Università di Perugia
Medicina del Lavoro, Malattie Respiratorie e Tossicologia
Professionali e Ambientali

Malattie cronico-degenerative e fumo di tabacco

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Cenni storici sul tabacco

- 1826: isolata la nicotina
- Durante la guerra in Crimea nasce la sigaretta, usando le cartine della polvere da sparo
- 1854: Philip Morris, un tabaccaio londinese, inizia a produrre e vendere sigarette fatte a mano
- La sigaretta si diffonde tra le truppe della Prima Guerra Mondiale

TOBACCO EPIDEMIC DEATH TOLL

100 million dead in the 20th century

Currently 5.4 million deaths every year

Unless urgent action is taken:

By 2030, there will be more than 8 million deaths every year

By 2030, more than 80% of tobacco deaths will be in developing countries

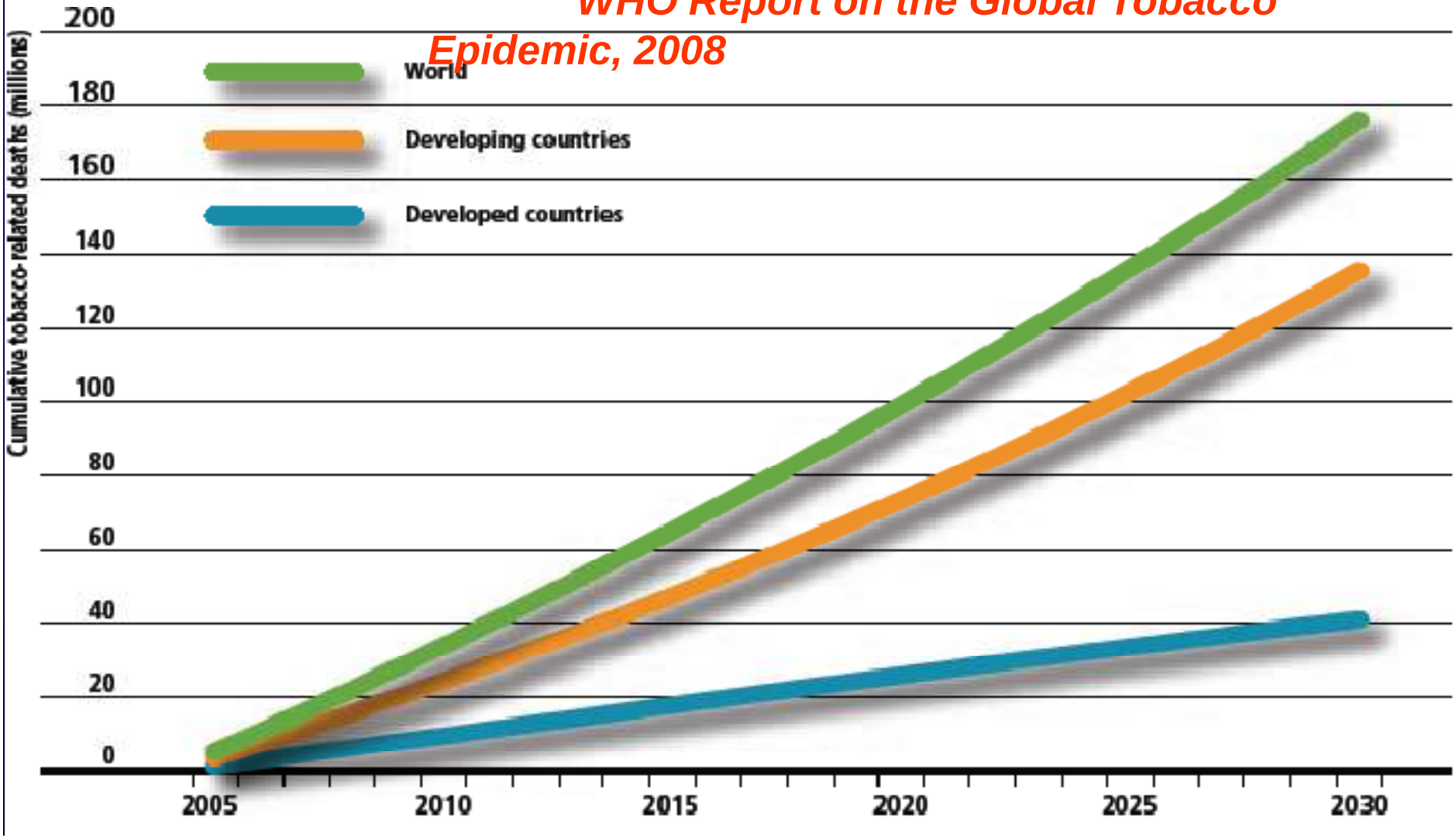
One billion estimated deaths during the 21st century

WHO Report on the Global Tobacco Epidemic, 2008

TOBACCO WILL KILL OVER 175 MILLION PEOPLE WORLDWIDE BETWEEN NOW AND THE YEAR 2030

Cumulative tobacco-related deaths, 2005–2030

WHO Report on the Global Tobacco Epidemic, 2008



Caratteristiche chimico-fisiche del fumo di tabacco

Fumo di tabacco

Miscela complessa (oltre 4000 composti) derivante dalla combustione delle foglie di *Nicotiana Tabacum*

5% del peso del fumo

95% del peso del fumo

Materiale "particolato"

(nicotina, benzo[a]pirene, cadmio, nickel, amine aromatiche, acidi, ...)

Sostanze allo stato di vapore

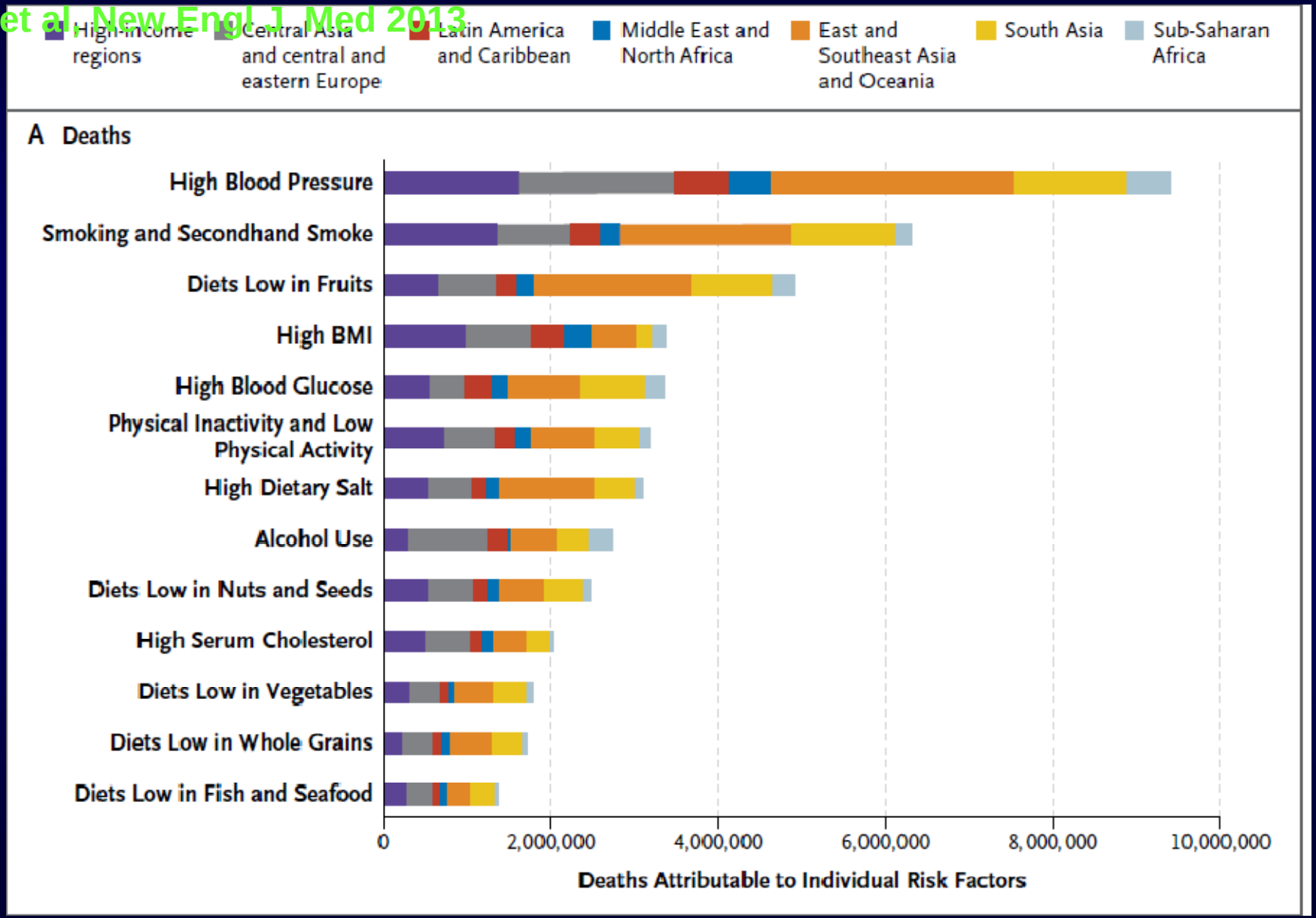
(CO, nitrosamine, benzene, acido cianidrico, formaldeide, ...)

H_2O, nicotina, altri alcaloidi

Catrame

Deaths and Burden of Disease Attributable to Selected Behavioral and Dietary Risk Factors in 2010 and the Metabolic and Physiological Mediators of Their Hazardous Effects

Ezzati M et al. New Engl J Med 2013



Deaths and Burden of Disease Attributable to Selected Behavioral and Dietary Risk Factors in 2010 and the Metabolic and Physiological Mediators of Their Hazardous Effects

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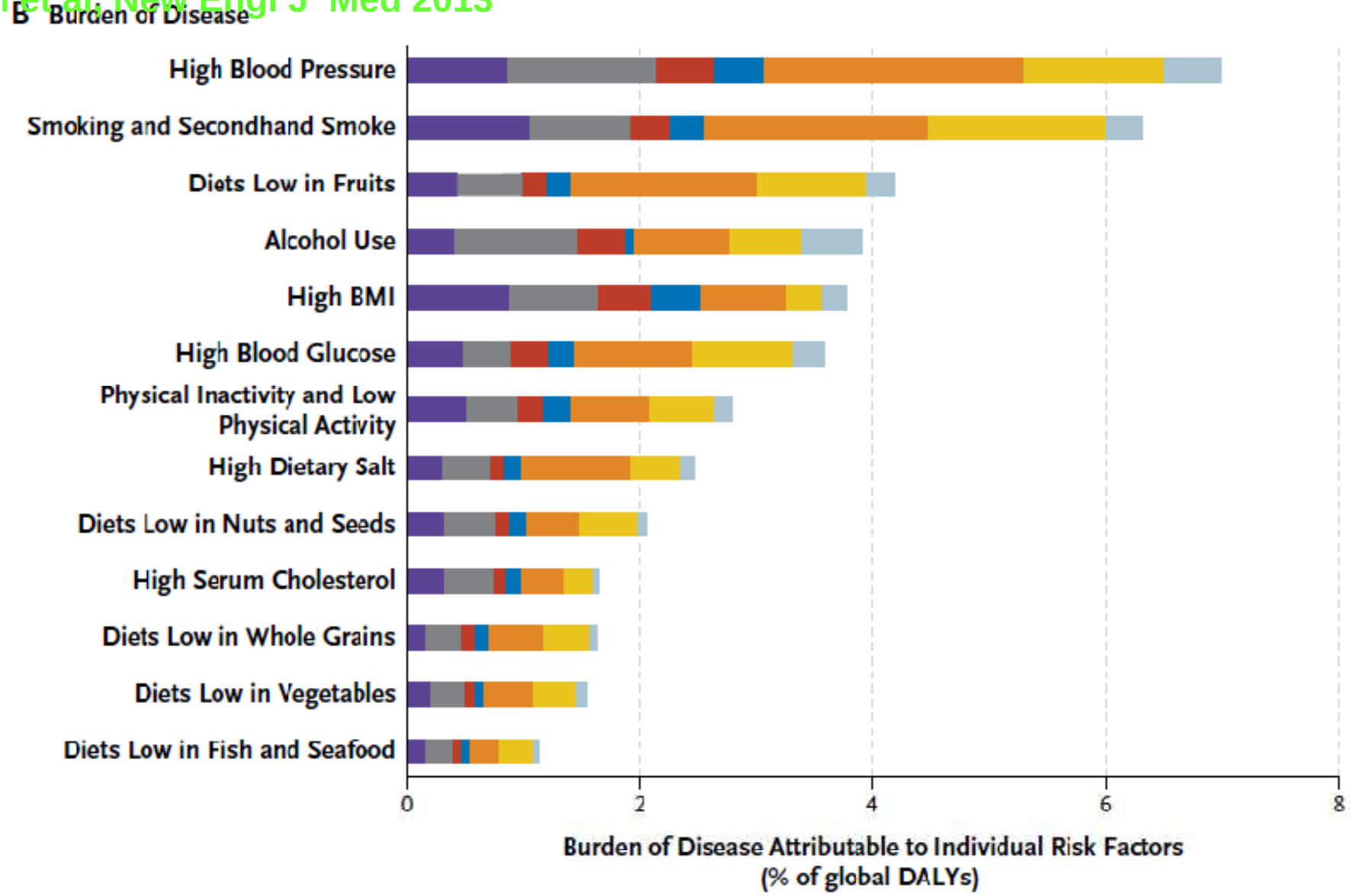
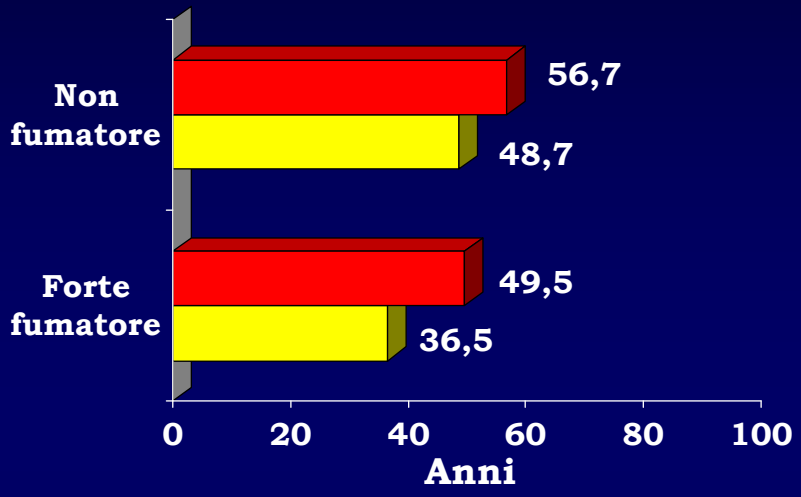


