.[c]	222	235
I	50 (22.5)	50 (21.3)
II	148 (66.7)	157 (66.8)
III	23 (10.4)	28 (11.9)
IV	1 (0.4)	0



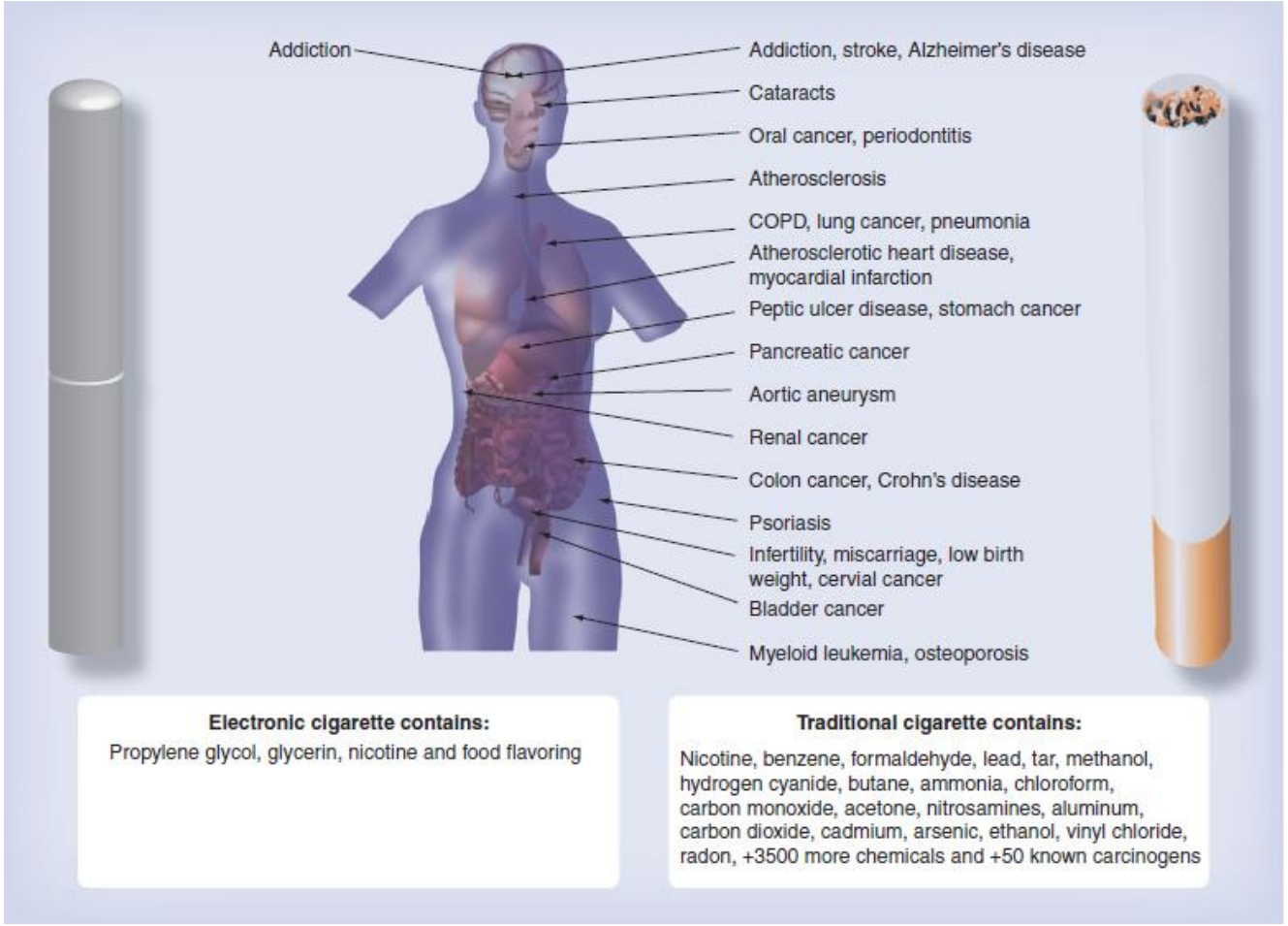
Chest 2011;139(3):591-599

The emerging phenomenon of electronic cigarettes



Expert Rev Resp Med 2012;6(1):63-74

The emerging phenomenon of electronic cigarettes



Expert Rev Resp Med 2012;6(1):63-74

Effect of an e-Cigarette on smoking reduction and cessation : a prospective 6-month pilot study

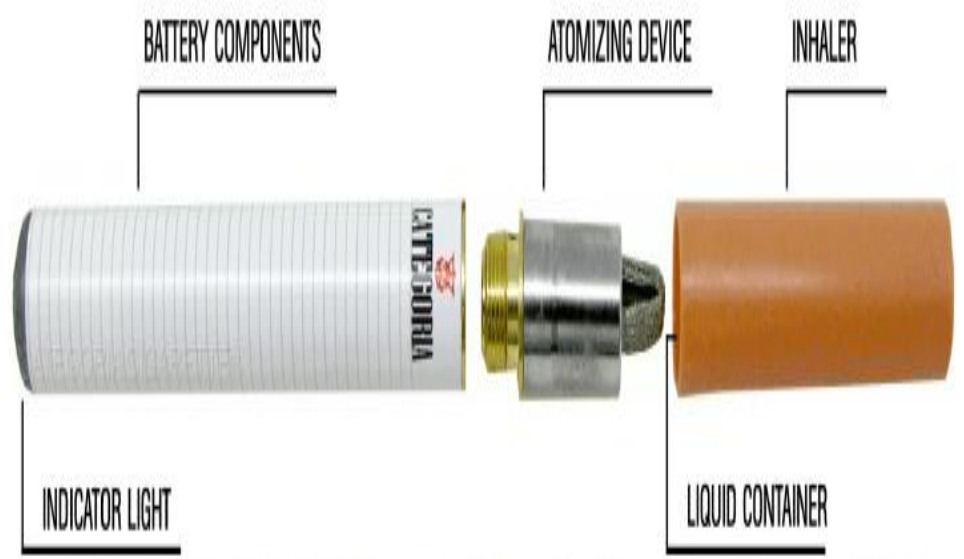
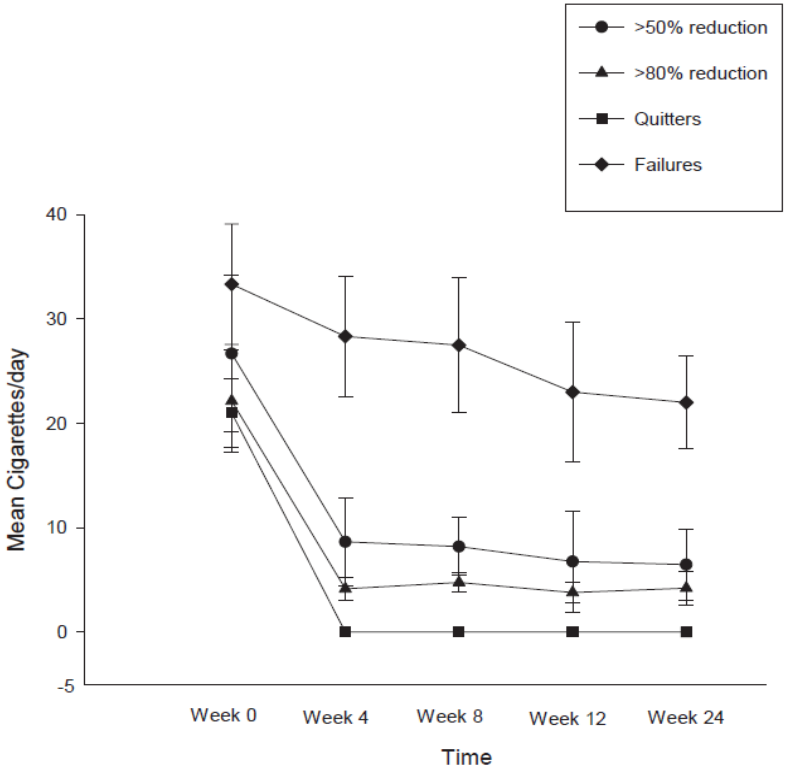
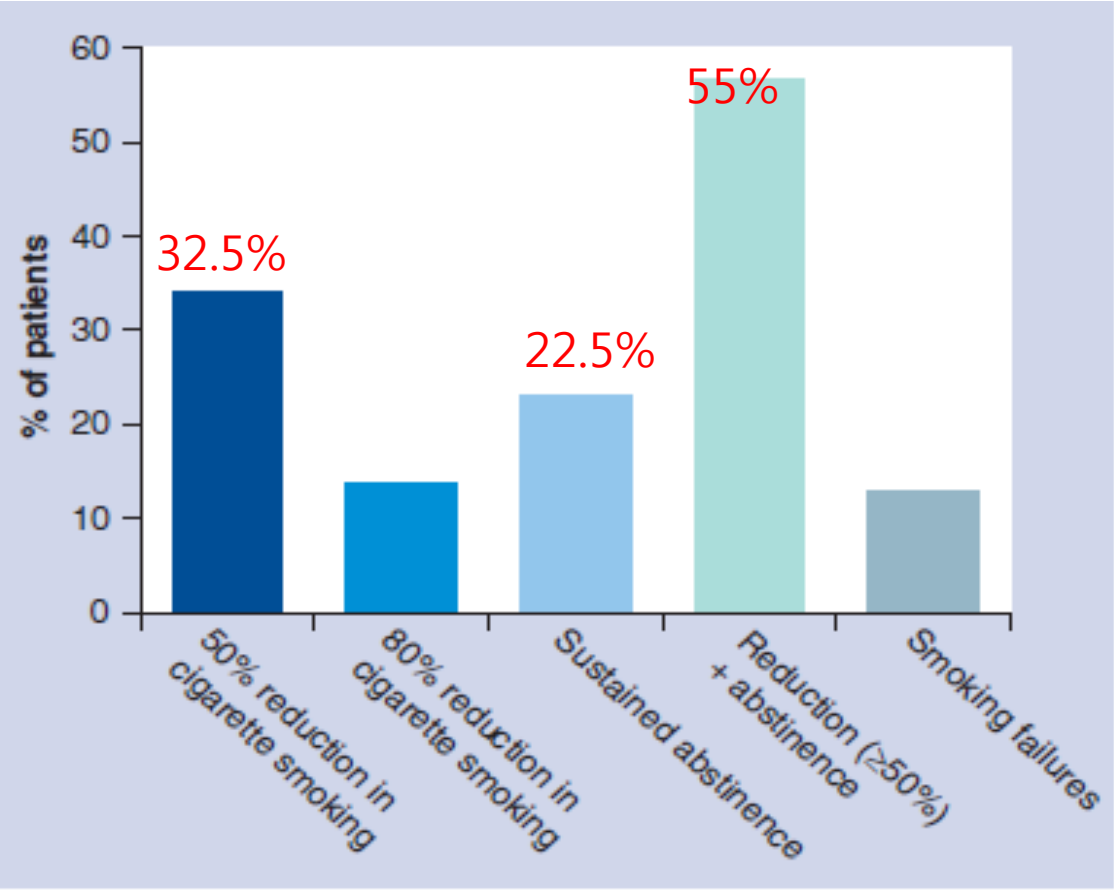


Figure 1 Structure of the 'Categoria' electronic-cigarette (e-Cigarette). The e-Cigarette is a battery-powered electronic nicotine delivery



BMC Pulblic Health 2011;11:786

Participant's smoking status after 24 weeks of electronic cigarette use



Expert Rev Resp Med 2012;6(1):63-74

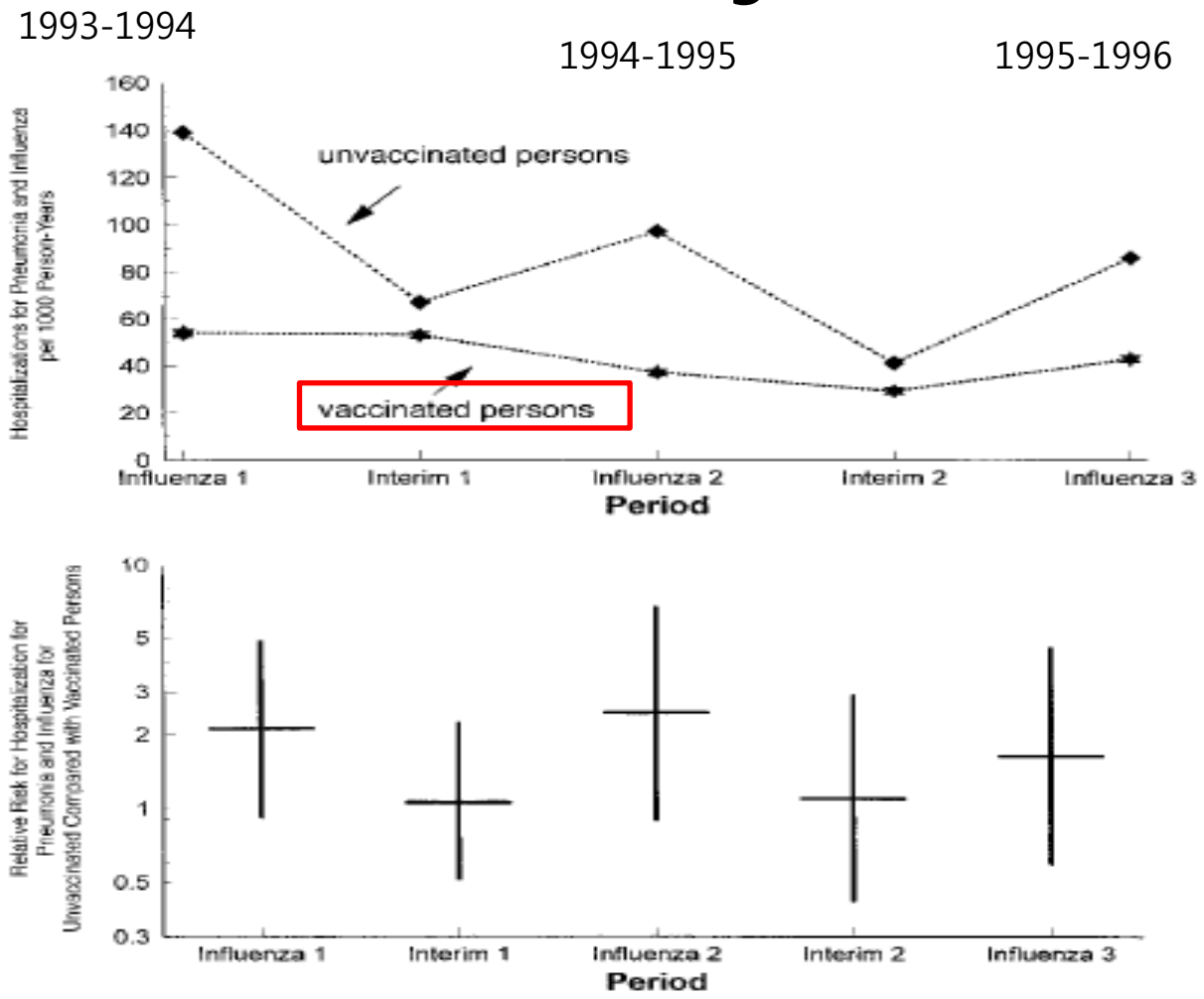
Relation between Influenza vaccination and outpatient visits, hospitalization, and mortality in Elderly persons with Chronic Lung Disease