Attesa di vita in uomini e donne di 20 anni d'età

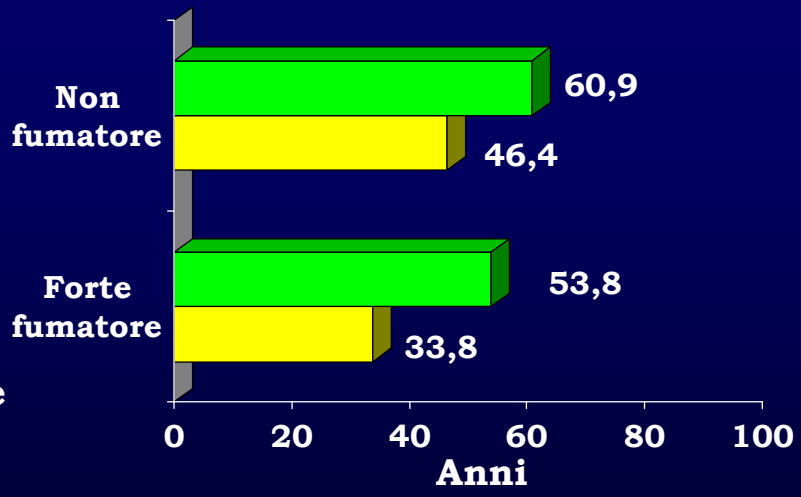


Uomini

Attesa di vita

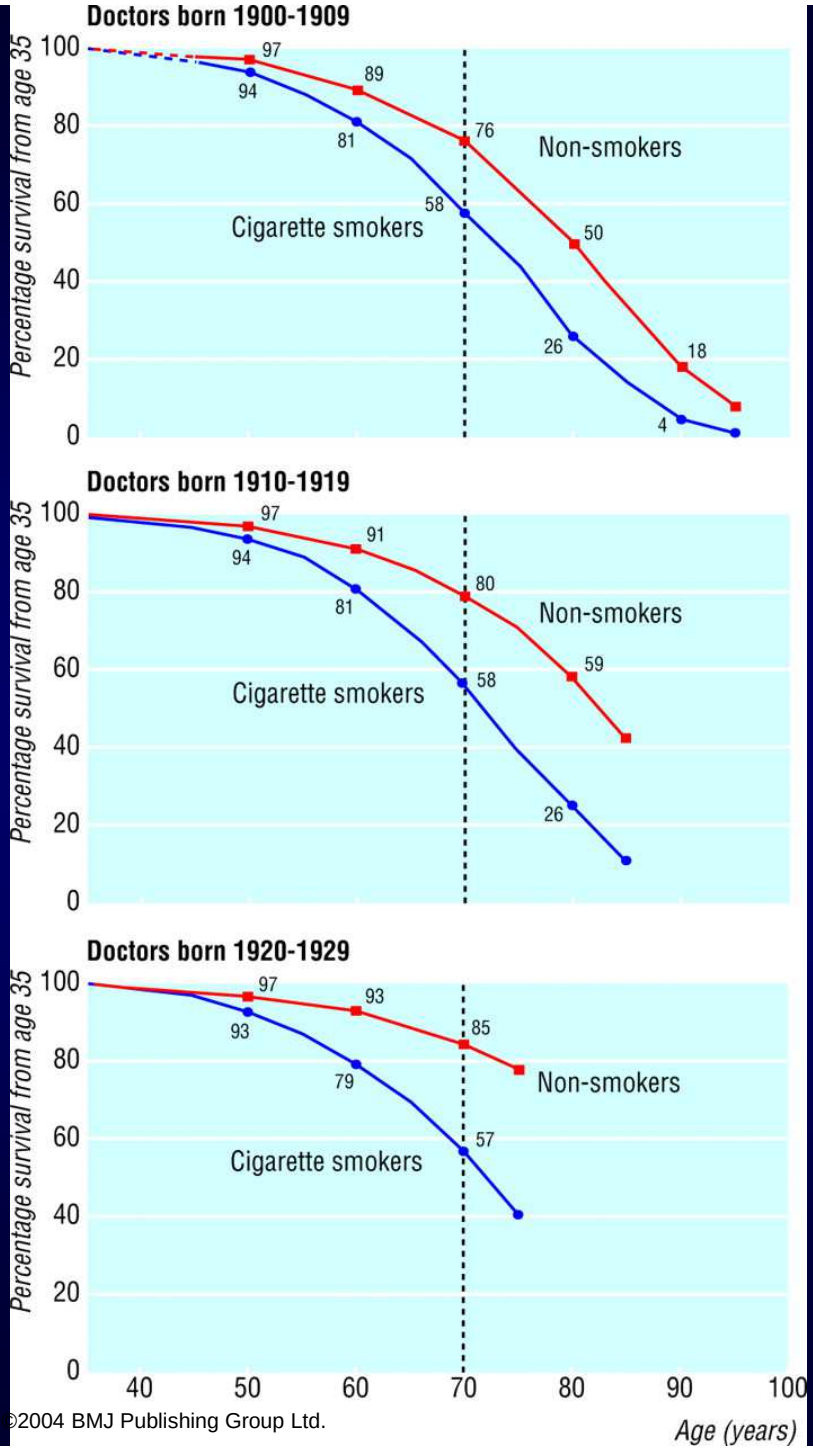
Anni in buona salute

Donne



Attesa di vita

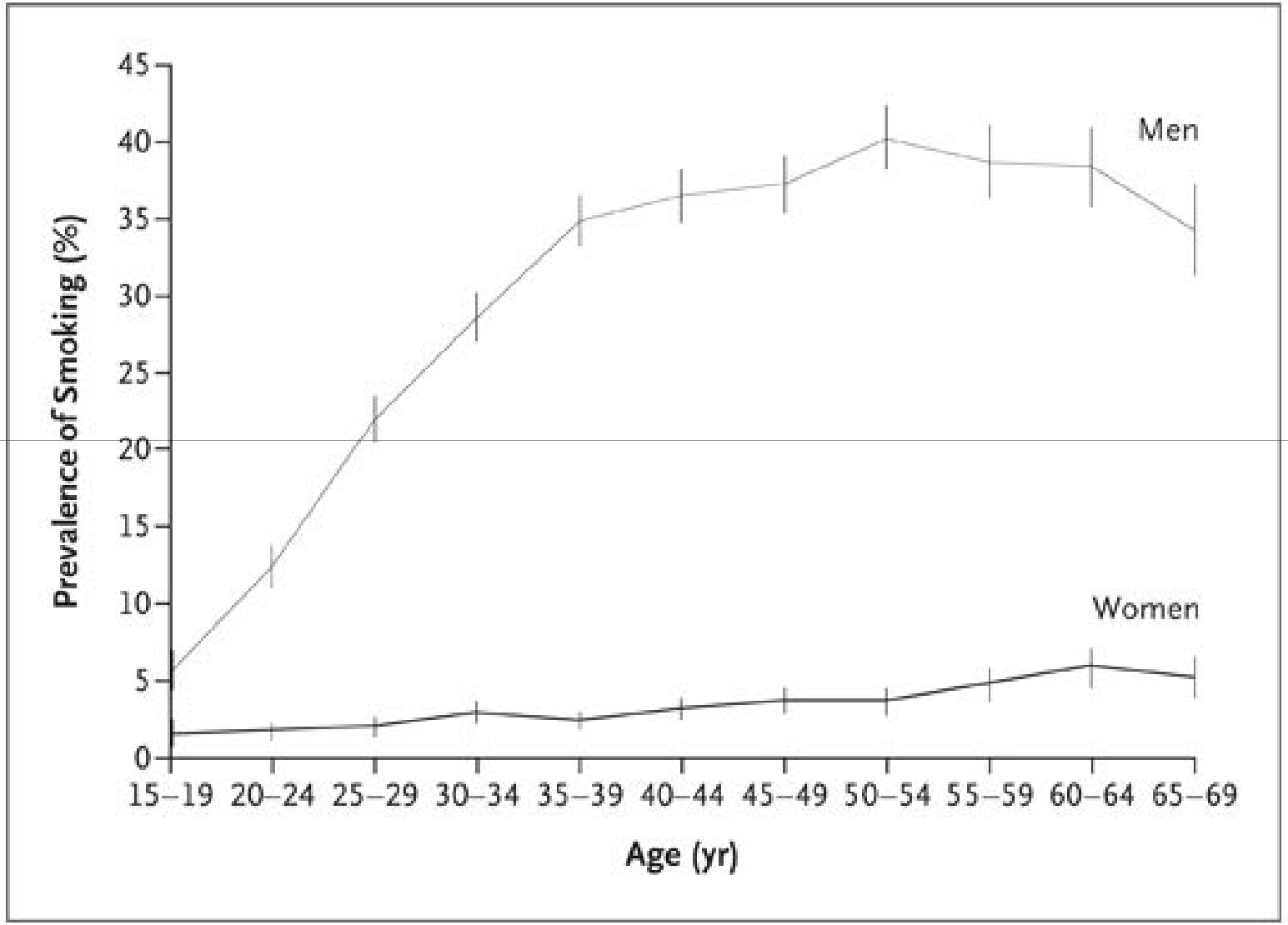
Anni in buona salute



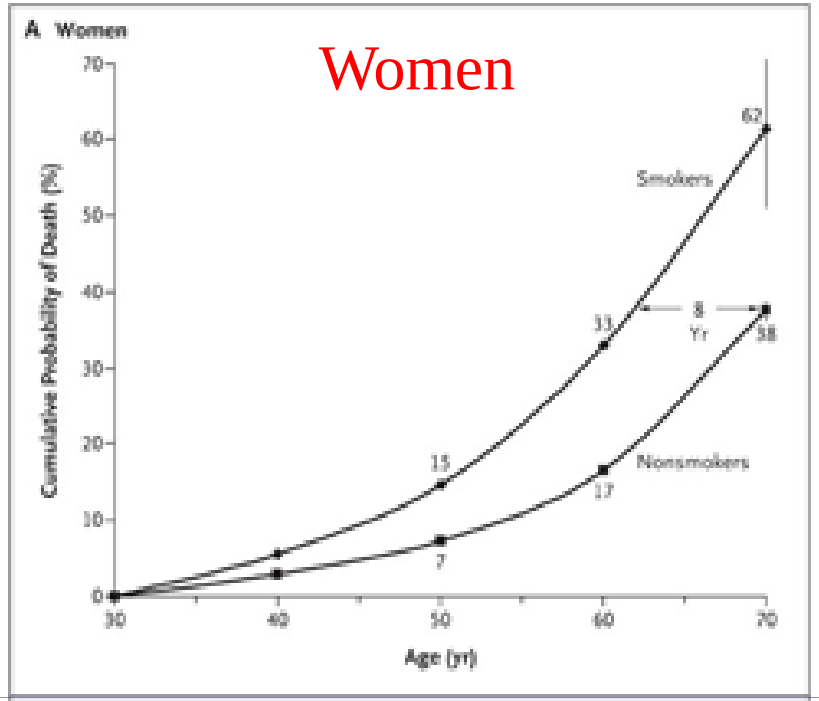
Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1909, 1910-1919, and 1920-1929, with percentages alive at each decade of age

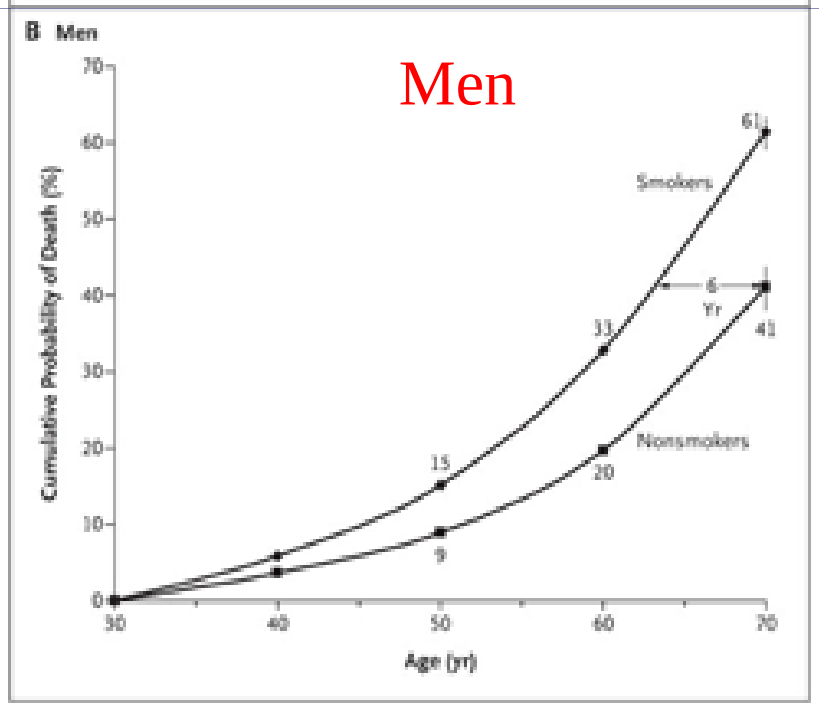
Doll, R. et al. BMJ 2004;328:1519

Prevalence of Smoking in India, According to Age and Sex



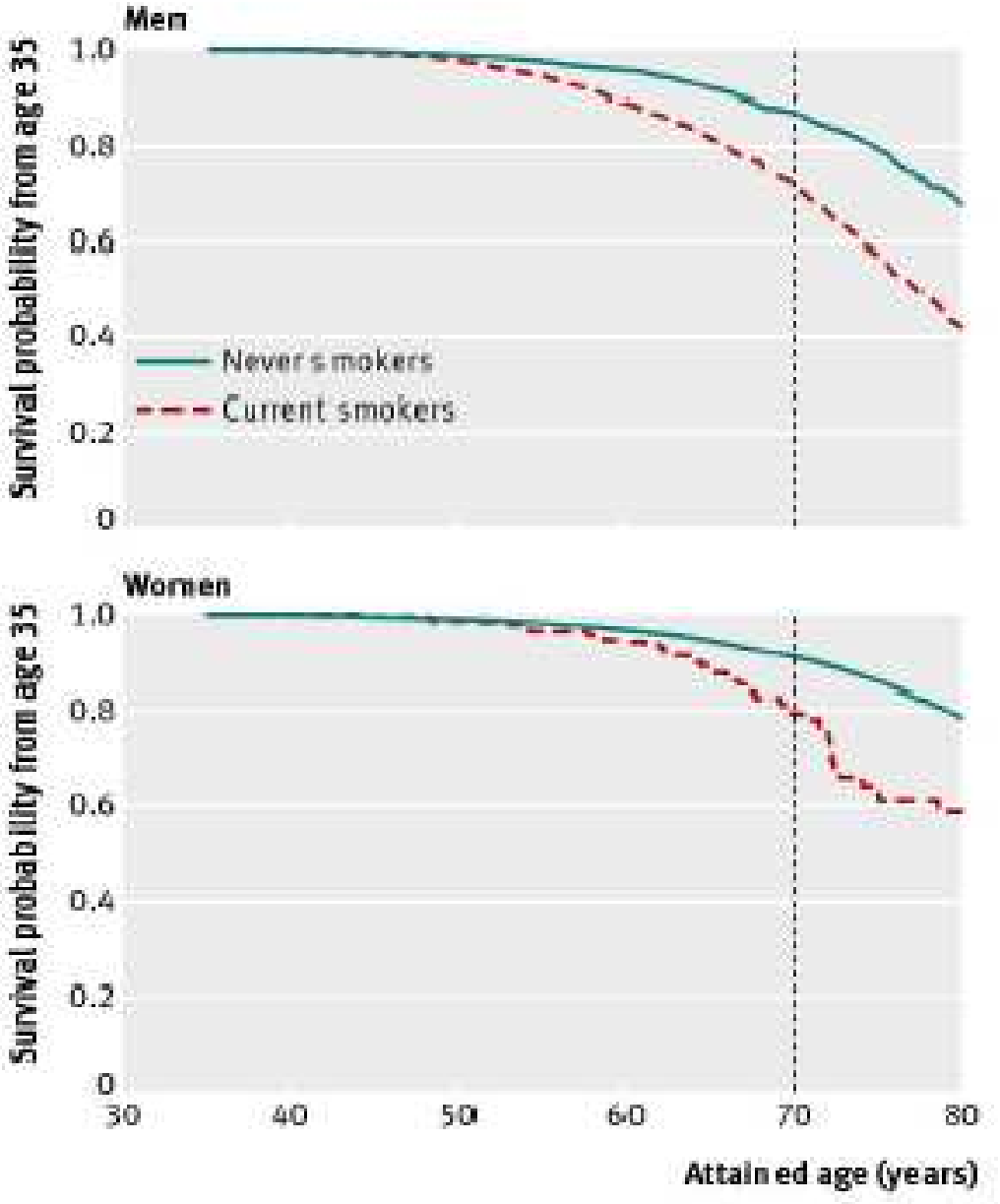
Jha P et al. N Engl J Med 2008;358:1137-1147





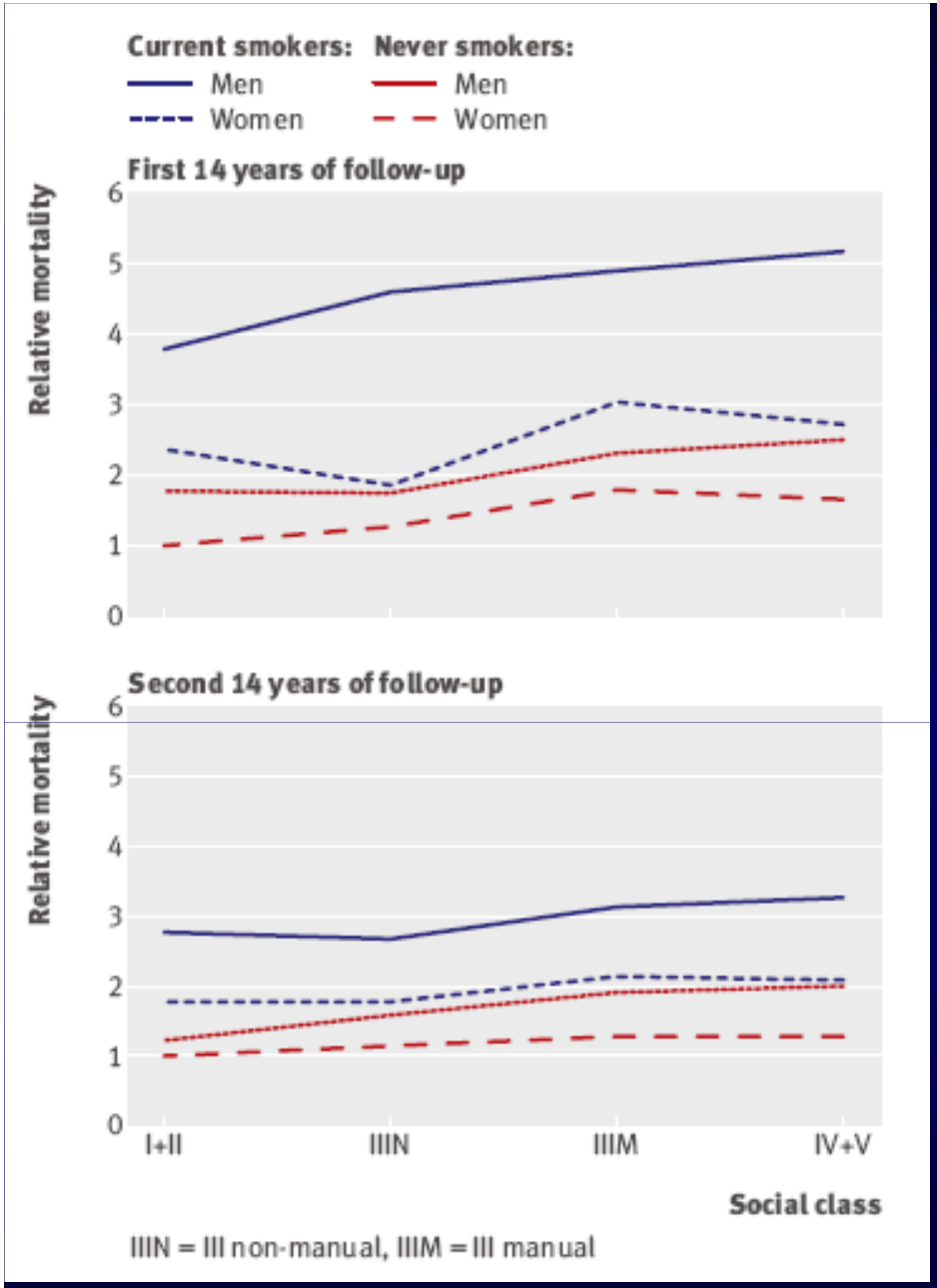
Cumulative Probability of Death from Any Cause among Smokers and Nonsmokers between the Ages of 30 and 69 Years.

Jha P et al. N Engl J Med, 2008



Survival from age 35 years for **Japanese men and women born between 1920 and 1945** who were never smokers or who started to smoke before age 20 years and continued smoking (mean smoking intensity among smokers of 23 cigarettes/day for men and 17 cigarettes/day for women).

Sakata R, et al. BMJ, 2012



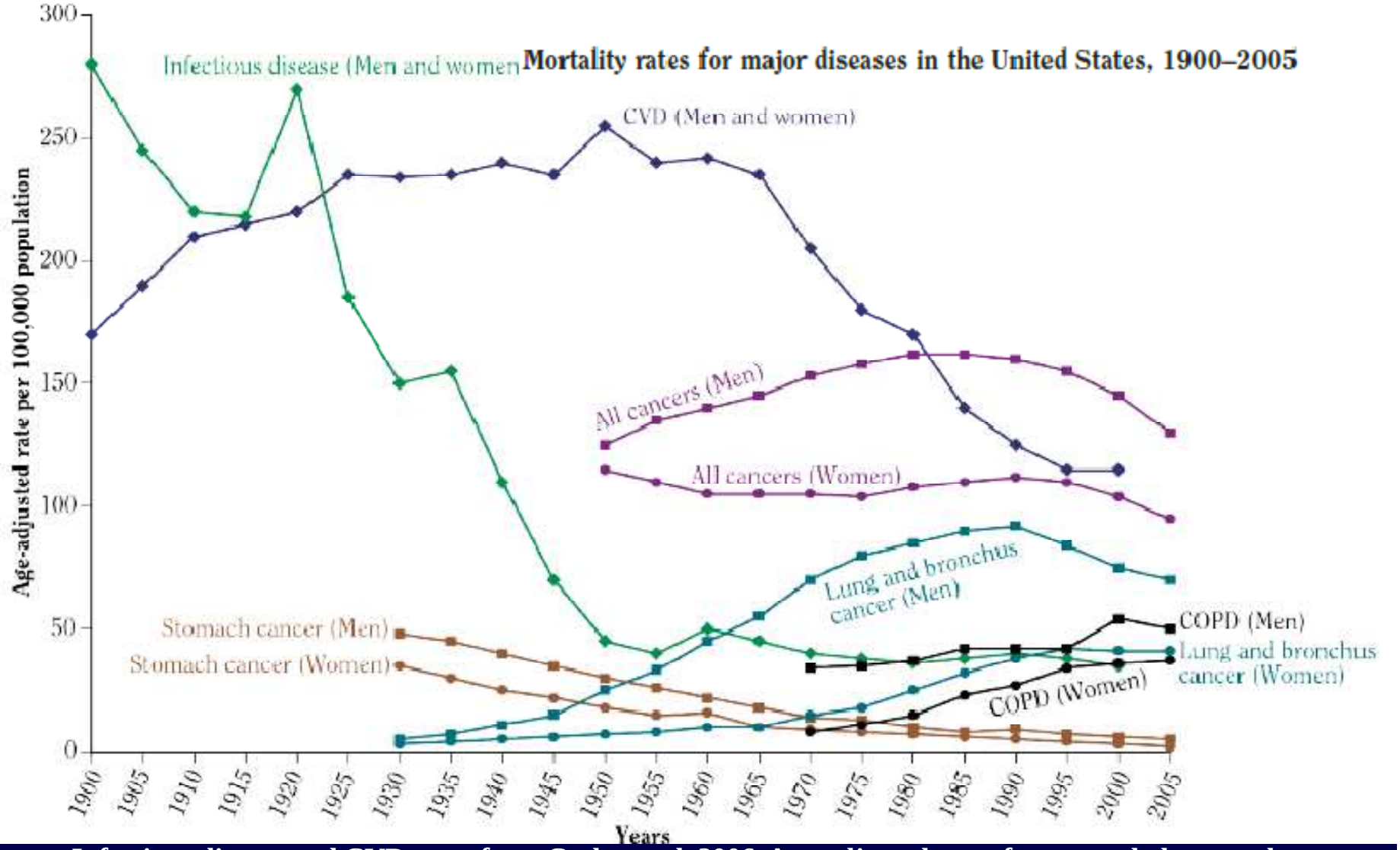
Age adjusted, relative, all cause mortality in the first and second 14 years of follow-up of women and men aged 45-64 years and who never smoked or currently smoked at recruitment **categorised by social class** (with women in social classes I and II who never smoked as the reference group)