Table 1. Characteristics of Study Cohort before the First Influenza Season*

Characteristic	Vaccinated Persons (n = 1366)	Unvaccinated Persons (n = 532)	P Value
Mean age ± SD, y	73.5 ± 5.3	75.0 ± 6.9	<0.001
Median age (25th, 75th percentiles), n	72.8 (69.4, 76.6)	73.5 (70.0, 79.4)	
Age ≥ 80 years, %	14.8	26.3	<0.001
Male sex, %	51.2	42.7	0.001
Previous diagnoses, %			
Heart disease	34.4	39.5	0.04
Diabetes	16.5	18.4	>0.2
Stroke or dementia	3.4	12.0	<0.001
Chronic renal disease	2.9	3.8	>0.2
Rheumatologic disease	2.8	3.4	>0.2
Cancer	16.5	21.4	0.01
History of pneumonia, %	16.5	20.3	0.06
Pneumococcal vaccination, %	49.6	31.2	<0.001
Mean physician visits ± SD, n	18.5 ± 13.1	16.5 ± 13.3	0.003
Median physician visits (25th, 75th percentiles), n	16.0 (9.0, 24.0)	13.0 (7.2, 22.0)	

Ann Intern Med. 1999;130:397-403

Relation between Influenza vaccination and outpatient visits, hospitalization, and mortality in Elderly persons with Chronic Lung Disease



Ann Intern Med. 1999;130:397-403

Relation between Influenza vaccination and outpatient visits, hospitalization, and mortality in Elderly persons with Chronic Lung Disease

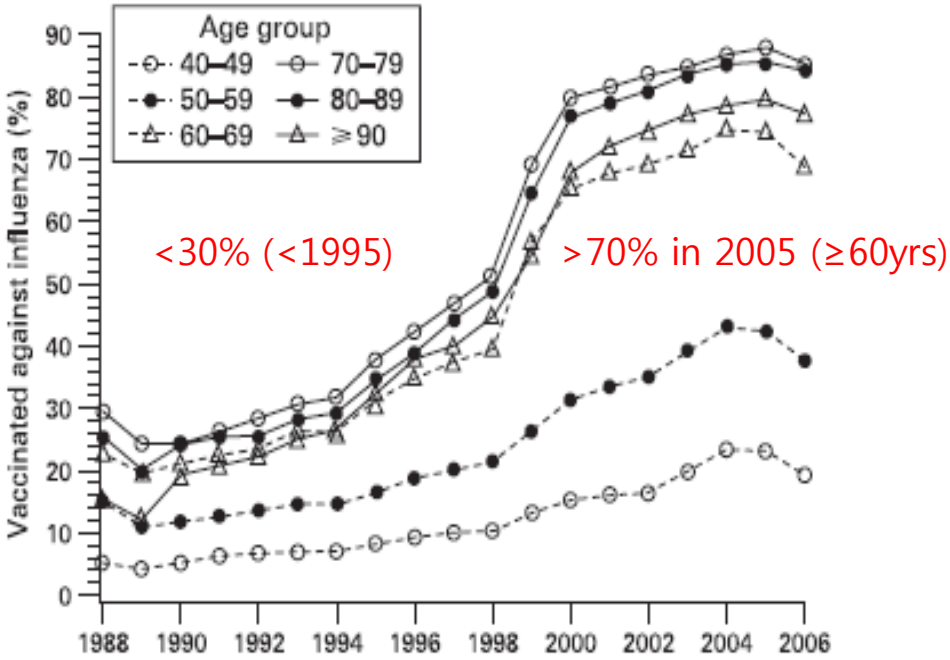
Table 2. Risk for Hospitalizations, Death, and Outpatient Visits among Vaccinated and Unvaccinated Persons during Three Influenza Seasons

Outcome	Risk Ratio or Odds Ratio (95% CI)*	*P* Value
Hospitalizations for pneumonia and influenza	0.48 (0.28–0.82)	0.008
Hospitalizations for all respiratory conditions	0.76 (0.53–1.09)	0.13
Death	0.30 (0.21–0.43)	<0.001
Outpatient visits for pneumonia and influenza		
≥1 outpatient visit	0.95 (0.73–1.25)	>0.2
Number of outpatient visits†	0.64 (0.49–0.84)	0.002
Outpatient visits for all respiratory conditions		
≥1 outpatient visit	0.95 (0.84–1.07)	>0.2
Number of outpatient visits†	0.89 (0.83–0.96)	0.002

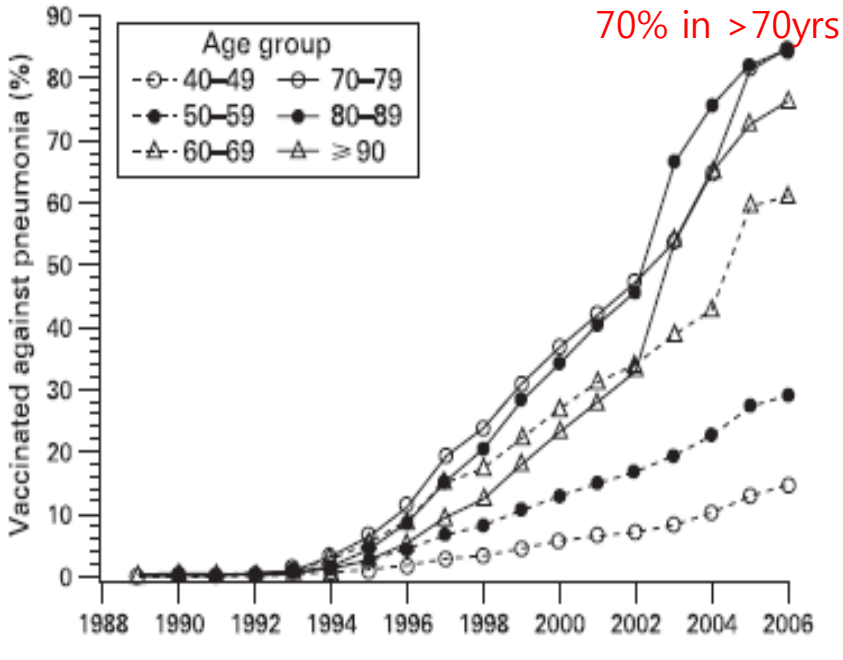
Ann Intern Med. 1999;130:397-403

Influenza but not pneumocccal vaccination protects against all-cause mortality in patients in patients with COPD

177,120 pts (65yrs), 6.8yrs



Influenza vaccination



Pneumococcal vaccination

Thorax 2009;64:567-572

Adjusted Relative Risks (RRs) for all-cause mortality in COPD

Risk factor	RR (95% CI)
Gender (men vs women)	1.41 (1.38 to 1.43)
Age	
40–49	0.1 (0.11 to 0.13)
50–59	0.3 (0.35 to 0.38)
60–69	1.00
70–79	2.1 (2.06 to 2.18)
80–89	3.7 (3.66 to 3.88)
≥90	6.7 (6.49 to 7.00)
Season (December to March vs April to November)	1.3 (1.33 to 1.40)
Unexpected influenza strain	1.1 (1.13 to 1.25)
Myocardial infarction	1.2 (1.23 to 1.30)
Congestive heart disease	2.1 (2.12 to 2.22)
Peripheral vascular disease	1.3 (1.33 to 1.40)
Cerebrovascular disease	1.3 (1.34 to 1.40)
Dementia	2.3 (2.22 to 2.44)
Rheumatic disease	1.1 (1.09 to 1.18)
Peptic ulcer disease	1.1 (1.07 to 1.14)
Mild liver disease	2.1 (1.86 to 2.42)
Diabetes	1.2 (1.25 to 1.32)
Diabetes with chronic disorders	1.0 (0.90 to 1.19)
Hemiplegia or paraplegia	1.4 (1.35 to 1.61)
Renal disease	1.7 (1.71 to 1.87)
Any malignancy	1.4 (1.39 to 1.45)
Moderate or severe liver disease	2.9 (2.49 to 3.57)
Metastatic solid tumour	3.9 (3.70 to 4.21)

Thorax 2009;64:567-572

Adjusted Relative Risks (RRs) associated with influenza and pneumonia vaccination for all-cause mortality in COPD

		December to March		April to November	
		Vaccinated against pneumonia		Vaccinated against pneumonia	
	Vaccinated against influenza	No	Yes	No	Yes
Deaths	No	1	1.68 (1.58 to 1.78)	1	1.28 (1.20 to 1.36)
	Yes	0.59 (0.57 to 0.61)	0.53 (0.51 to 0.56)	0.98 (0.95 to 1.01)	0.88 (0.85 to 0.91)
Deaths associated with a respiratory event	No	1	1.78 (1.55 to 2.04)	1	1.45 (1.25 to 1.79)
	Yes	0.63 (0.58 to 0.68)	0.61 (0.56 to 0.67)	1.03 (0.96 to 1.11)	1.03 (0.96 to 1.12)
Deaths with a respiratory event recorded as cause of death	No	1	2.29 (1.80 to 2.91)	1	1.93 (1.52 to 2.46)
	Yes	0.63 (0.55 to 0.77)	0.87 (0.74 to 1.03)	1.00 (0.85 to 1.19)	1.26 (1.09 to 1.46)

Thorax 2009;64:567-572

Interaction between influenza vaccination and season for all-cause mortality rates and death associated with a respiratory event in COPD

	December to November	December to March	April to November	December to March vs April to November
Patients not vaccinated against pneumonia				
Deaths	0.79 (0.77 to 0.80)	0.59 (0.57 to 0.61)	0.97 (0.94 to 1.00)	0.60 (0.58 to 0.63)
Deaths associated with a respiratory event	0.82 (0.77 to 0.86)	0.60 (0.53 to 0.68)	1.03 (0.96 to 1.11)	0.61 (0.55 to 0.68)
Deaths with a respiratory event recorded as cause of death	0.80 (0.70 to 0.92)	0.61 (0.51 to 0.75)	0.98 (0.83 to 1.17)	0.63 (0.49 to 0.81)
Patients vaccinated against pneumonia				
Deaths	0.46 (0.44 to 0.48)	0.30 (0.28 to 0.32)	0.64 (0.60 to 0.68)	0.47 (0.43 to 0.51)
Deaths associated with a respiratory event	0.47 (0.42 to 0.52)	0.32 (0.28 to 0.37)	0.65 (0.56 to 0.76)	0.49 (0.40 to 0.60)
Deaths with a respiratory event recorded as cause of death	0.50 (0.48 to 0.52)	0.37 (0.30 to 0.46)	0.63 (0.510.79)	0.59 (0.43 to 0.80)

Thorax 2009;64:567-572

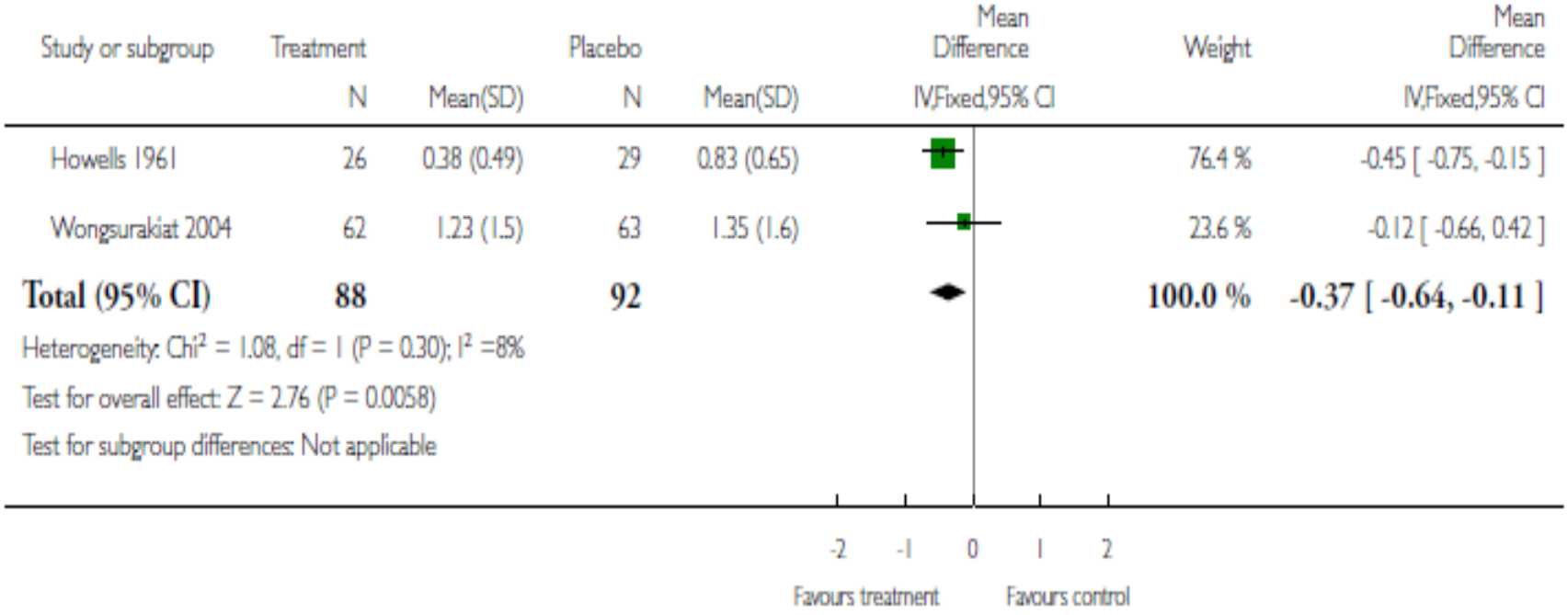
The Effect of influenza vaccination on the incidence of COPD exacerbations in the immediate postvaccination period

Age	37-89 yrs
Median age	68
M:F ratio	1.84:1
GOLD stage I	16 (2.7%)
GOLD stage II	358(61.1%)
GOLD stage III	176(30.0%)
GOLD stage IV	36 (6.1%)

	Control exacerbated	Control did not exacerbate
Vaccinated patient exacerbated	0	11
Vaccinated patient did exacerbate	21	261

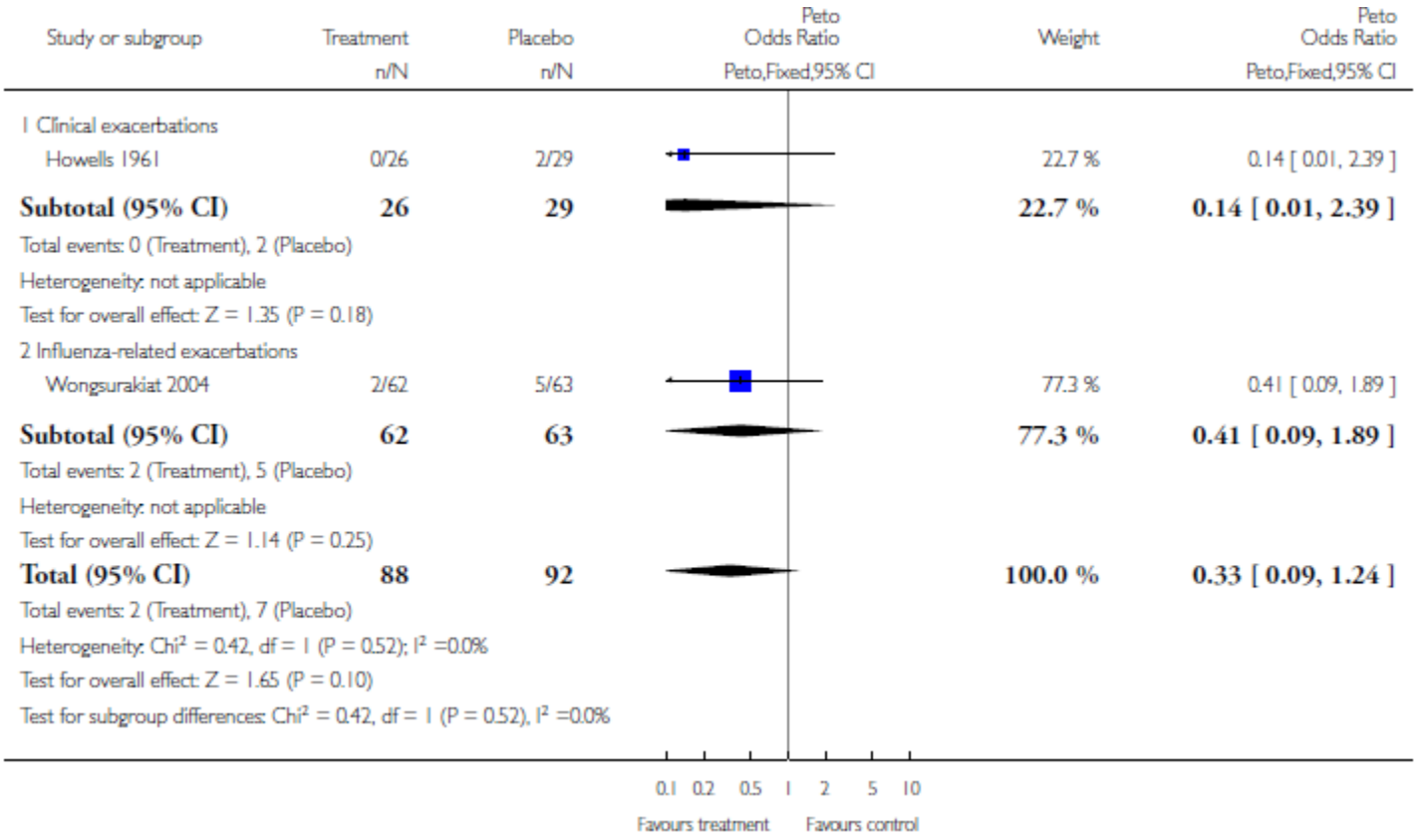
J Epidemiol Community Health 2011;65:157-159