Social class—classes I plus II (highest), III non-manual, III manual, and IV plus V (lowest)

Gruer L, et al. BMJ 2009;338:b48

Abitudine al fumo e specifiche cause di morte

- Il fumo rappresenta la *principale causa di neoplasia polmonare*: il rischio di morire per Cr polmonare nel sesso maschile è circa *21 volte* maggiore rispetto ai non fumatori
- Il fumo è responsabile di circa il *50% delle BPCO (Lundback B et al, 2003)* : il rischio di morire per tale patologia è circa *10 volte* superiore nei fumatori rispetto ai non fumatori
- Il rischio di morte per *patologie coronariche* è da *2 a 4 volte* superiore rispetto ai non fumatori
- Il rischio di *ictus cerebri* è *doppio* rispetto ai non fumatori

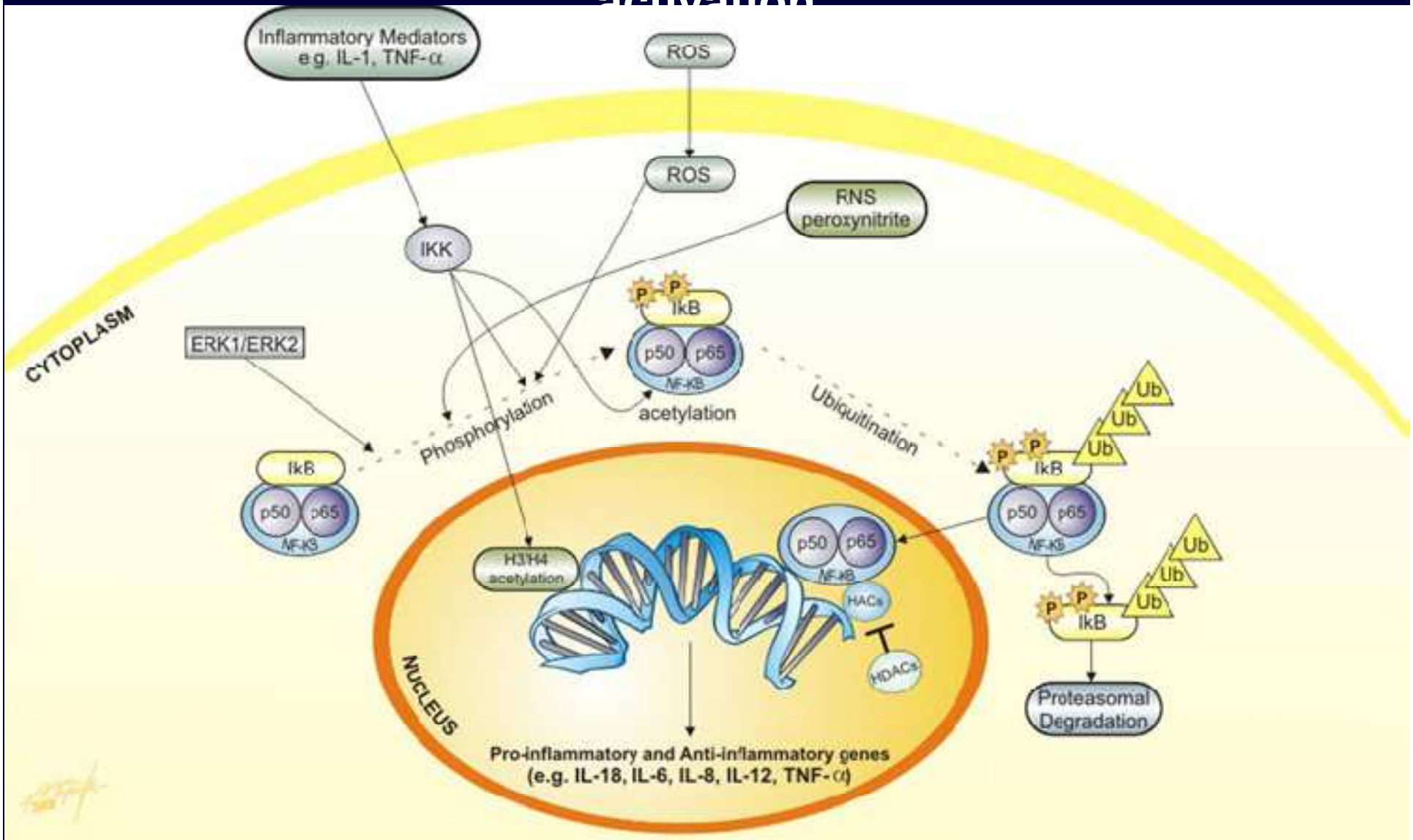


Source: **Infectious disease and CVD rates from Cutler et al. 2006. Age-adjusted rates for stomach, lung, and bronchus cancer from American Cancer Society 2009. Age-standardized rate for all cancers from World Health Organization Mortality Database 2012. Age-adjusted rates for COPD from National Center for Health Statistics 2012.**

Note: **COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease.**

U.S. Dep. of Health and Human Services - A Report of the Surgeon General, 2014

A model for the pathological effects of smoking on transcriptional control of inflammatory genes via NF-kB activation



Goncalves RB et al, Inflamm Res, 2013

Disease category	Total		
	SAD	No. of deaths	%SAD
Malignant neoplasms			
Lip, oral cavity, pharynx	1685	2785	60.5
Esophagus	1060	1757	60.3
Stomach	1595	10485	15.2
Pancreas	1713	9811	17.5
Larynx	1277	1672	76.4
Trachea, lung, bronchus	25987	32888	79.0
Cervix uteri	39	408	9.6
Kidney and renal pelvis	667	3078	21.7
Urinary bladder	1856	5479	33.9
Acute myeloid leukemia	229	1870	12.2
Cardiovascular diseases			
Ischemic heart disease	8242	75050	11.0
Other heart disease	4607	51294	9.0
Cerebrovascular disease	4212	61447	6.9
Atherosclerosis	322	2833	11.4
Aortic aneurysm	1936	3773	51.3
Other arterial disease	293	2726	10.7
Respiratory diseases			
Pneumonia, influenza	955	7429	12.9
Bronchitis, emphysema	3037	3841	79.1
Chronic airway obstruction	11733	16787	69.9
Other causes of death	0	273986	0.0
Total	71445	569399	12.5

Smoking attributable deaths (SAD) by sex, according to cause of death (Italy, 2010)

Estimated 71,445 deaths (52,707 men and 18,738 women, 12.5% of total mortality) caused by smoking

Total resident in 2010 was 60,340,328 (29,287,403 males and 31,052,925 females)