Influenza vaccination vs placebo (total exacerbation / patient) in COPD



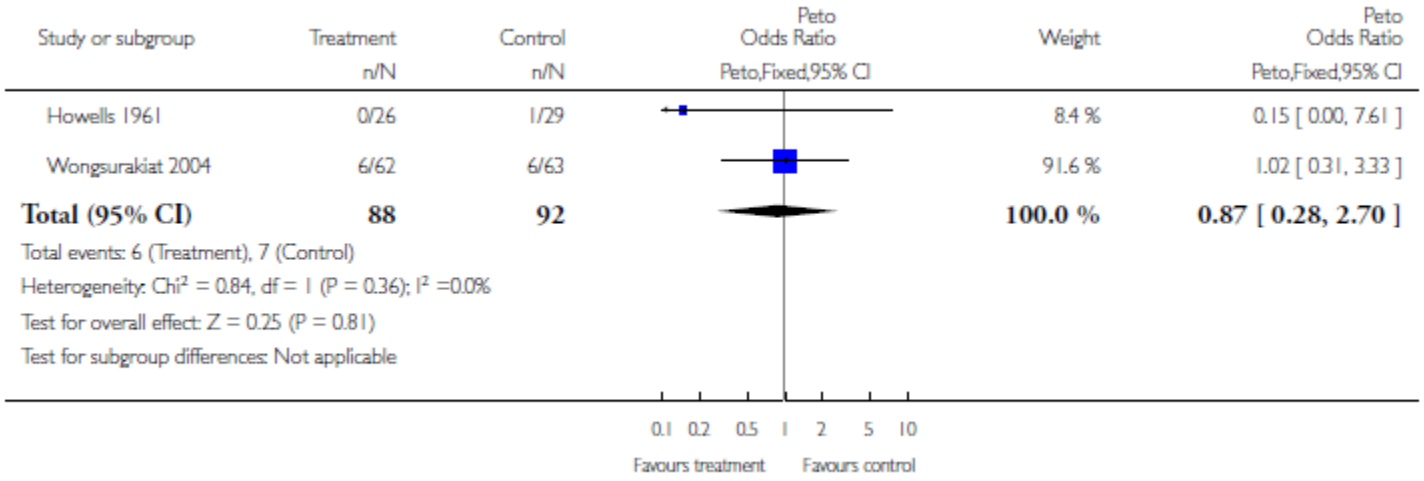
The Cochrane Library 2006.

Influenza vaccination vs placebo (Hospitalization) in COPD



The Cochrane Library 2006.

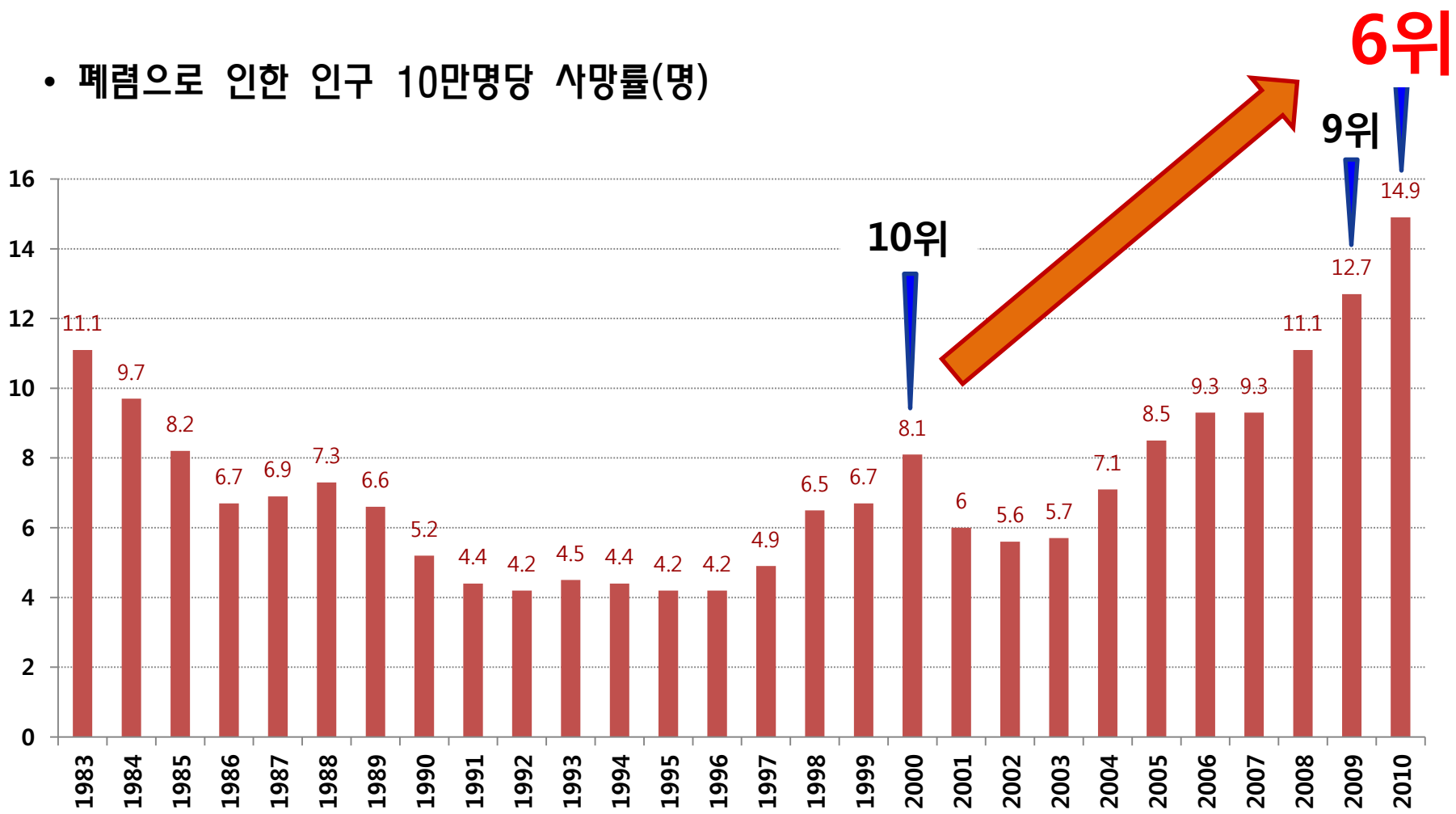
Influenza vaccination vs placebo (Mortality)



The Cochrane Library 2006.

연도별 폐렴 사망률 (한국)

- 폐렴으로 인한 인구 10만명당 사망률(명)



통계청「2010년 사망원인통계」

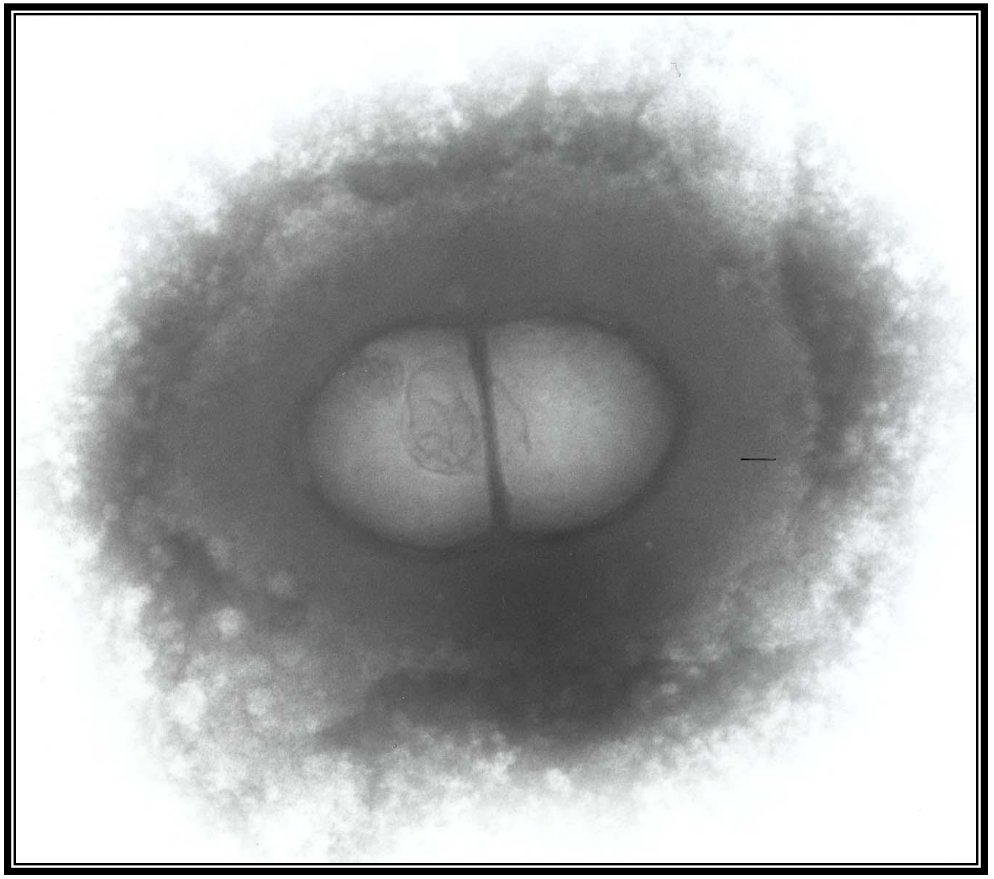
S. pneumoniae Is the Most Commonly Identified Organism Causing CAP: Meta-Analysis of 127 Study Cohorts

Agent	Patients	% Contribution
S. Pneumoniae	**4432**	**24.2**
Hemophilus influenzae	833	4.5
Mycoplasma pneumoniae	507	2.8
Mixed bacteria	301	1.6
Legionella	272	1.5
Viruses	197	1.1
Coxiella burnetti	182	1.0
Staphylococcus aureus	157	0.9
Other bacteria	182	1.0
Unknown	11,229	61.3
Total	**18,292**	**100.00**

Fine MJ et al. *JAMA*. 1996;275:134-141.

Streptococcus pneumoniae: Causative Agent of Pneumococcal Disease

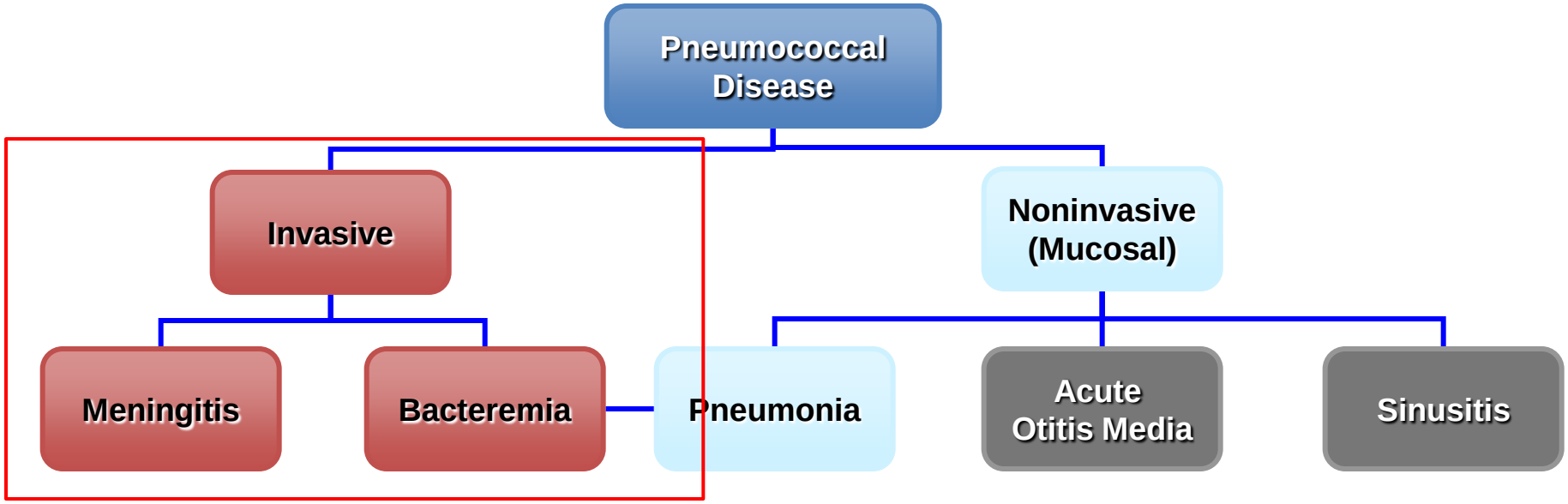
- **Gram+ bacterium[1]**
- **Polysaccharide capsule[1,2]**
  - Virulence factor
  - Defines serotype
  - Vaccine target
- **90 known serotypes[1,2]**
  - 11 serotypes account for 70% to 93% of cases of invasive disease worldwide[3]



Serotype 19F; Photograph by Rob Smith. **Bar=100 nm**

1. CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases.* 11th ed. 2009;217-230.
2. WHO. Acute Respiratory Infections (Update February 2009). http://www.who.int/vaccine_research/diseases/ari/en/print.html. Accessed May 27, 2009.
3. Hausdorff WP et al. *Clin Infect Dis.* 2000;30:100-121.