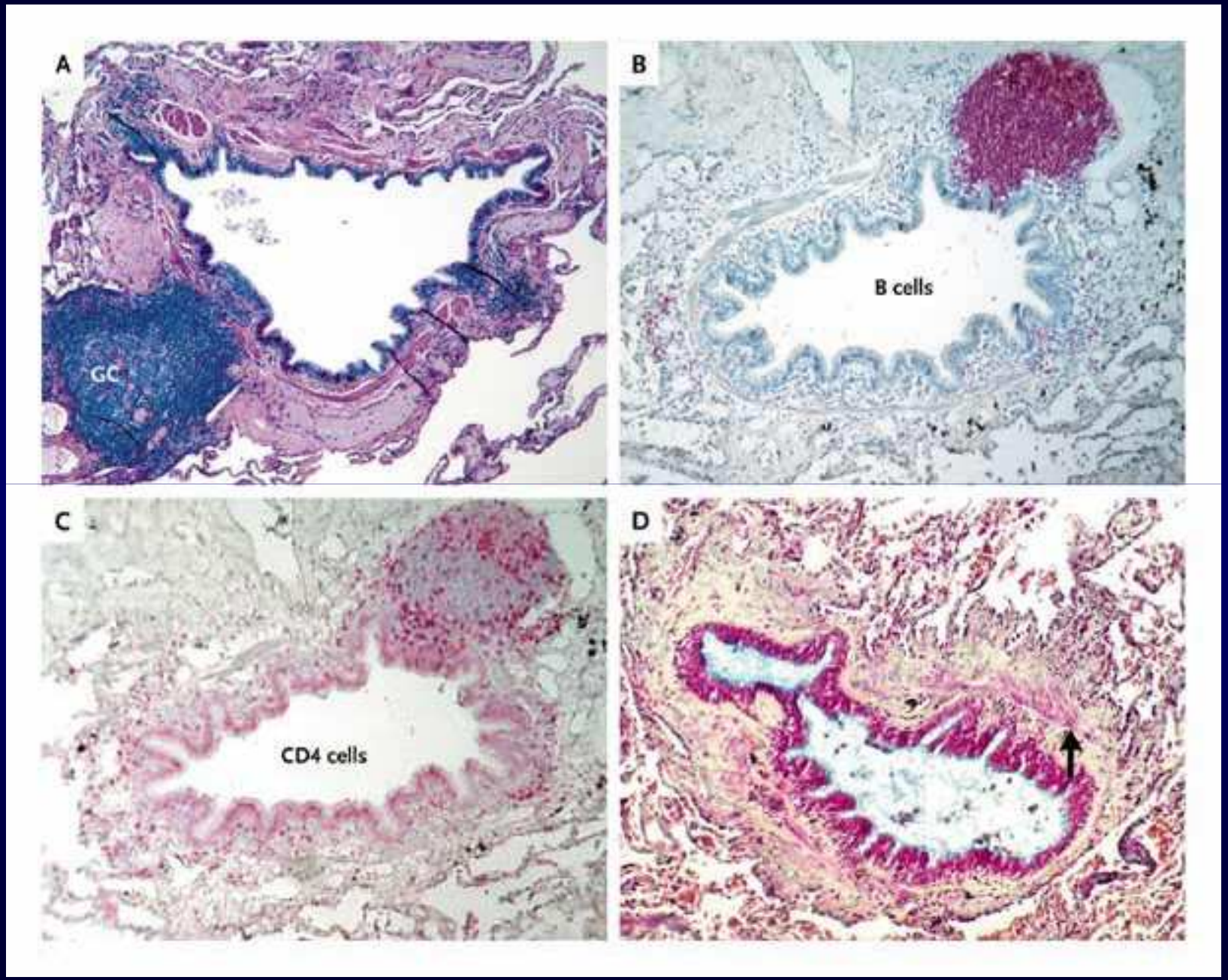
Gallus S, et al. Prev Med, 2011

Bronco-pneumopatia cronica ostruttiva

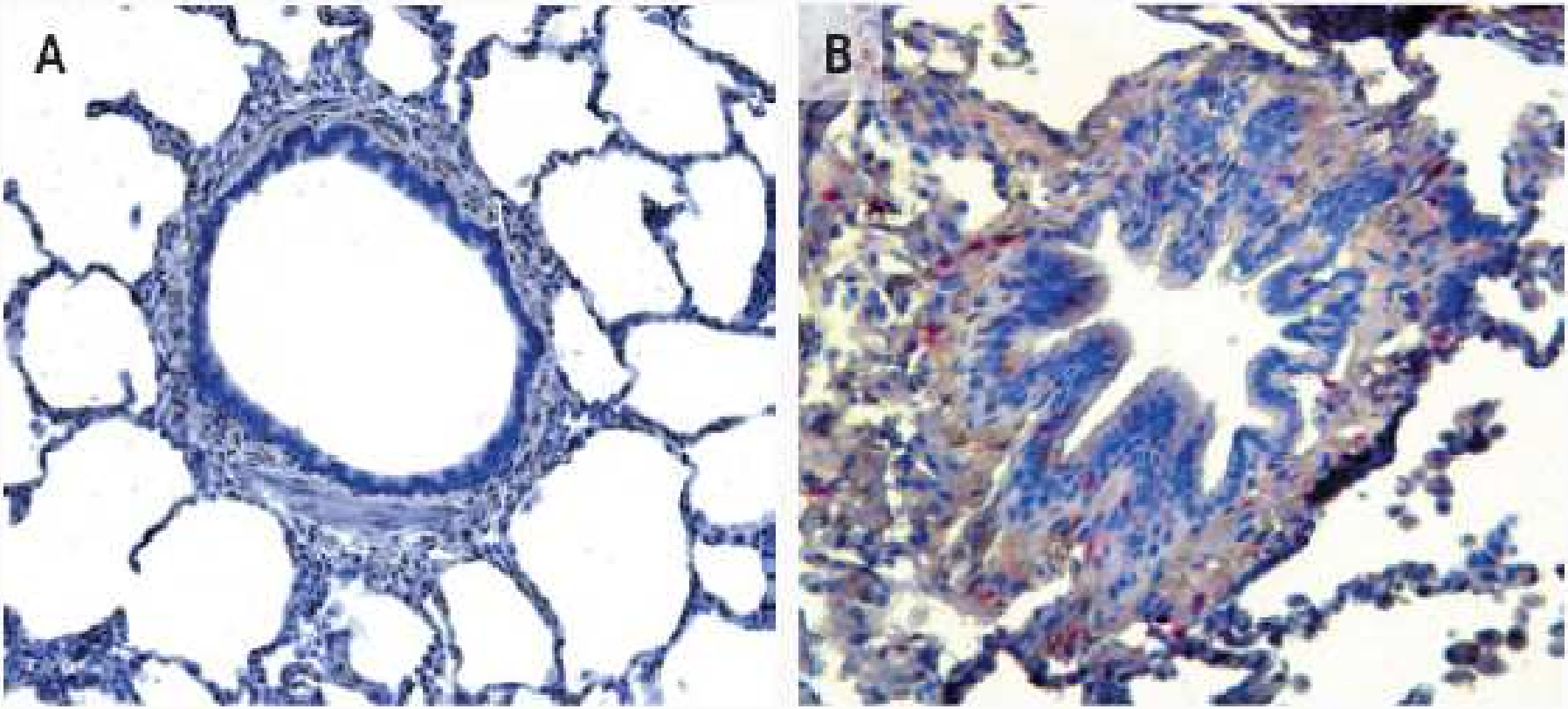
Broncopneumopatia cronica ostruttiva

- 5% adulti nei paesi industrializzati (maschi e femmine)
- 20% dei fumatori sviluppa BPCO
- Progressione legata a:
  - numero delle riacutizzazioni
  - maggiore declino annuale del VEMS
  - comparsa di enfisema polmonare
- Mortalità influenzata da:
  - età di inizio precoce
  - continuità dell'abitudine
  - entità dell'esposizione *("quantità di fumo")*

Pathological Findings in Patients with COPD



Hogg J et al. N Engl J Med 2004;350:2645-2653



Specimens from the Small Airways in the Healthy Lung of a Nonsmoker and the Lung of a Smoker with COPD.

Cosio MG, N Engl J Med, 2009

Enfisema polmonare

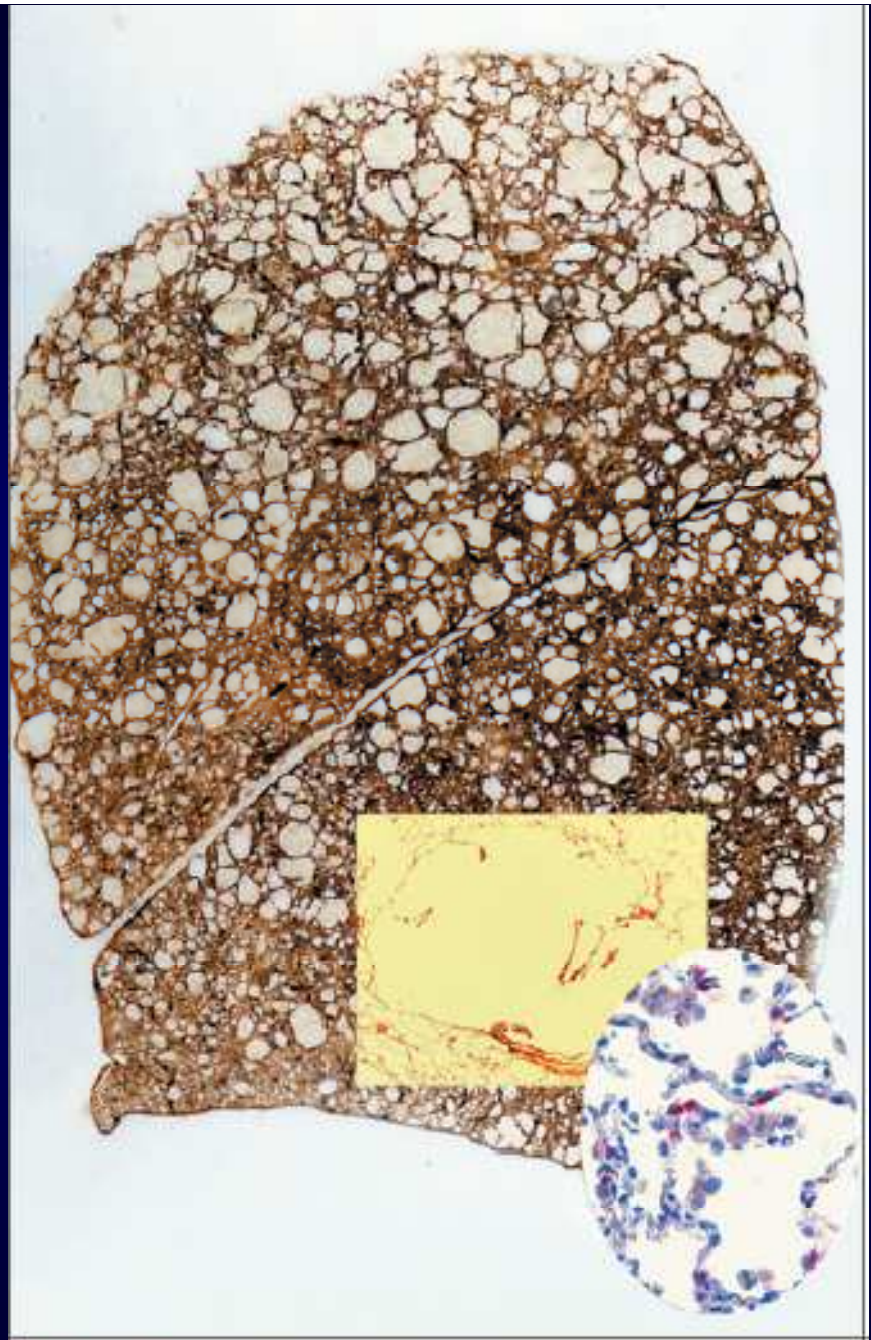
Patogenesi

Neutrofili (proteasi) → Elastasi, Collagenasi, Catepsina G, Proteinasi 3

Elastasi, Collagenasi → Metallo-proteinasi

Macrofagi → Incremento proteasi

Aumentati di 2-4 volte nei fumatori

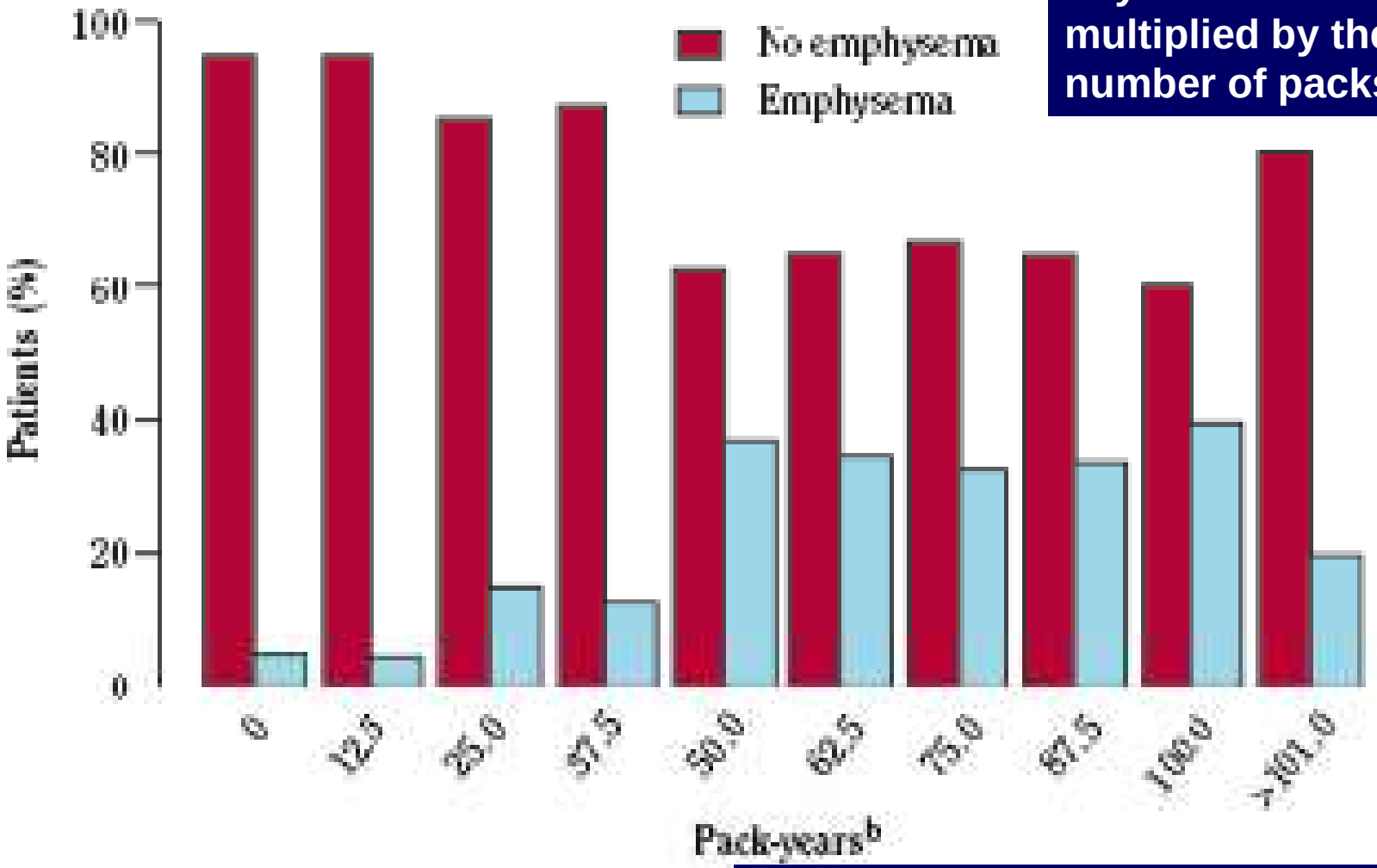


Lung Specimen from a Patient with Emphysema and COPD.