Major Clinical Forms of Pneumococcal Disease



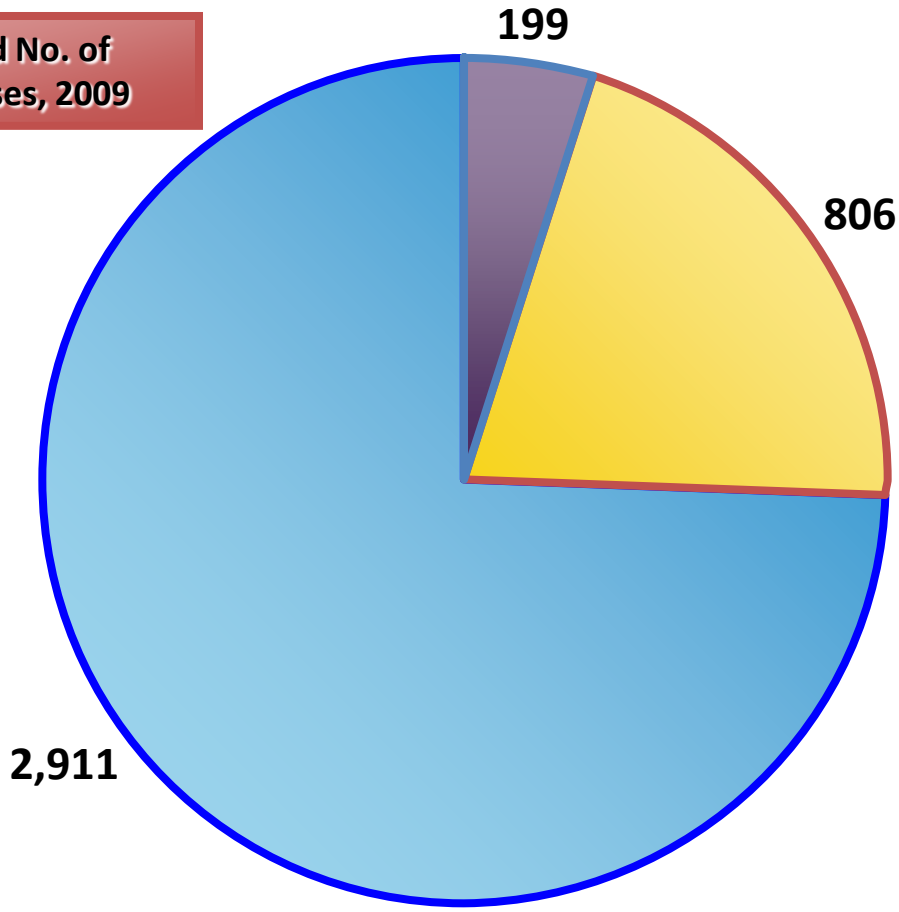
- Pneumococcal disease can be broadly grouped into categories of invasive disease and noninvasive (also termed *mucosal*) disease[1]
- Noninvasive forms of disease may become invasive (eg, pneumonia when accompanied by bacteremia)[2]
- Serotype is associated with disease severity and invasiveness[3]

1. WHO. Acute Respiratory Infections (Update September 2009). www.who.int/vaccine_research/diseases/ari/en/print.html. Accessed December 20, 2010.
2. CDC. *Epidemiology and prevention of vaccine-preventable diseases.* 11th ed. 2009;217-230.
3. Jansen AG et al. *Clin Infect Dis.* 2009;49:e23-e29.

Major Clinical Syndromes of Invasive Pneumococcal Disease in Adults: US

IPD is defined as the isolation of *S. pneumoniae* from a normally sterile site

Estimated No. of Annual Cases, 2009



- Meningitis
- Bacteremia without focus
- Pneumonia with bacteremia

Age, years	Cases, rate*
18–49	16
50–64	21.2
≥65	39.7

*Cases per 100,000 population for ABCs area.

Invasive pneumococcal disease in Korea

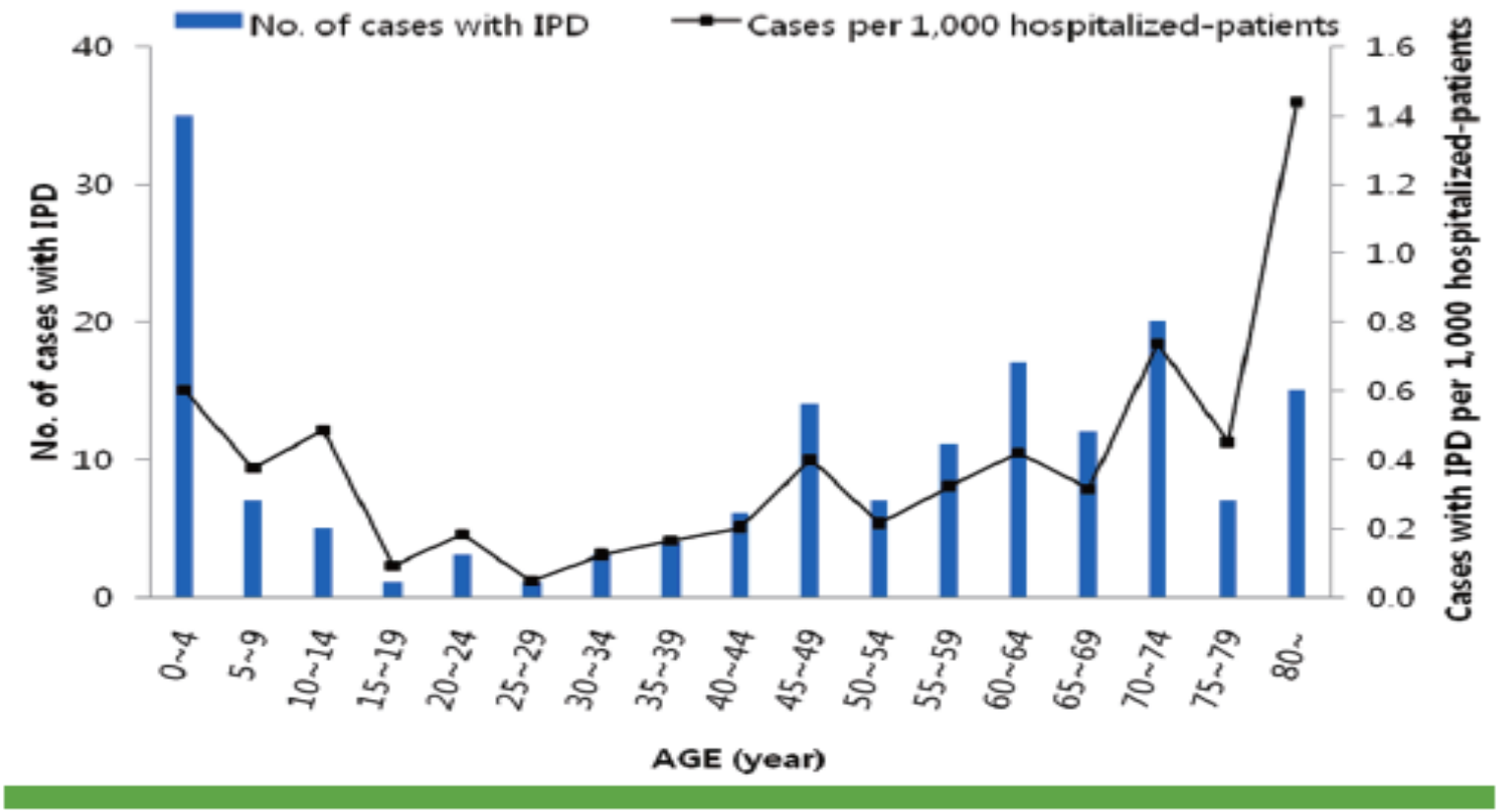


Figure 1. Age distribution of cases with invasive pneumococcal disease (IPD) in 3 university hospitals in Korea from January 2002 to December 2007.

Multiple Adult Populations Are at Increased Risk for Pneumococcal Disease

Diseases/Conditions
COPD[2-4]
Asthma[2]
Diabetes mellitus[2-4]
Chronic CVD and other chronic diseases[1-4] • eg, renal failure, alcoholism
Sickle cell disease[3]
Immunodeficiency[1,2,4]

Circumstances
Age ≥65 years old[1] Infants
Cigarette smoking[1]
Living in a crowded environment[1,2] • eg, nursing home or other long-term care facility, correctional facility
Race/ethnicity: [1,2] • African American, Alaskan Native, American Indian

COPD=chronic obstructive pulmonary disease; CV

1. Whitney CG et al. Clin Infect Dis. 2001;33:662-675.
2. CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases. 11th ed. 2009;217-230.
3. Fletcher MA et al. Int J Pract. 2006;60:450-456.
4. Kyaw MH et al. J Infect Dis. 2005;192:377-386.

S. pneumoniae: Capsule Influence on Disease

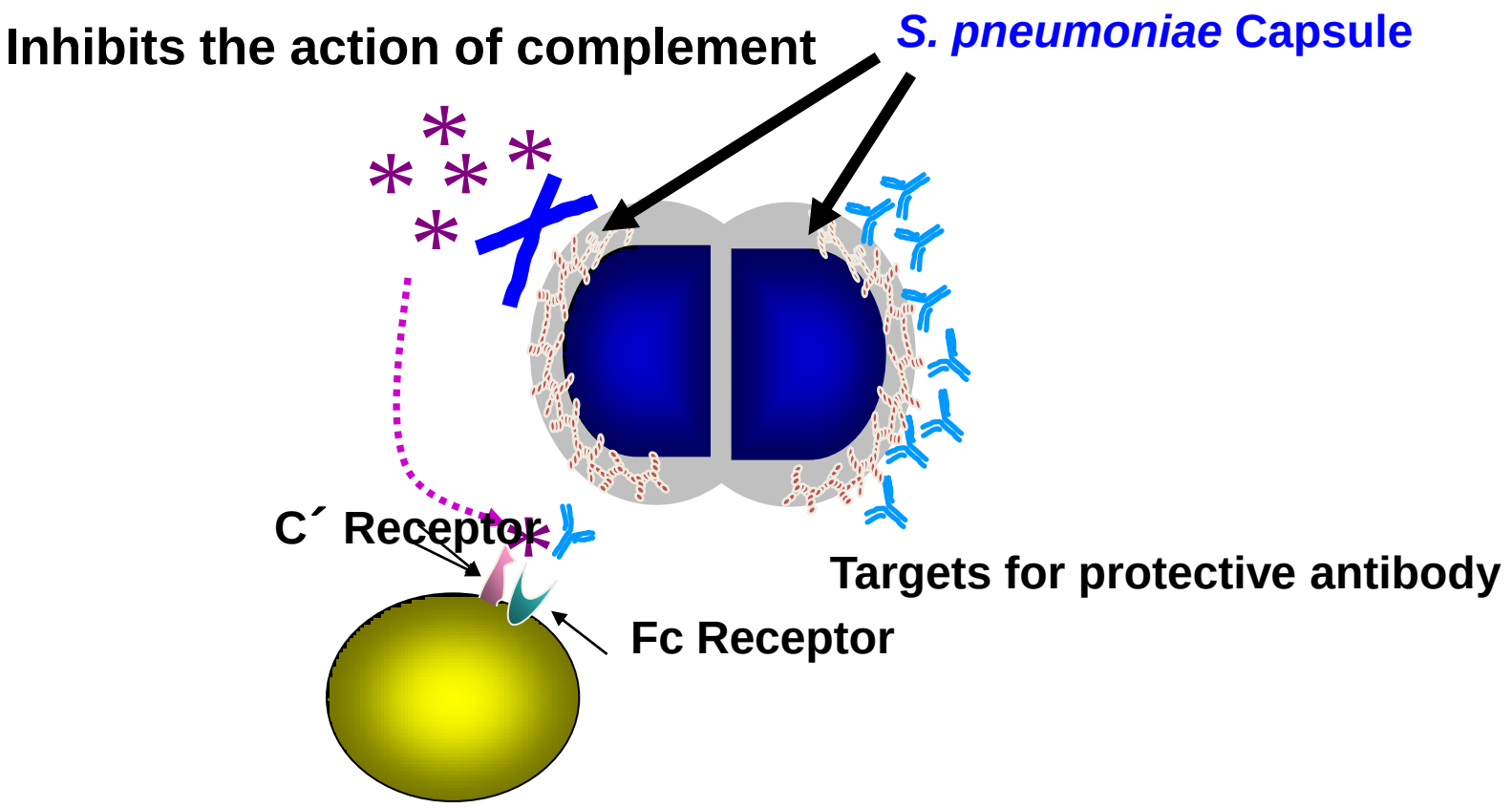


Image courtesy of Dr. David Goldblatt

1. CDC. *Epidemiology and prevention of vaccine-preventable Diseases.* 11th ed. 2009:217-233.
2. WHO. Acute Respiratory Infections (Update September 2009). http://www.who.int/vaccine_research/diseases/ari/en/print.html. Accessed March 16, 2009.

The history of Pneumococcal vaccines

1. Austrian R. *Drugs Aging*. 1999;15(suppl 1):1-10.
2. Fedson DS. *Drugs Aging*. 1999;15(suppl 1):21-30.
3. Summary of basis for approval. Pneumococcal vaccine, polyvalent. June 1983.

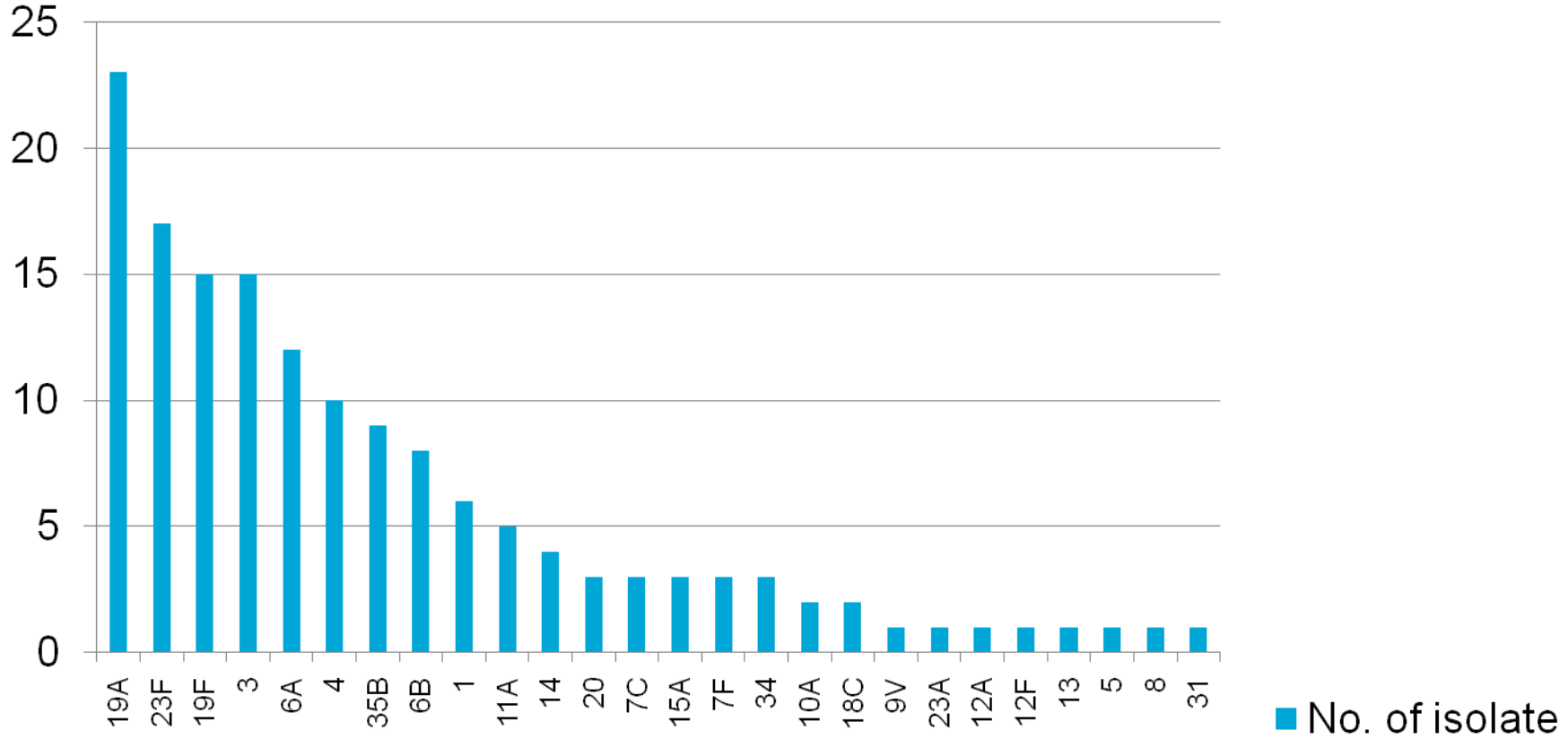
Most common serotypes of *Streptococcus pneumoniae*

Serotype	1	2	3	4	5	6A	6B	9V	12F	14	18C	19A	19F	23C	23F	35
New Zealand[1]				✓			✓	✓		✓			✓	✓		
Taiwan[2]			✓	✓						✓			✓		✓	
South Korea[3]						✓				✓		✓			✓	✓
China[4]	✓	✓			✓	✓				✓		✓				
Japan[5-6]			✓	✓						✓					✓	

- **11 serotypes account for 70% to 93% of cases of invasive disease**

1. PCV13 Advisory Board, Dec 2008; 2. Chen YY, et al. J Med Microbiol. 2006;55:1109-1114; 3. Acute respiratory infections survey, KCDC 2005-2006; 4. Zhonghua Liu Xing Bing Xue Za Zhi. 1989;10(3):133-7 ; 5. PCV13 Advisory Board, Dec 2008; 6. Chiba N et al., Epidemiol Infec 2009;Jun 19:1-8 (Epub ahead of print).

Distribution of serotypes in 158 isolates from pneumococcal pneumonia patients(adults)



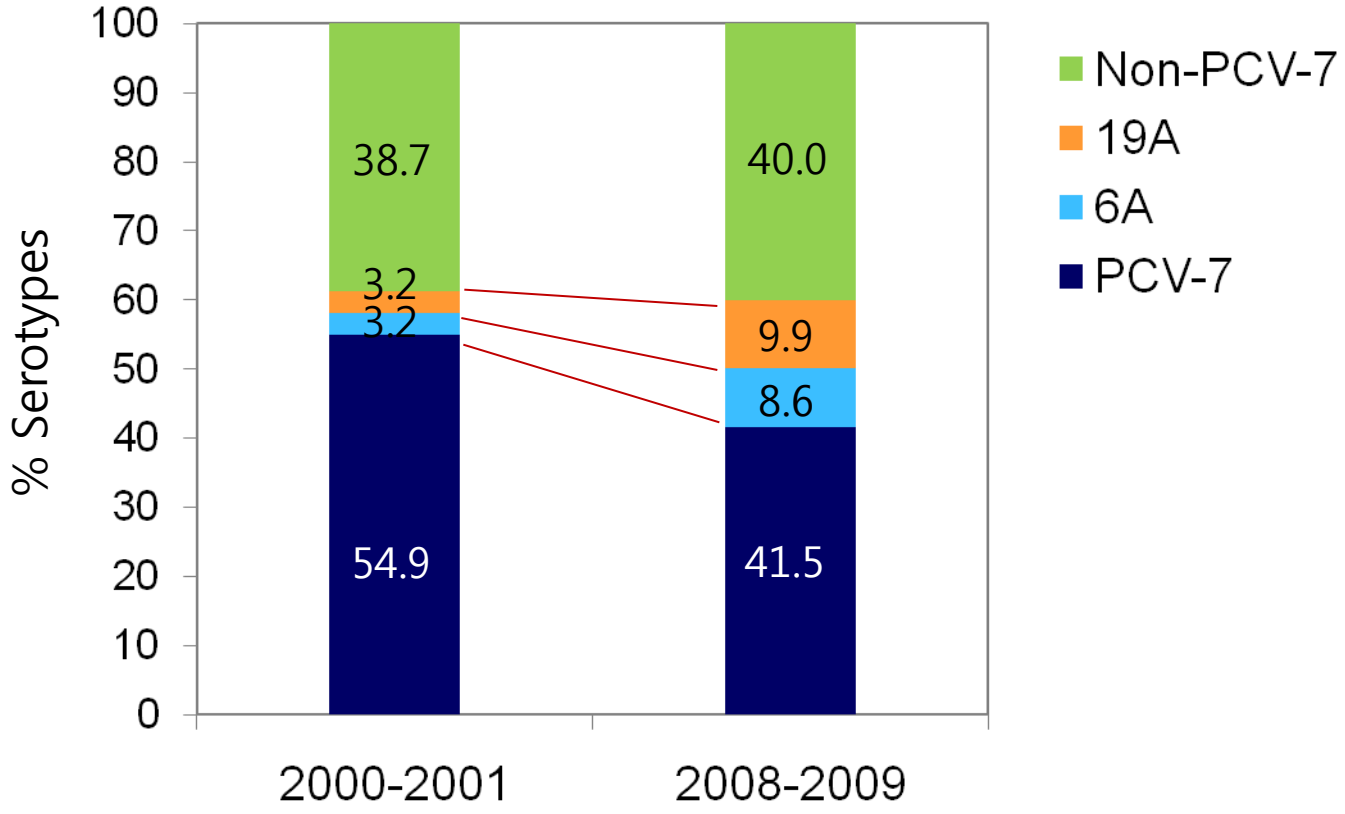
PCV13 coverage: 117/158(74.1%)

PPV23 coverage: 117/158(74.1%)

Data from KCDC 2009

Emergence of non-PCV-7 serotypes

- Increase of 19A & 6A in Korea



Song JH & ANSORP. AAC. 2004, 48:2101-2107;
ANSORP surveillance project 2008-2009

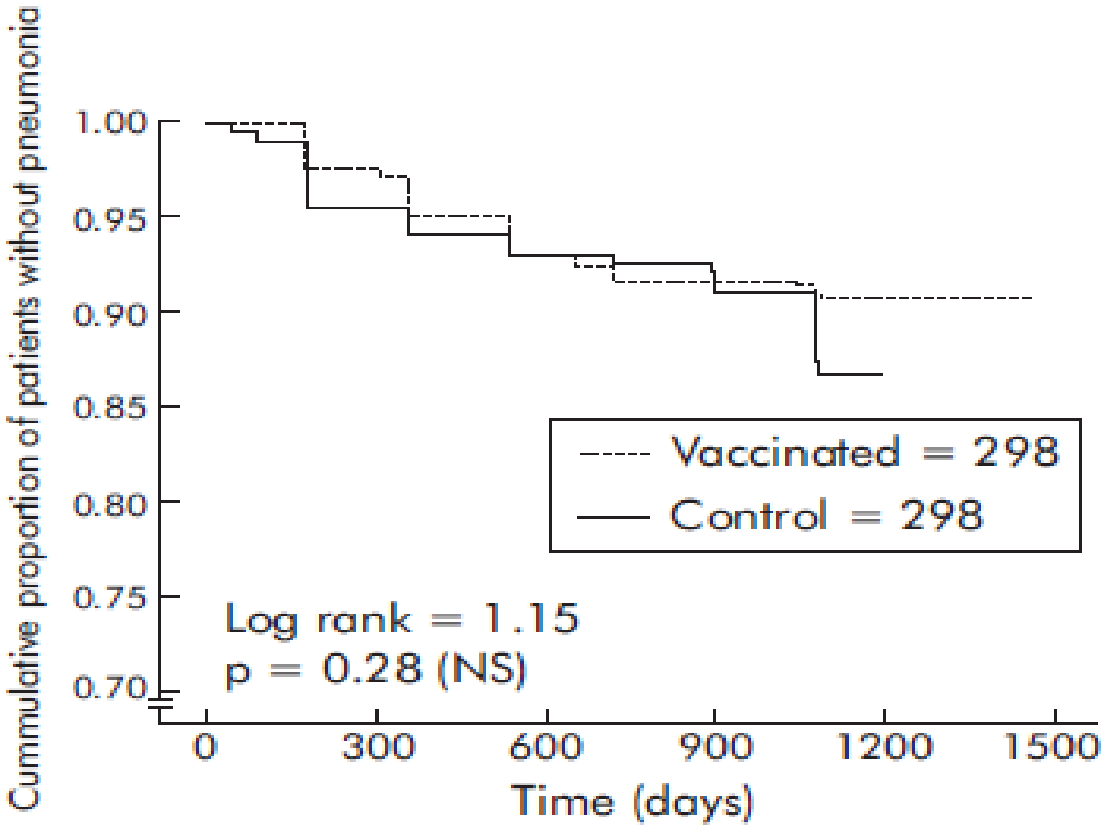
Clinical efficacy of anti-pneumococcal vaccination in patients with COPD

Table 1 Clinical and functional characteristics of study patients

	Intervention group (N = 298)	Non-intervention group (N = 298)	p value
% Male	96.6%	93.3%	0.09
Follow up			0.77
Mean (days)	980.0	977.8	
Range (days)	20–1454	21–1183	
Total (person-years)	800.1	798.0	
FVC (l)	2.0 (1.6–2.5)	2.1 (1.7–2.6)	0.17
FVC (%)	62 (50–73)	63 (52–74)	0.21
FEV_1 (l)	1.1 (0.8–1.4)	1.2 (0.8–1.5)	0.02
FEV_1 (%)	42 (32–54)	43 (33–55)	0.21
FEV_1%FVC	53 (45–62)	55 (45–64)	0.21
Age (years)	69 (62–73)	68 (61–73)	0.23
Age group			
<65 years	91 (31%)	116 (39%)	0.04
≥65 years	207 (69%)	182 (61%)	
Severity of COPD			
Severe (FEV_1 <40%)	132 (44%)	114 (38%)	0.13
Non-severe (FEV_1 ≥40%)	166 (56%)	184 (62%)	
Currently smoking	65 (22%)	77 (26%)	0.25
Previous pneumonia	58 (19.5%)	52 (17.4%)	0.53
Pneumonia in previous 5 years	33 (11%)	28 (9.4%)	0.50
Previous TB	22 (7.4%)	33 (11.1%)	0.12
Neoplasia during follow up	18 (6%)	16 (5.3%)	0.72
Death from any cause	57 (19.1%)	58 (19.5%)	0.92
Death from pneumonia	6 (2%)	6 (2%)	1.00

Thorax 2006;61:189-195

Clinical efficacy of anti-pneumococcal vaccination (PPV23) in patients with COPD



Thorax 2006;61:189-195

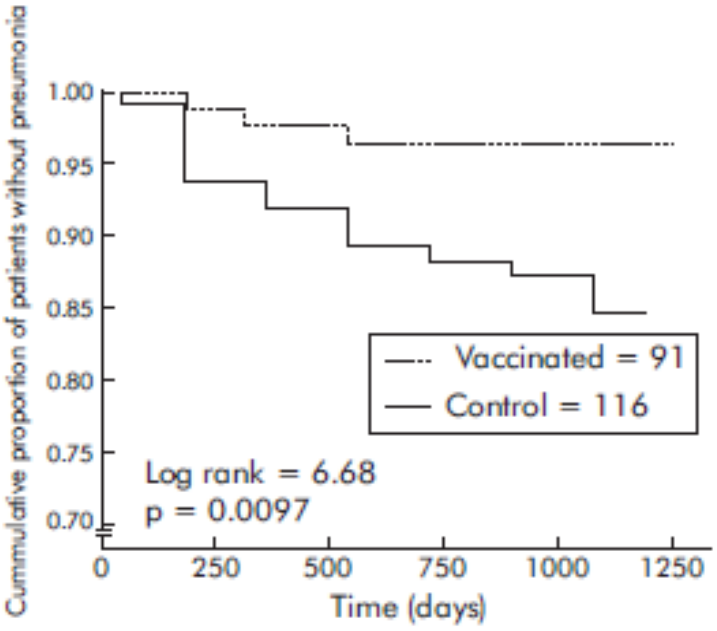
Clinical efficacy of anti-pneumococcal vaccination in patients with COPD

Table 3 Numbers of pneumonia patients (first episode) in a prospective randomised trial showing efficacy of 23-serotype pneumococcal vaccine

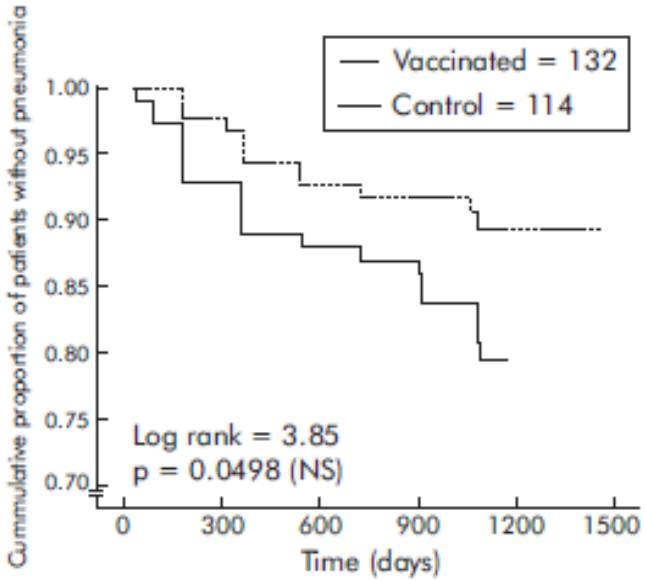
	Intervention group		Non-intervention group		Vaccine efficacy*			NNT	
	n	N	n	N	%	95% CI	p value†	n	95% CI
CAP-PN									
All patients	25	298	33	298	24	(−24 to 54)	0.333		
<65 years	3	91	16	116	76	(20 to 93)	0.013	10	(6 to 31)
≥65 years	22	207	17	182	−14	(−107 to 38)	0.801		
FEV_1 <40%	12	132	20	114	48	(−7 to 80)	0.076		
FEV_1 ≥40%	13	166	13	184	−11	(−132 to 47)	0.945		
Age <65 years and FEV_1 <40%	1	46	10	40	91	(35 to 99)	0.002	3	(2 to 4)
Pneumococcal pneumonia	0	298	5	298			0.061		

Thorax 2006;61:189-195

Clinical efficacy of anti-pneumococcal vaccination in patients with COPD



Patients <65years



Patients with severe COPD (FEV1<40%)

Thorax 2006;61:189-195

Protective Effects of the 23-Valent PPV in the Elderly population : the EVAN-65 Study

Table 1. Baseline characteristics of 11,241 cohort members, according to their pneumococcal vaccination status, before the start of the study.

Characteristics	No. (%) of subjects		P^a
	Unvaccinated subjects (n = 6255)	Vaccinated subjects (n = 4986)	
Age[b]			
65–74 years	3903 (62.4)	2302 (46.2)	<.001
75–84 years	1780 (28.5)	2080 (41.7)	
≥85 years	572 (9.1)	604 (12.1)	
Sex			
Male	2716 (43.4)	2176 (43.6)	.814
Female	3539 (56.6)	2810 (56.4)	
No of outpatient visits during previous 2 years[c]			
0–14	2553 (40.8)	659 (13.2)	<.001
15–29	2038 (32.6)	1841 (36.9)	
≥30	1664 (26.6)	2486 (49.8)	
History of hospitalization for pneumonia in previous 2 years	51 (0.8)	85 (1.7)	<.001
Influenza vaccination in previous year	1917 (30.6)	4115 (82.5)	<.001
Medical condition or risk factor			
Chronic heart disease	623 (10.0)	717 (14.4)	<.001
Diabetes mellitus	1294 (20.7)	1356 (27.2)	<.001
Chronic lung disease	598 (9.6)	701 (14.1)	<.001
Hypertension	2988 (47.8)	3002 (60.2)	<.001
Obesity	937 (15.0)	1038 (20.8)	<.001
Smoking	569 (9.1)	361 (7.2)	<.001
Chronic liver disease	114 (1.8)	101 (2.0)	.435
Chronic nephropathy	182 (2.9)	228 (4.6)	<.001
Active neoplasia	133 (2.1)	171 (3.4)	<.001
Receipt of immunosuppressive medication	296 (4.7)	396 (7.9)	<.001
Immunocompromised status[d]	652 (10.4)	794 (15.9)	<.001

2003-3005

Clin Infect dis 2006;43:860-8

Protective Effects of the 23-Valent PPV in the Elderly population : the EVAN-65 Study

Table 2. Incidence and risk of invasive pneumococcal disease (IPD) and pneumococcal pneumonia in relation to pneumococcal vaccination status.