Cosio MG, N Engl J Med, 2009

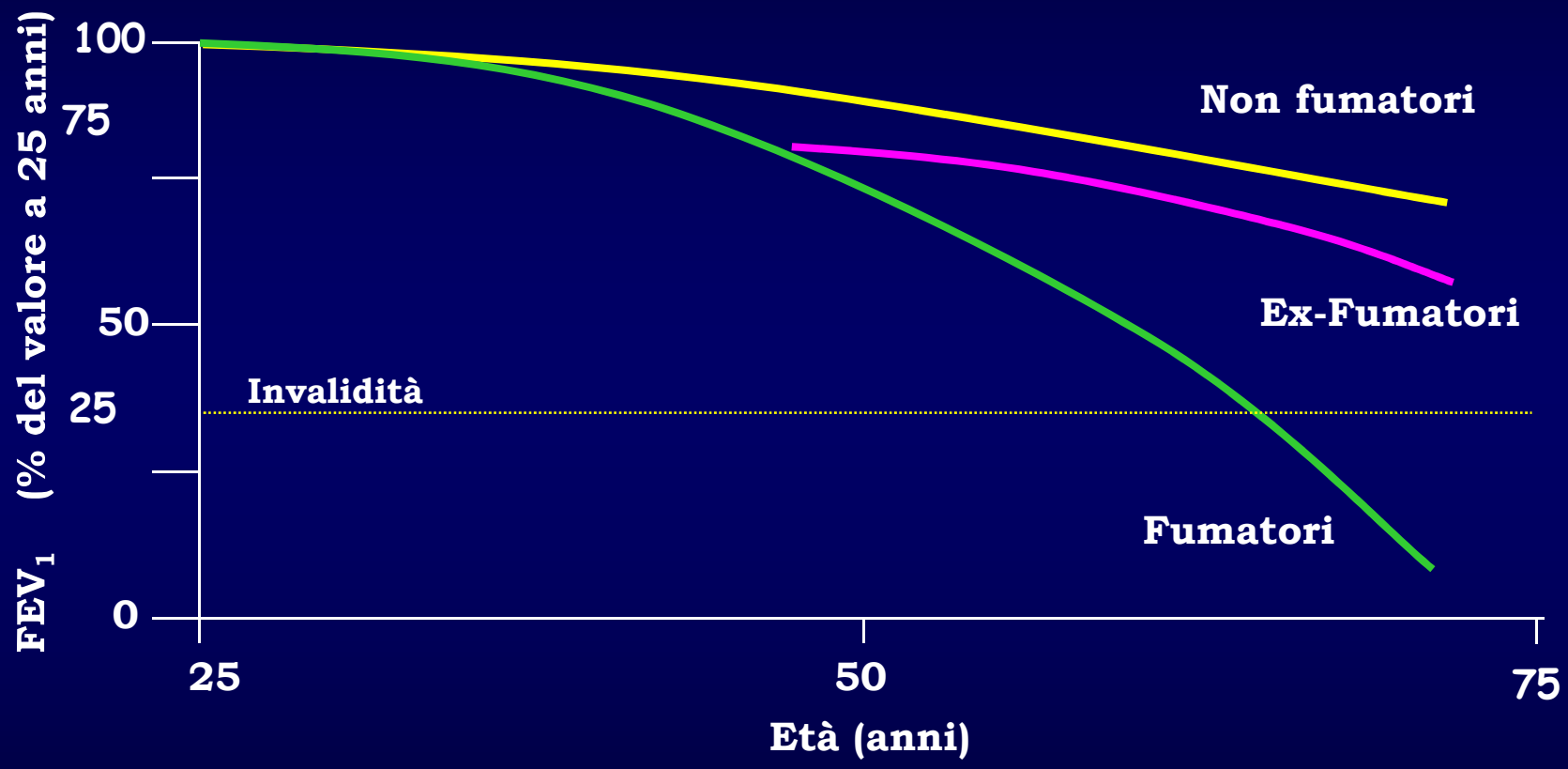
Dose-response relationship between level of smoking and the percentage of 408 patients in the St. Paul's Lung Study with morphologic evidence of significant emphysema in their lu

Pack-years = the number of years of smoking multiplied by the number of packs of



Hogg J et al. N Engl J Med 2004;350:2645-2653

Abitudine al fumo e riduzione del FEV_1



Fletcher e Peto, BMJ, 1977 (modificata)

COPD- Genere

La mortalità per COPD è aumentata in modo drammatico nei decenni passati

1) Il fumo è il principale rischio di COPD negli uomini e nelle donne; **donne potenzialmente più suscettibili** ad esposizioni più basse

2) E' possibile che le donne sviluppino una **severa COPD ad età più giovani** rispetto agli uomini e con minore esposizione cumulativa a fumo di sigaretta

3) Uomini e donne attualmente presentano **simili rischi relativi (RR) di mortalità per COPD**

4) Donne: **significativamente minore enfisema**, nonostante una simile severità di COPD valutata come livello di FEV_1

5) Donne fumatrici: declino di FEV1 maggiore rispetto ai maschi

U.S. Dep. of Health and Human Services - A Report of the Surgeon General, 2014

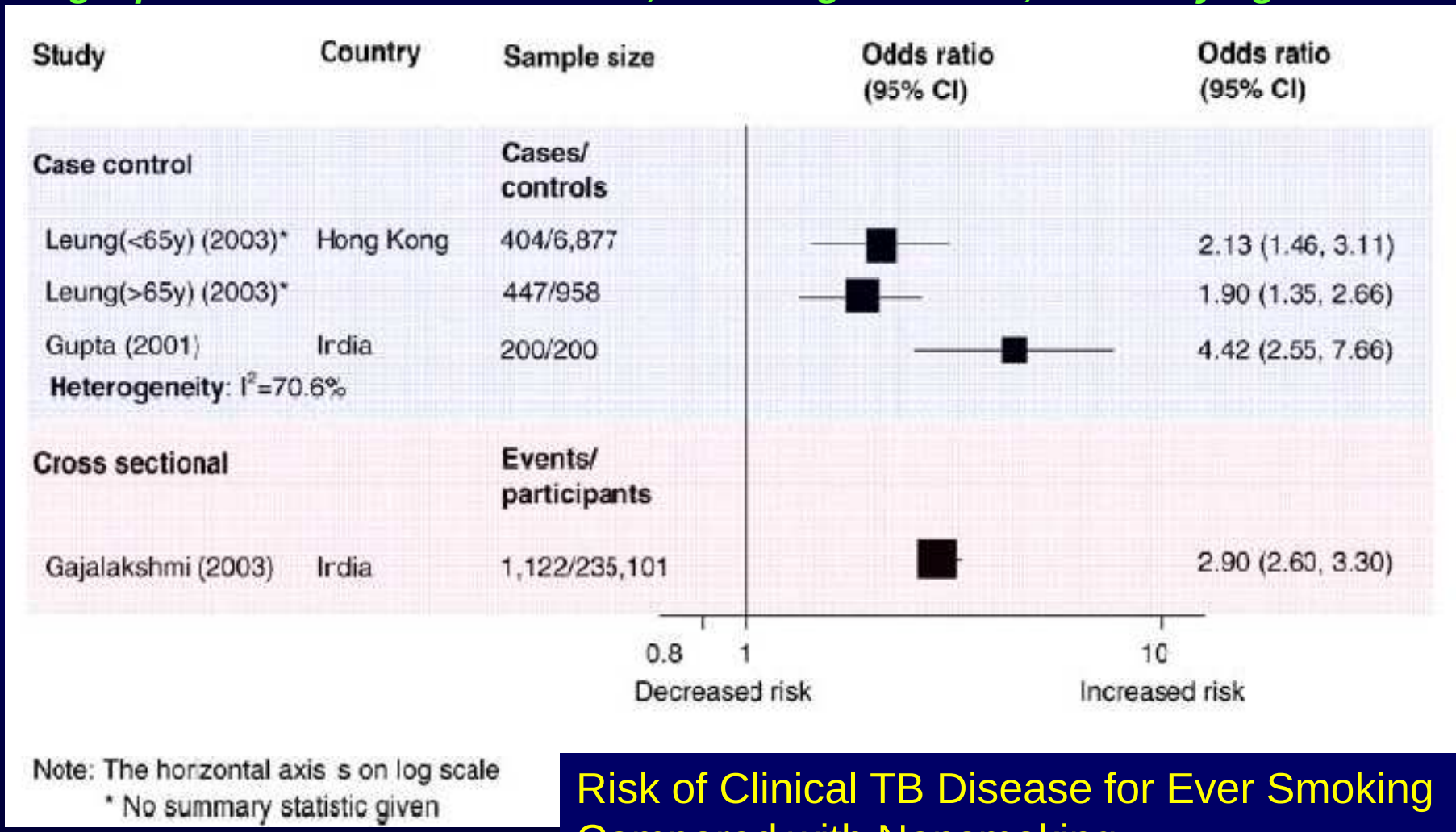
Pneumopatie interstiziali correlate con il fumo di tabacco

- **Pneumopatia interstiziale desquamativa (DIP) o alveolite macrofagica**
- **Bronchiolite respiratoria e malattia interstiziale polmonare (RB-ILD)**
- **Istiocitosi polmonare con cellule di Langerhans**
- **Fibrosi polmonare idiopatica (UIP) (?)**

Ryn J.H. et al., Eur Respir J, 2001

Tobacco Smoke, Indoor Air Pollution and Tuberculosis: A Systematic Review and Meta-Analysis

Compared with people who do not smoke, smokers have an increased risk of having a positive tuberculin skin test, of having active TB, and of dying from TB



Risk of Clinical TB Disease for Ever Smoking Compared with Nonsmoking

Lin HH et al, PLoS Med 4(1): e20, 200

Tobacco smoking and cancer: A meta-analysis

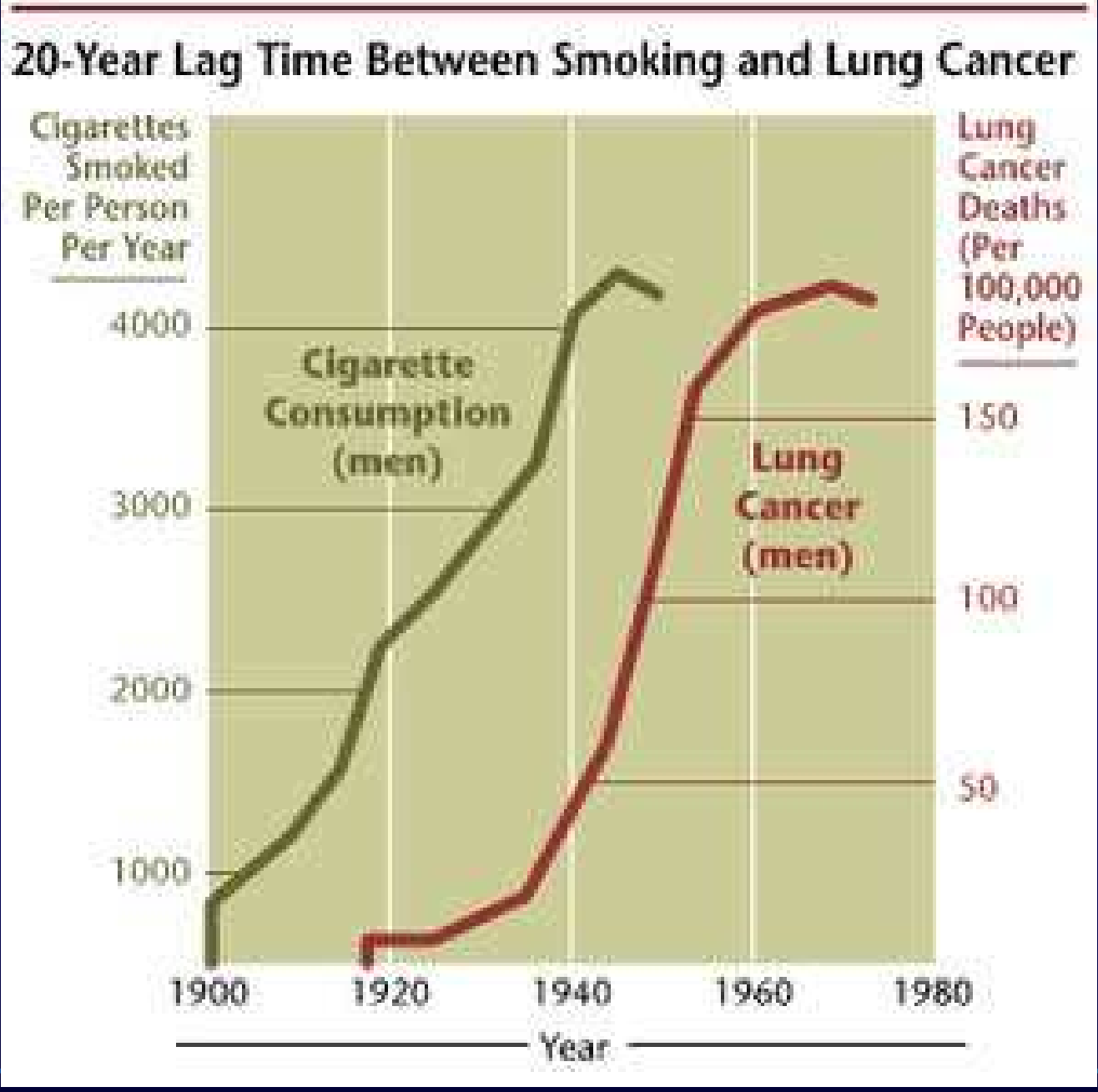
Sara Gandini, Edoardo Botteri, Simona Iodice, Mathieu Bonio, Albert B. Lowenfels, Patrick Maisonneuve and Peter Boyle