	IPD		Pneumococcal pneumonia		
Parameter	Vaccine and vaccine-related serotypes	All IPD cases[a]	With bacteremia	Without bacteremia	Overall[b]
No. of events					
Unvaccinated subjects	8	14	12	26	38
Vaccinated subjects	3	8	6	26	32
Unadjusted rate per 1000 person-years					
Unvaccinated subjects	0.48	0.85	0.73	1.58	2.30
Vaccinated subjects	0.17	0.46	0.34	1.49	1.84
Unadjusted HR for all subjects					
HR (95% CI)	0.38 (0.10–1.42)	0.56 (0.23–1.34)	0.51 (0.19–1.35)	0.84 (0.49–1.45)	0.74 (0.46–1.19)
P	.149	.194	.174	.533	.217
Age- and sex-adjusted HR for all subjects					
HR (95% CI)	0.39 (0.10–1.50)	0.50 (0.21–1.20)	0.41 (0.15–1.11)	0.71 (0.41–1.24)	0.61 (0.38–0.99)
P	.169	.120	.080	.230	.046
Multivariable-adjusted HR for all subjects					
HR (95% CI)	0.61 (0.13–2.76)[c]	0.60 (0.22–1.65)[d]	0.45 (0.15–1.40)[e]	0.61 (0.35–1.06)[f]	0.55 (0.34–0.88)[g]
P	.517	.324	.452	.081	.013

Clin Infect dis 2006;43:860-8

Protective Effects of the 23-Valent PPV in the Elderly population : the EVAN-65 Study

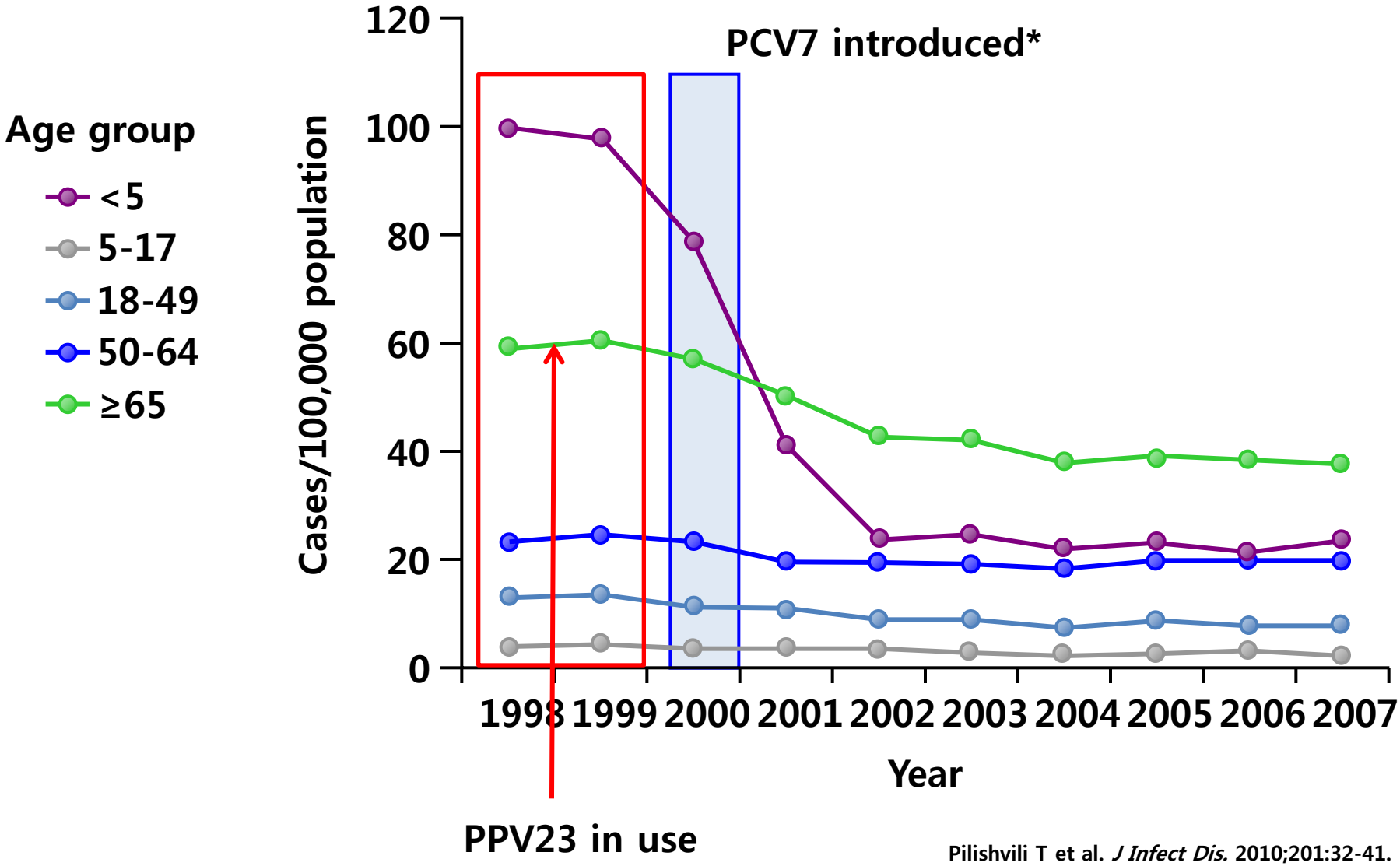
Table 3. Incidence and risk of hospitalization for pneumonia, outpatient pneumonia, overall pneumonia, and death due to pneumonia or to any cause, according to pneumococcal vaccination status.

	CAP			Death		
Type of event	Hospitalization for pneumonia[a]	Outpatient pneumonia[b]	Overall pneumonia[c]	Death due to pneumococcal infection	Death due to pneumonia	Death due to any cause
No. of events						
Unvaccinated subjects	161	46	207	5	34	696
Vaccinated subjects	194	72	266	5	26	801
Unadjusted rate per 1000 person-years						
Unvaccinated subjects	9.75	2.78	12.54	0.30	2.03	41.61
Vaccinated subjects	11.15	4.13	15.29	0.28	1.46	45.10
Unadjusted HR for all subjects						
HR (95% CI)	1.12 (0.91–1.39)	1.43 (0.99–2.08)	1.19 (0.99–1.43)	0.83 (0.24–2.88)	0.70 (0.42–1.18)	1.06 (0.95–1.17)
P	.275	.057	.057	.765	.180	.296
Age- and sex-adjusted HR for all subjects						
HR (95% CI)	0.96 (0.78–1.19)	1.31 (0.90–1.91)	1.03 (0.86–1.24)	0.74 (0.21–2.60)	0.55 (0.33–0.91)	0.83 (0.75–0.92)
P	.739	.159	.716	.636	.022	.000
Multivariable-adjusted HR for all subjects						
HR (95% CI)	0.74 (0.59–0.92)[d]	0.90 (0.59–1.37)[e]	0.79 (0.64–0.98)[f]	0.50 (0.13–2.02)[g]	0.41 (0.23–0.72)[h]	0.97 (0.86–1.09)[i]
P	.007	.619	.032	.332	.002	.595

Clin Infect dis 2006;43:860-8

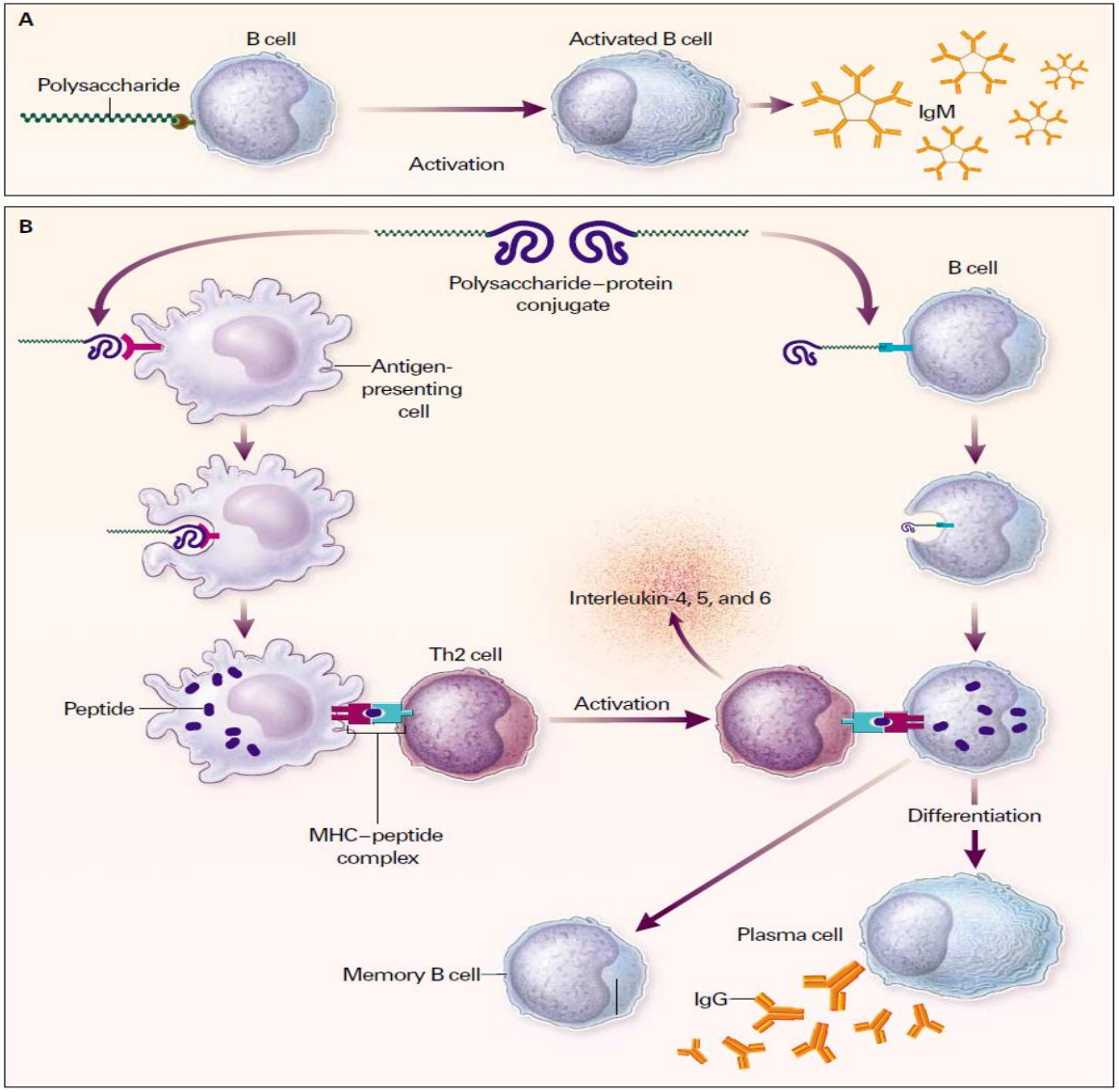
PPV23의 한계 – 침습성 질환을 감소시키지 못했다`

•No sizable impact on reducing IPD in the US

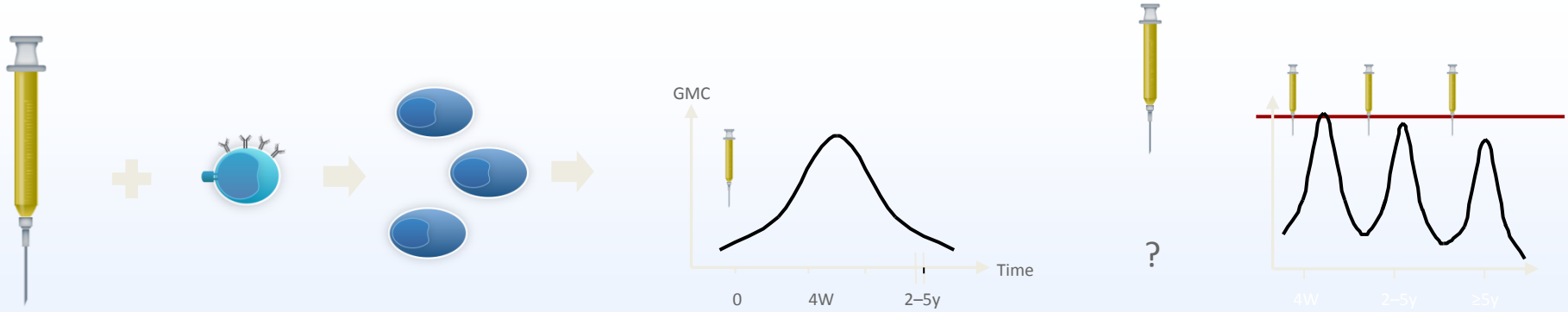


Pilishvili T et al. *J Infect Dis.* 2010;201:32-41.

Polysaccharide Ag 과 Polysaccaride – Protein congugates에 대한 antibody response



Immune response to polysaccharide vaccines in Adults



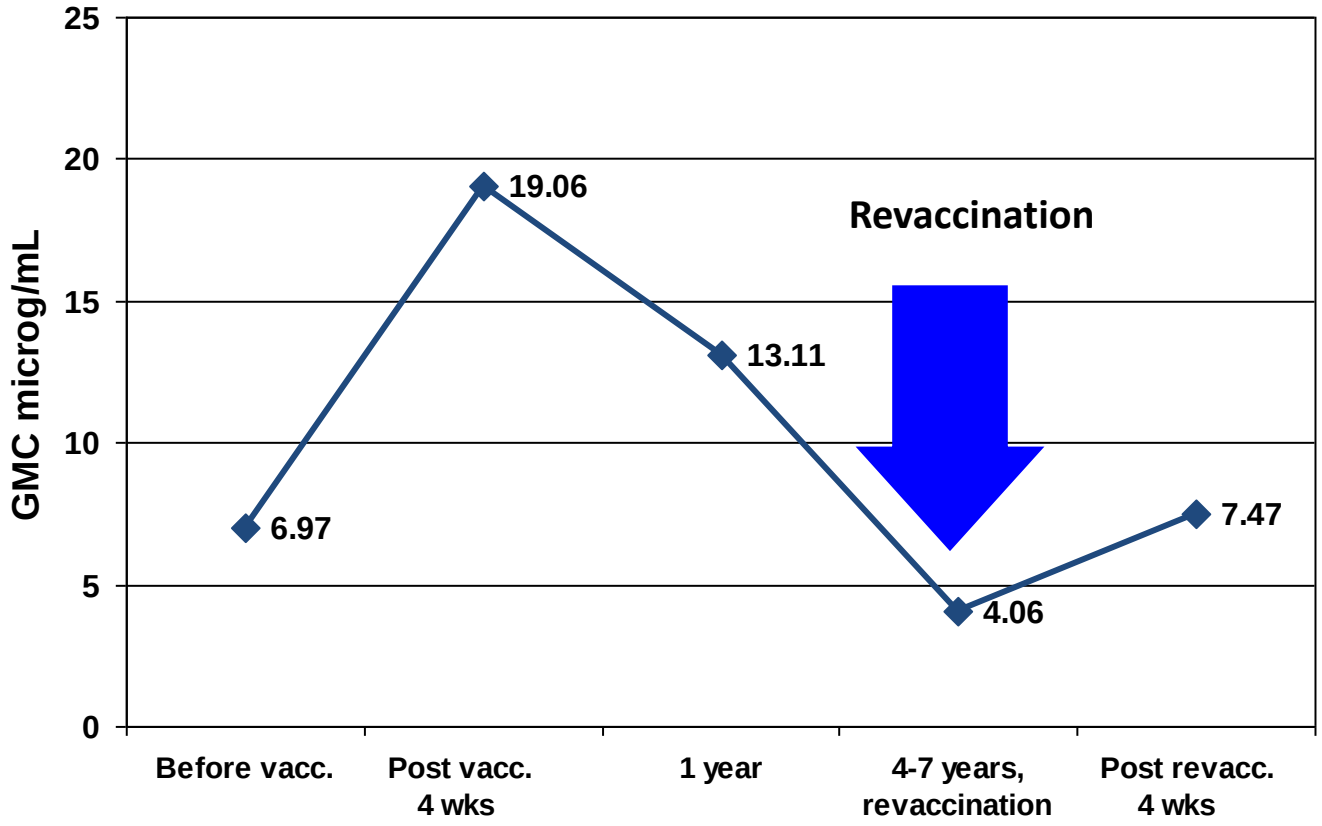
PS + Naive B-cell → Plasma Cells → Antibody Production → Repeated PS-dosing no