Int J Cancer. 2008

We conducted a systematic meta-analysis of observational studies on cigarette smoking and cancer from 1961 to 2003. The aim was to quantify the risk for 13 cancer sites, recognized to be related to tobacco smoking by the International Agency for Research on Cancer (IARC), and to analyze the risk variation for each site in a systematic manner. We extracted data from 254 reports published between 1961 and 2003 (177 case-control studies, 75 cohorts and 2 nested case-control studies) included in the 2004 IARC Monograph on Tobacco Smoke and Involuntary Smoking

As expected, pooled RRs for respiratory cancers were greater than the pooled estimates for other sites

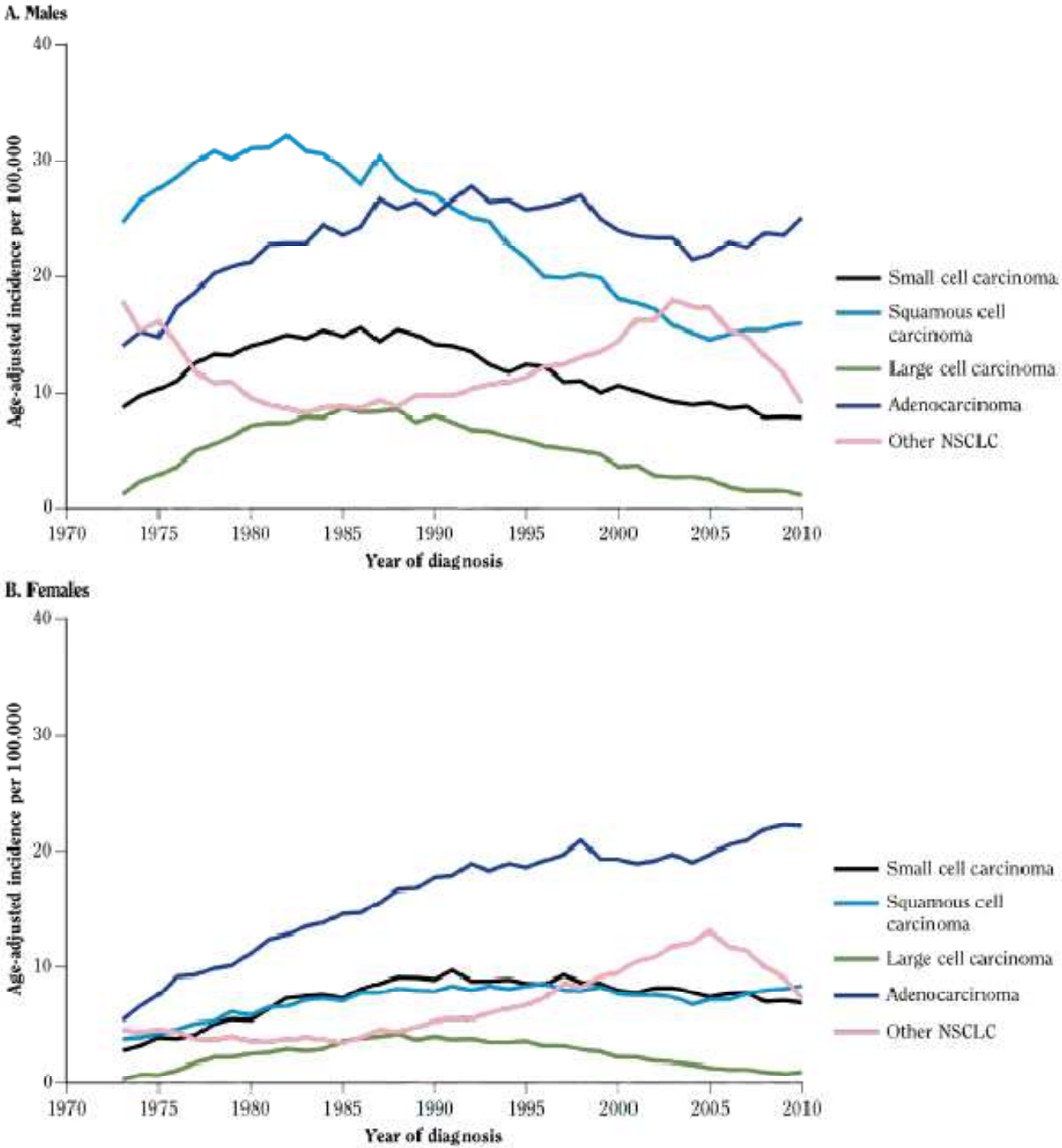
The analysis of heterogeneity showed that study type, gender and adjustment for confounding factors significantly


20-Year Lag Time Between Smoking and Lung Cancer
Cigarettes Smoked Per Person Per Year
4000
3000
2000
1000
Cigarette Consumption (men)
Lung Cancer (men)
Lung Cancer Deaths (Per 100,000 People)
150
100
50
1900
1920
1940
1960
1980
Year

Carcinoma polmonare

Ruolo svolto dal fumo di sigaretta:

- il fumo è stato messo in relazione con la comparsa di **mutazioni specifiche**
- **aumento di incidenza** del carcinoma polmonare nei fumatori rispetto ai non fumatori
- **relazione dose-risposta** tra quantità di sigarette fumate al giorno e rischio di carcinoma polmonare
- tale associazione è più evidente per gli istotipi **squamocellulare**, a **piccole cellule e, più recentemente, per l'adenocarcinoma**
- l'esposizione a **fumo passivo** aumenta l'incidenza di tumore polmonare in soggetti non fumatori



Standardized incidence of lung cancer, by gender and histology (age adjusted to 2000 U.S. population), 1973–2010

U.S. Dep. of Health and Human Services - A Report of the Surgeon General, 2014

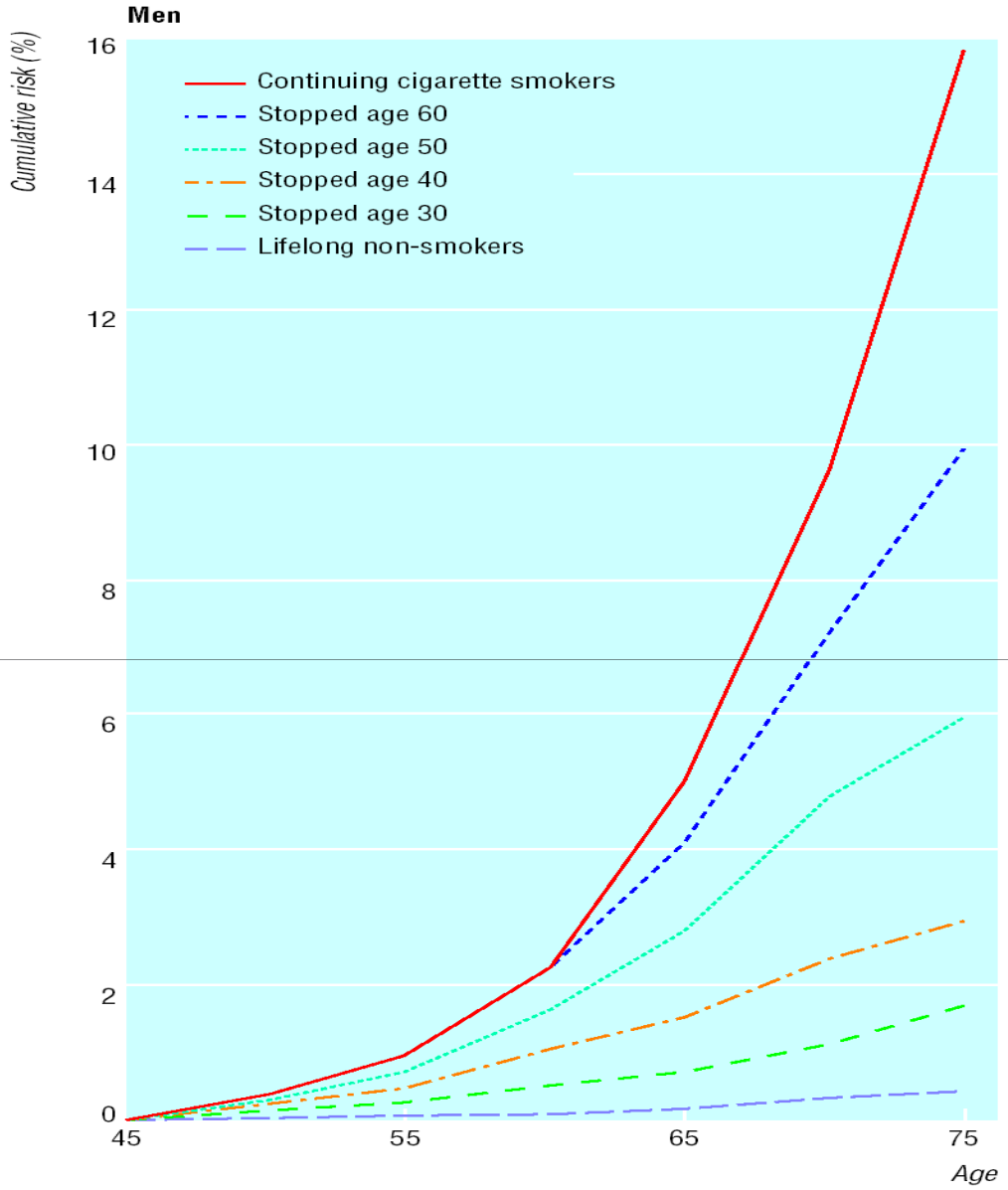


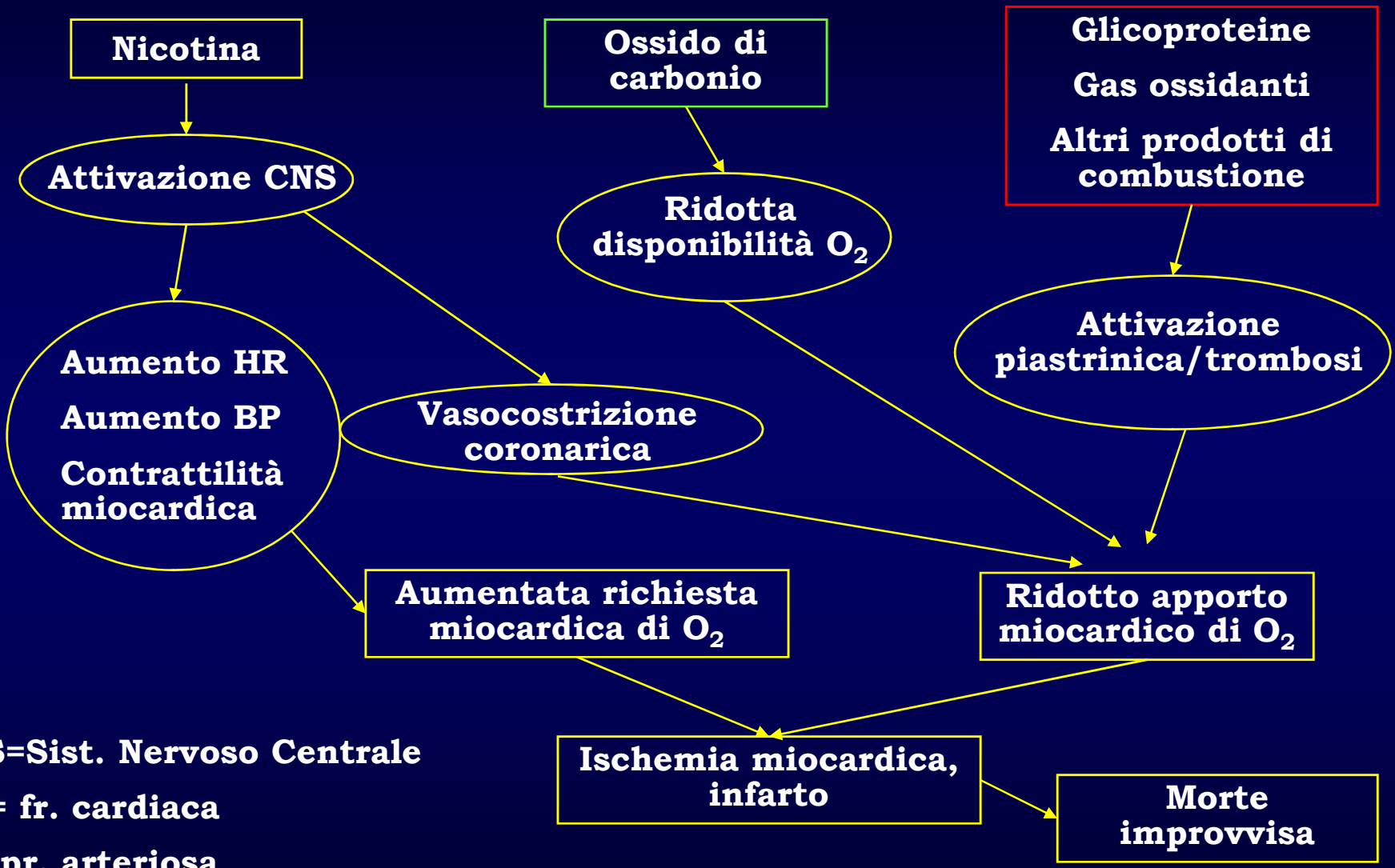
Fig 3 Effects of stopping smoking at various ages on the cumulative risk (%) of death from lung cancer up to age 75, at death rates for men in United Kingdom in 1990. (Non-smoker risks are taken from a US prospective study of mortality[14])