Plasma cells
- live 2-4 y only
- Cannot be boosted

Short life span
of Plasma cells
may be cause of hypor
esponsiveness

PPV Reduces the Response to Subsequent Doses of PPV

Combined Geometric Mean Pneumococcal Antibody Concentrations (GMC) to 6 Antigens

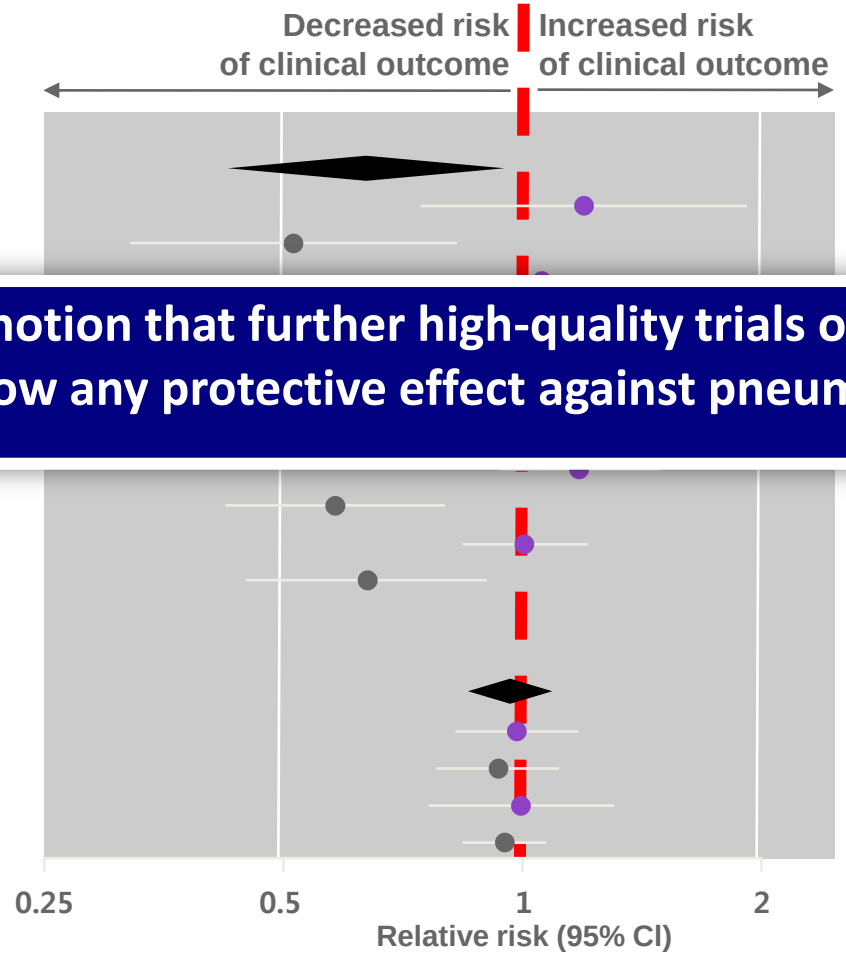


N=61 patients, median age 75

Meta-analysis of controlled clinical trials with PPV : Evidence of protection

Summary plot of meta-analyses of PPV

- Presumptive pneumococcal pneumonia
  - All trials
  - – Double-blind
  - – Other
  - – Adequate concealment of allocation
  - – Other
- Death from all causes
  - All trials
  - – Double-blind
  - – Other
  - – Adequate concealment of allocation
  - – Other



This study "… supports the notion that further high-quality trials of the [PPV] vaccine would fail to show any protective effect against pneumonia."

Summary plot of meta-analyses of pneumococcal polysaccharide vaccines that included 22 trials and 101,507 individuals. Purple circles show summary estimates from trials of higher methodologic quality.

Controversies: Recent meta-analysis

	Moberly, et al. Cochrane review 2008	Huss, et al. CMAJ, 2009
Protection:	Efficacy (95% CI)	Efficacy (95% CI)
Against Invasive pneumococcal disease	74% (56 to 85)	10% (0.77 to 54)
Against all-cause pneumonia	29% (3 to 48)	27% (6 to 44)
Against all cause mortality	13% (0.1 to 31)	3% (.09 to 13)

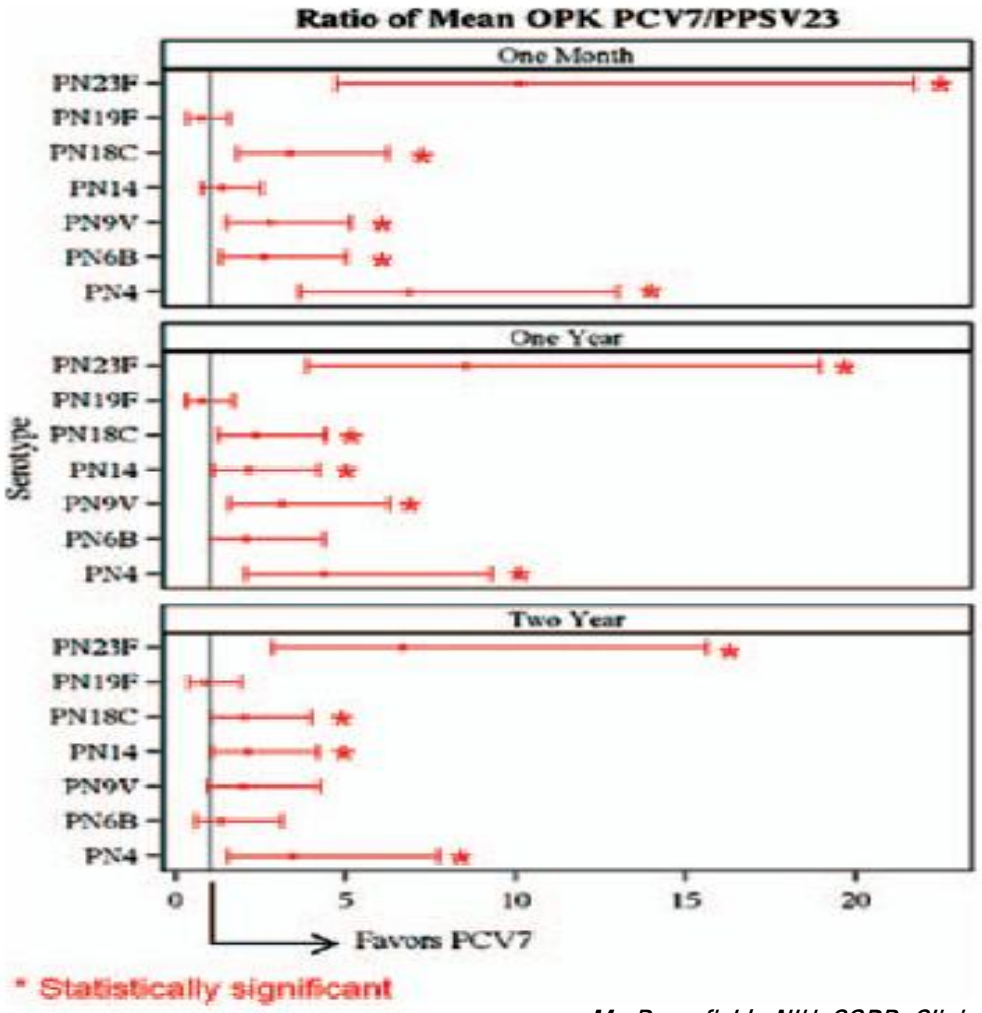
Different meta-analyses results highlight differences in vaccine efficacy amongst different population groups.

Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. *Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD000422. DOI: 10.1002/14651858.CD000422.pub2.*

Huss A, Scott P, Stuck A, et al. Efficacy of pneumococcal vaccination in adults:a meta-analysis. *CMAJ 2009;180(1):48-58*

COPD - PPV23 vs PCV7 면역원성

- COPD에서 접종후 항체양전률/항체가



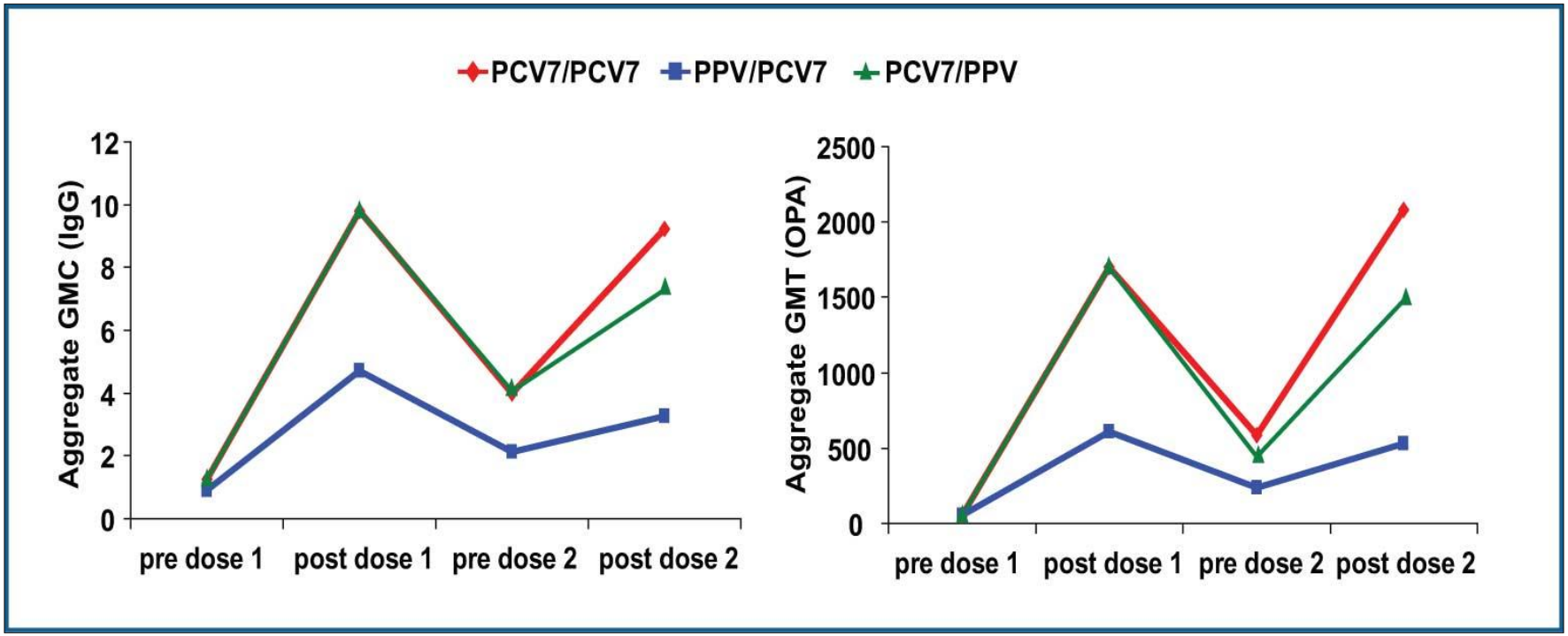
- 2년 추적

Opsonophagocytic killing index

: > 0.5
: 비열등, 우수

M. Dransfield, NIH COPD Clinical Research Network. Clinical Infectious Diseases 2012;55(5):e35-44

PCV7 Does Not Induce Hyporesponsiveness to a Subsequent Dose of PCV7, Whereas PPV Does

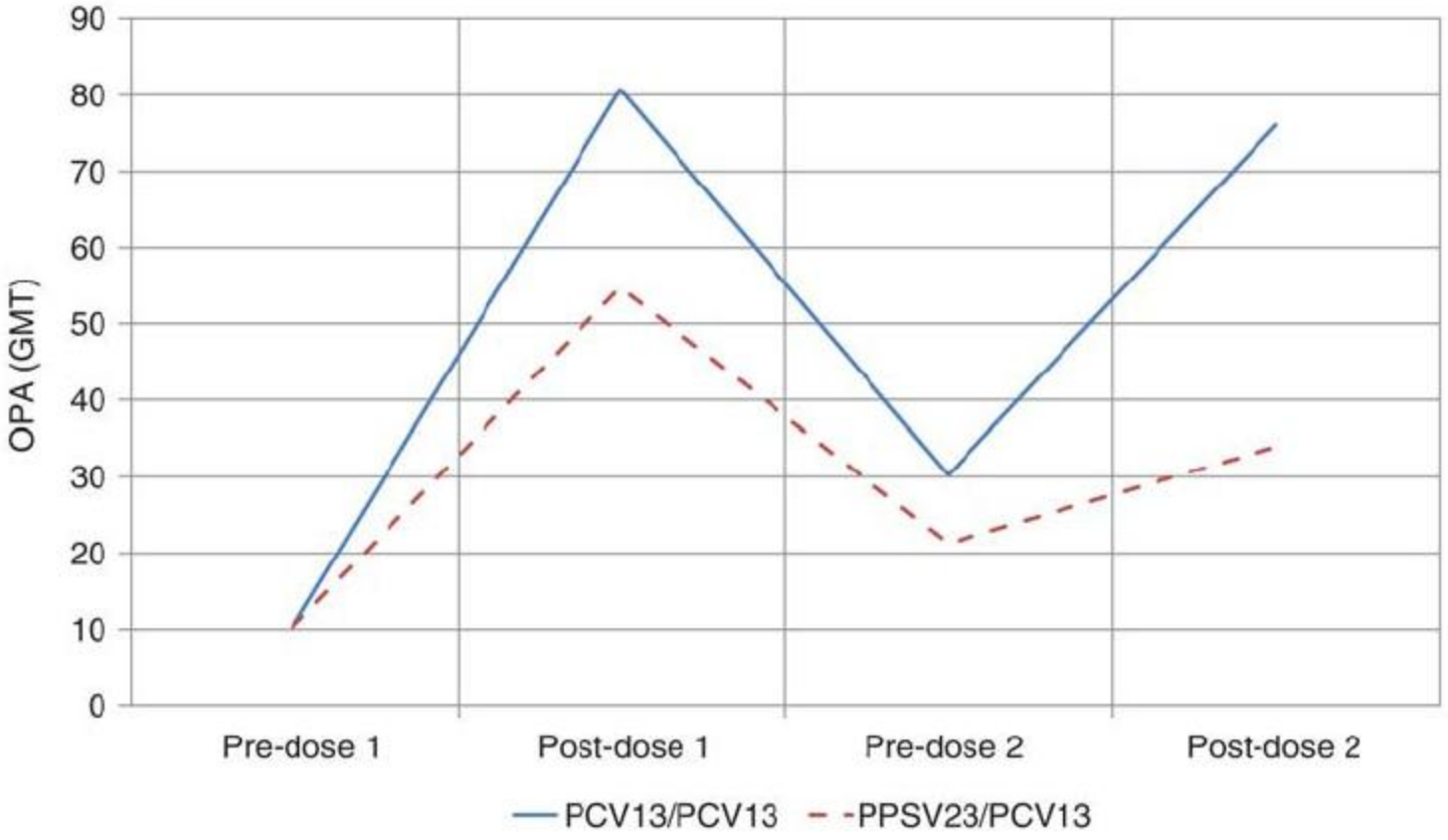


ELISA and OPA titers before and after each dose averaged for the 7 pneumococcal conjugate vaccine serotypes: vaccine-naïve subjects aged ≥70 years re-immunized at 1 year with a dose of PCV7 or PPV

de Roux A et al. *Clin Infect Dis*. 2008;46:1015-1023.

Average OPA of 12 common serotypes

PPSV23-Exposed Subjects ≥70 Years of Age



Peter R. Paradiso. Clinical Infectious Diseases 2012;55(2):259–64

성인에서 PCV 허가 - KFDA

- 50세 이상의 성인
- **폐렴구균(혈청형** 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F)**으로 인하여 생기는 폐렴 및 침습성 질환의 예방을 목적으로 접종함**
- 2012년 5월 25일

Sequence and spacing

- PCV13 / PPSV23
  - "…who have not previously received PCV13 or PPSV23, should receive a dose of PCV13 first, followed by a dose of PPSV23 at least 8 weeks later."
- PPSV23 / PCV13
  - " …should be given a PCV13 dose ≥1 year after the last PPSV23 dose was received"

- PPSV23 / PCV13 / PPSV23
  - "For those who require additional doses of PPSV23, the first such dose should be given no sooner than 8 weeks after PCV13 and at least 5 years after the most recent dose of PPSV23."

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Suggestions of pneumococcal vaccine in immunocompetent patients

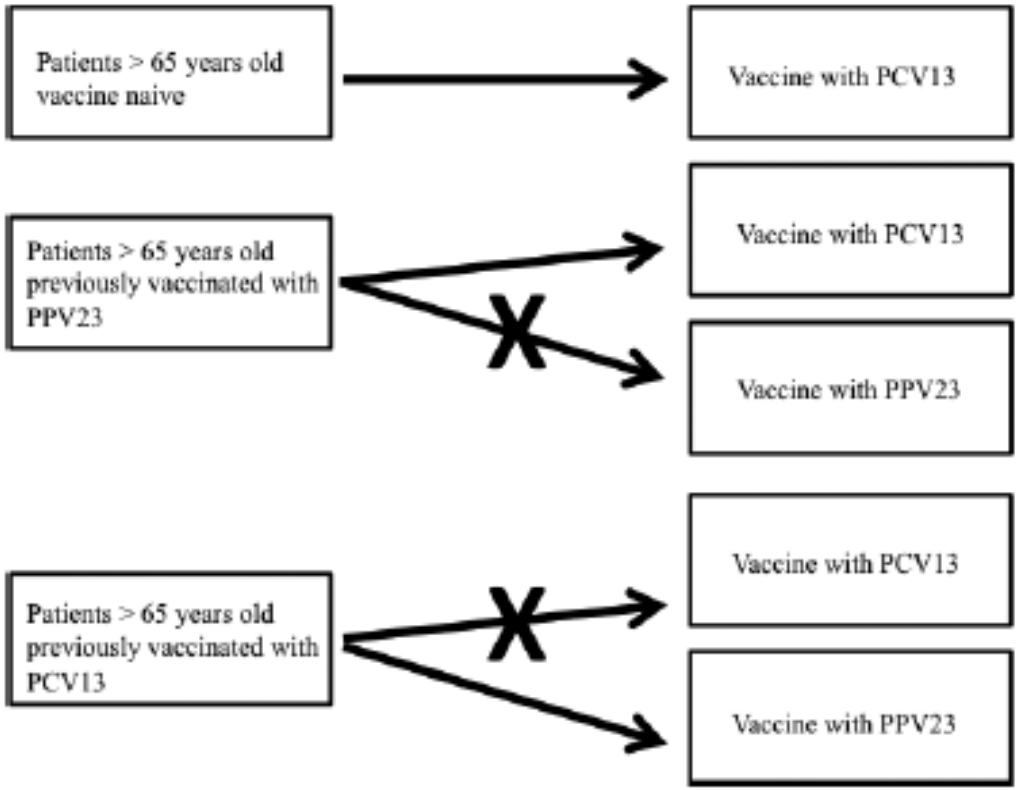


FIG. 1. PCV13 and PPV23: suggestions for pneumococcal vaccine use in immunocompetent patients. PCV13, pneumococcal 13-valent conjugate vaccine; PPV23, pneumococcal polysaccharide 23-valent vaccine.

Clin Microbial Infect 2014;20:52-58

Suggestions of pneumococcal vaccine in immunocompromised patients

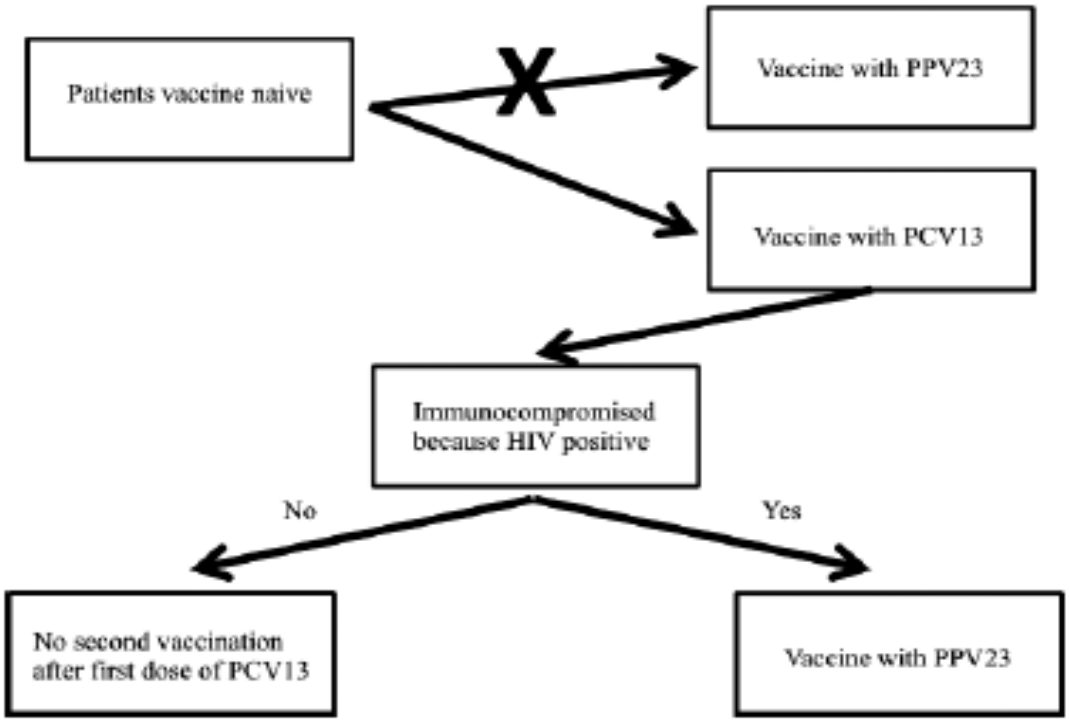
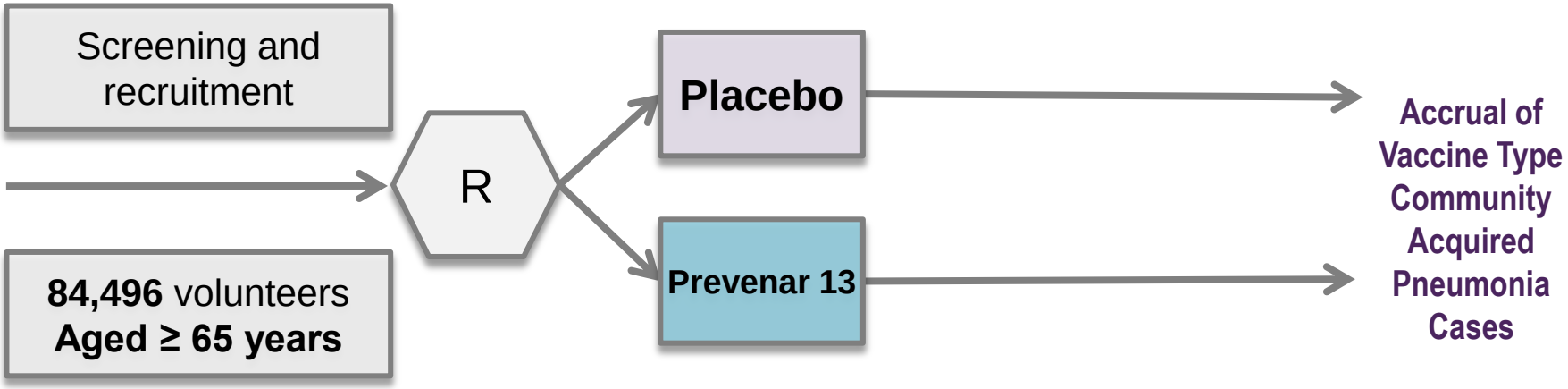
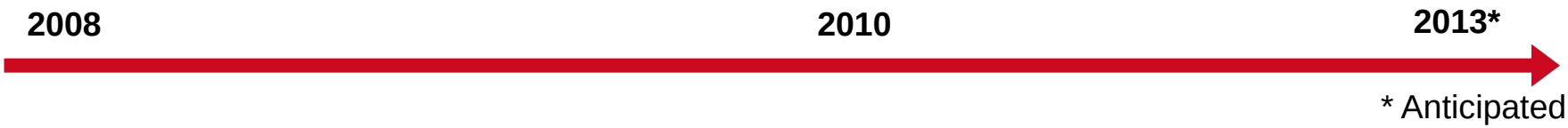


FIG. 2. PCV13 and PPV23: suggestion for pneumococcal vaccine use in immunocompromised patients. PCV13, pneumococcal 13-valent conjugate vaccine; PPV23, pneumococcal polysaccharide 23-valent vaccine; HIV, human immunodeficiency virus.

Clin Microbial Infect 2014;20:52-58

Clinical Trial Design and Timeline





* Anticipated

CAPiTA is an event-driven trial - timelines are dependent on accrual of sufficient number of cases of VT-CAP

Hak E, Grobbee DE, Sanders EAM, et al. Netherlands J Med. 2008;66:378-383.

- CAPiTA is the largest blinded prospective adult vaccine study conducted t o-date (~84,500 subjects)
  - Community-dwelling adults aged ≥65 years of age
  - Designed to fulfill regulatory requirements but important to determine the rol e of pneumococcal conjugate vaccines in the prevention of pneumococcal dis ease, especially CAP
- Primary objective is to establish efficacy of PCV13 in the prevention of a

16th International Congress on Infectious Disease (ICID) : Dr Bonten
PCV-13 : 45.5% effective at preventing a first episode of vaccine-type CAP
: 45.0% effective at preventing non-bacteremic pneumococcal CAP
: 75.5% effective at preventing invasive pneumococcal disease

  - Vaccine-type invasive pneumococcal disease
  - Vaccine-type non-bacteremic (non-invasive) pneumococcal CAP
- Safety
- Numerous exploratory objectives including immunogenicity, carriage and health outcomes

Hak E, Grobbee DE, Sanders EAM, et al. *Netherlands J Med.* 2008;66:378-383.

Recommended Adult Immunization Schedule—United States - 2014

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

Figure 1. Recommended adult immunization schedule, by vaccine and age group[1]

VACCINE ▼ / AGE GROUP ►	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza [2,*]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap) [3,*]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs					
Varicella [4,*]	2 doses					
Human papillomavirus (HPV) Female [5,*]	3 doses					
Human papillomavirus (HPV) Male [5,*]	3 doses					
Zoster [6]					1 dose	
Measles, mumps, rubella (MMR) [7,*]	1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13) [8,*]	1 dose					
Pneumococcal polysaccharide (PPSV23) [9,10]	1 or 2 doses					1 dose
Meningococcal [11,*]	1 or more doses					
Hepatitis A [12,*]	2 doses					
Hepatitis B [13,*]	3 doses					
Haemophilus influenzae type b (Hib) [14,*]	1 or 3 doses					

*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indication)

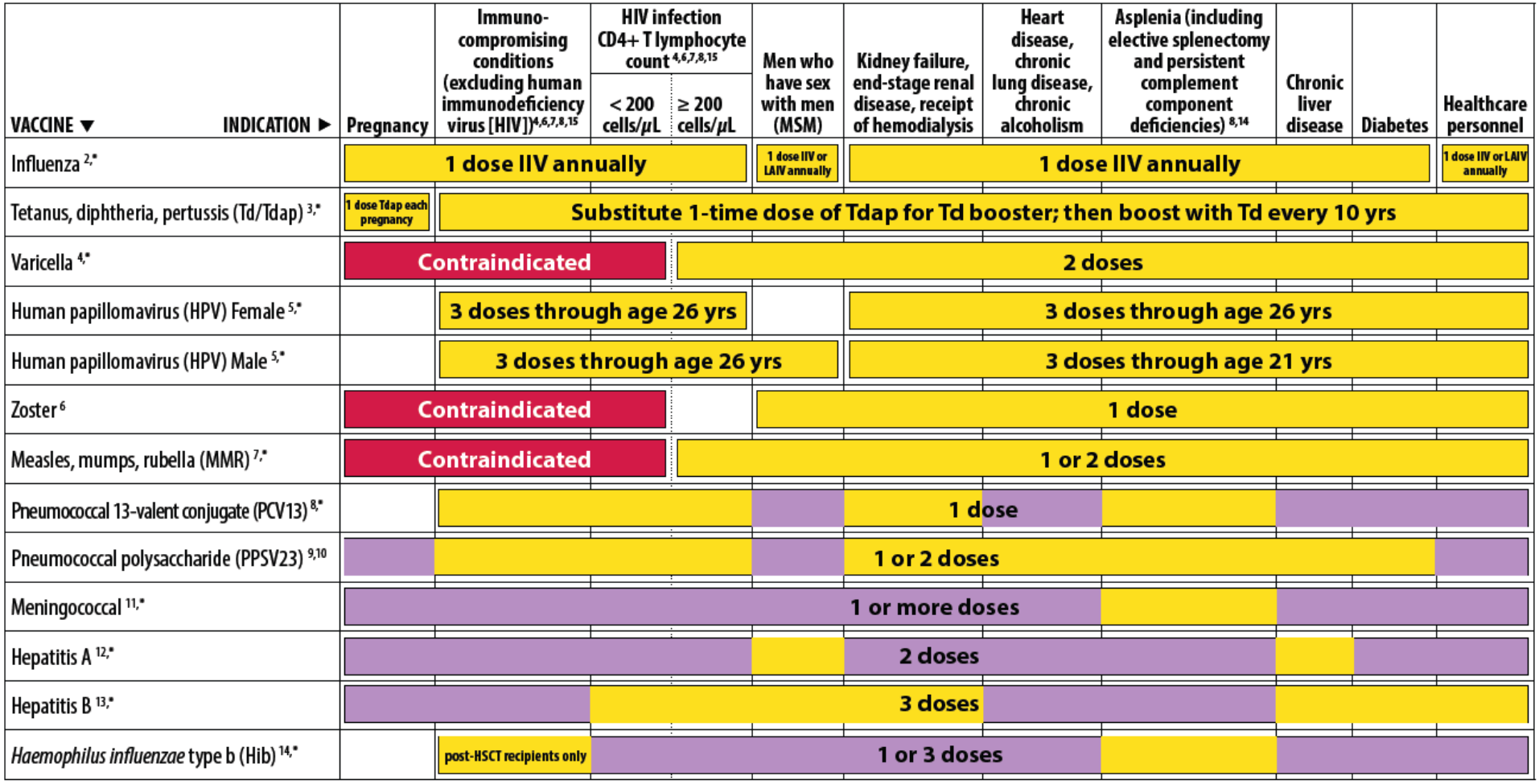
No recommendation

Recommended Adult Immunization Schedule—United States - 2014

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Figure 2. Vaccines that might be indicated for adults based on medical and other indications[1]



*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

Summary (1)

- In patients with establised COPD, the benefits of smoking cessation are immense, regardness of severity and in mild to moderate COPD, reduces the risk of disease progression as well as increasing survival and reducing morbidity for lung ca and CVD.
- The use of bupropion and varenicline in appropriate patients is cost-effective in fostering complete abstinence.
- Electronic cigarette is safe and effectiveness to serve as a long-term substitute for smoking.
- Influenza vaccination was associated with a reduced risk of all cause mortality in COPD patients but pneumococcal vaccination was not.

Summary (2)

- PPV23 is effective in preventing CAP in COPD patients aged less than 65 years and in those with severe airflow obstruction.
- In meta-analysis of controlled clinical trials , PPV23 vaccine would fail to show any protective effect against pneumonia.
- PCV7 induces a greater functional antibody response than PPV23 in COPD patent that persists for 2 years after vaccination.
- PCV 13 stimulates good antibody responses as well as mucosal immunity.
- The efficacy in adults of PCV13 in currently being investigated in CAPiTA study and results will be soon.

Thank you for your attention