Effetti della sospensione del fumo a diverse età sul rischio cumulativo di morte per tumore polmonare

BMJ, 2000;321:323-329

Abitudine al fumo
e
Malattie cardiovascolari

Fumo e malattie cardiovascolari

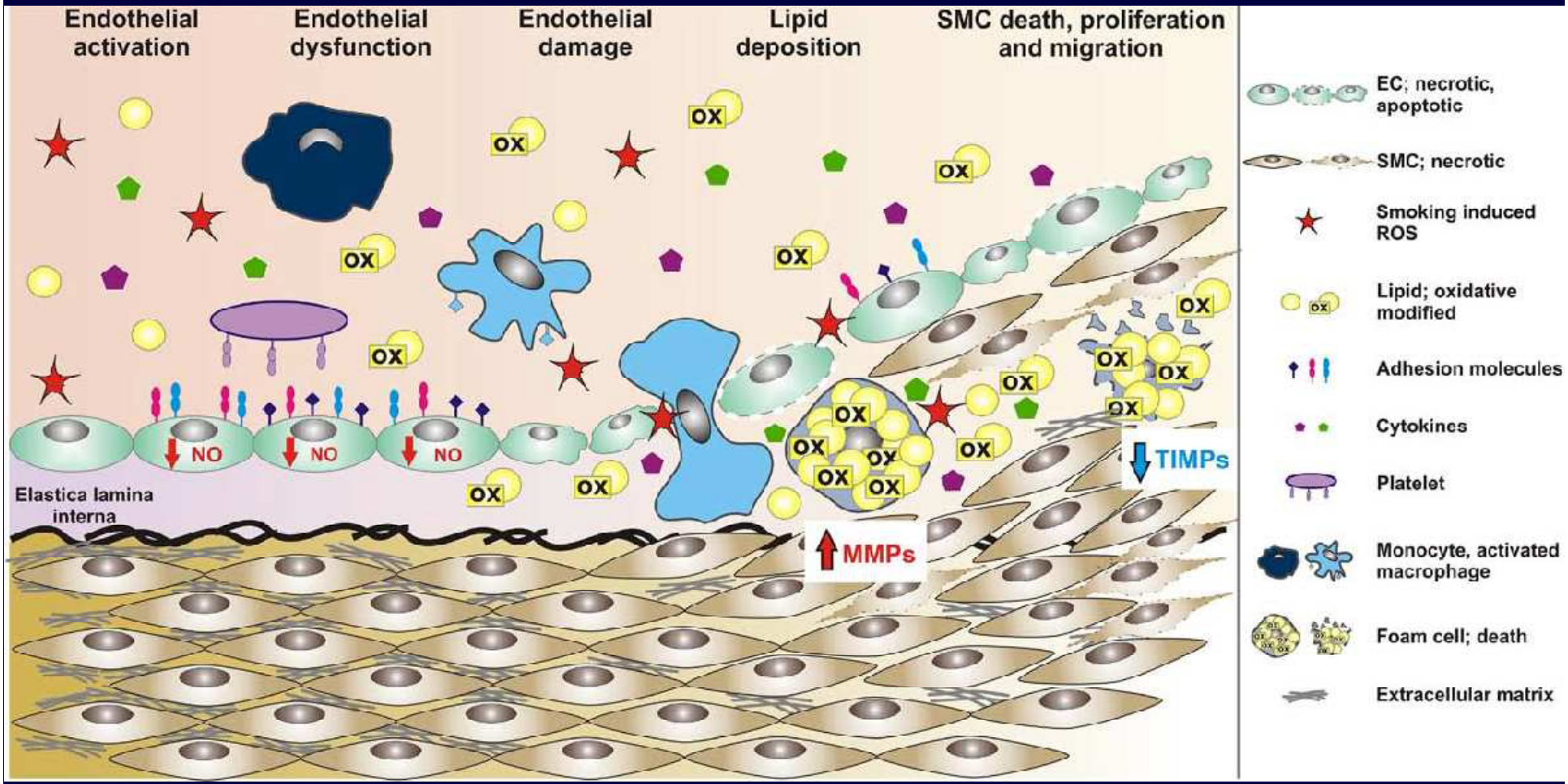


CNS=Sist. Nervoso Centrale

HR= fr. cardiaca

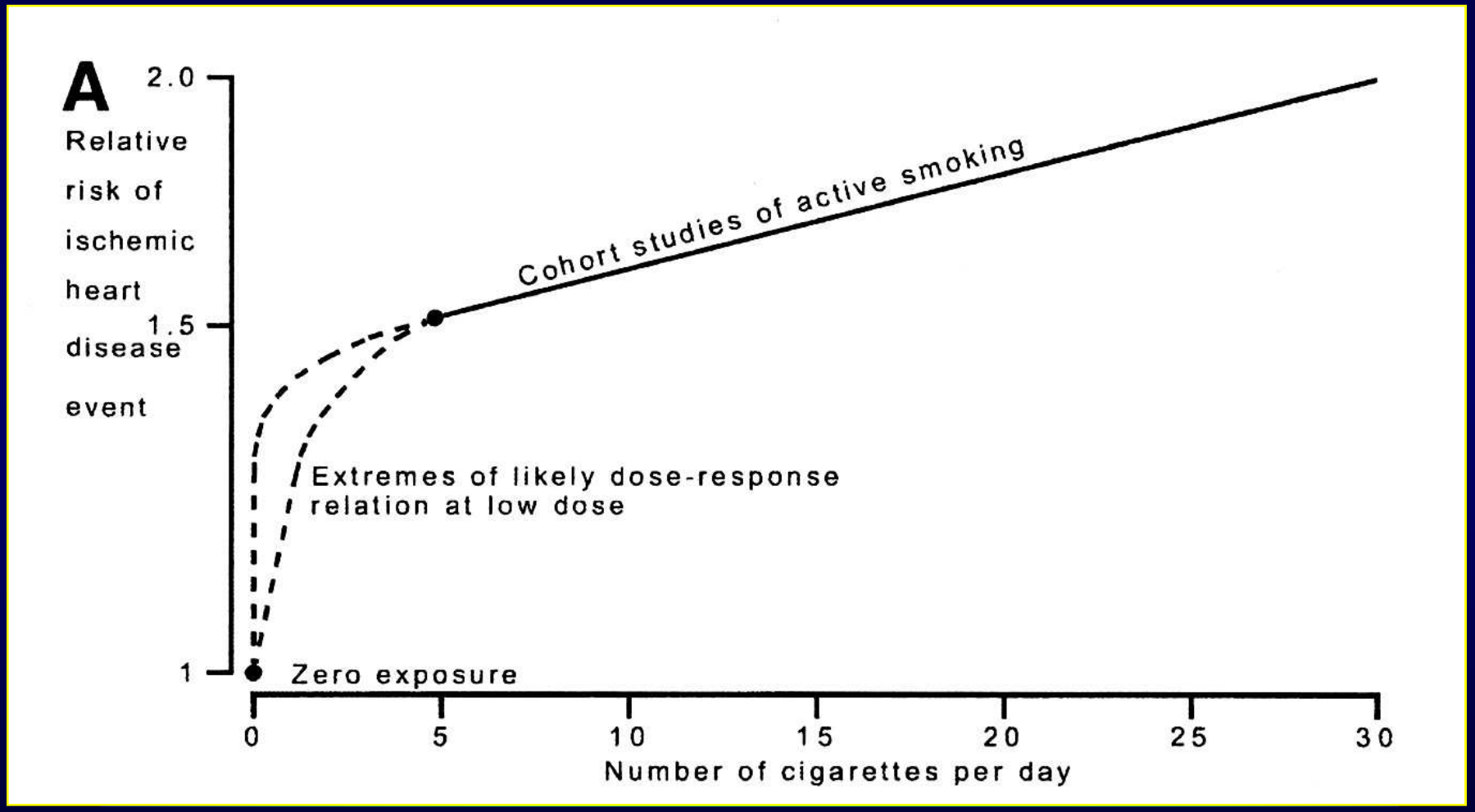
BP=pr. arteriosa

Smoking and Cardiovascular Disease
Mechanisms of Endothelial Dysfunction and Early Atherogenesi

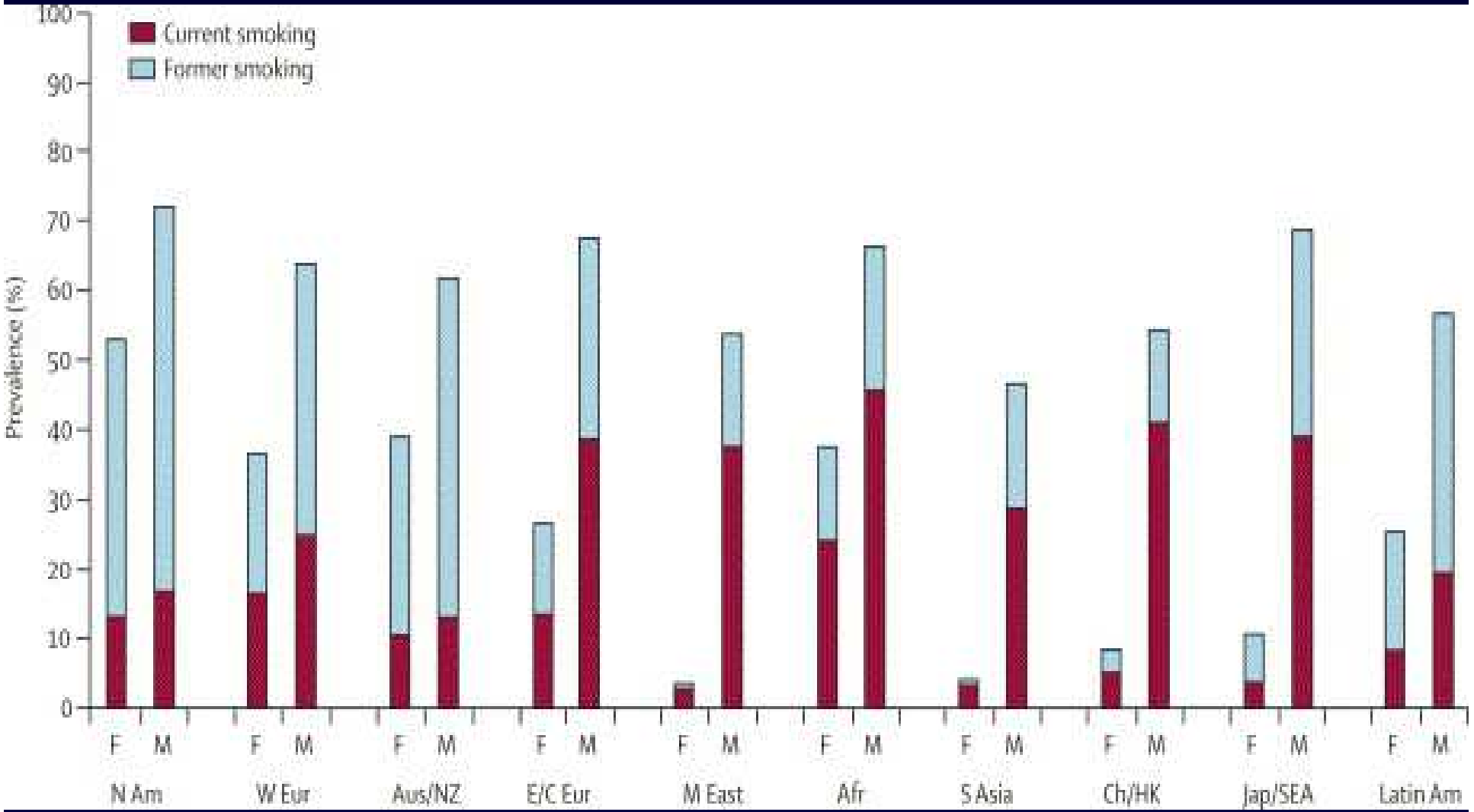


Messner B et al, Arteriosler Thromb Vasc Biol 2014

Relazione dose-risposta tra fumo attivo e rischio di cardiopatia ischemica

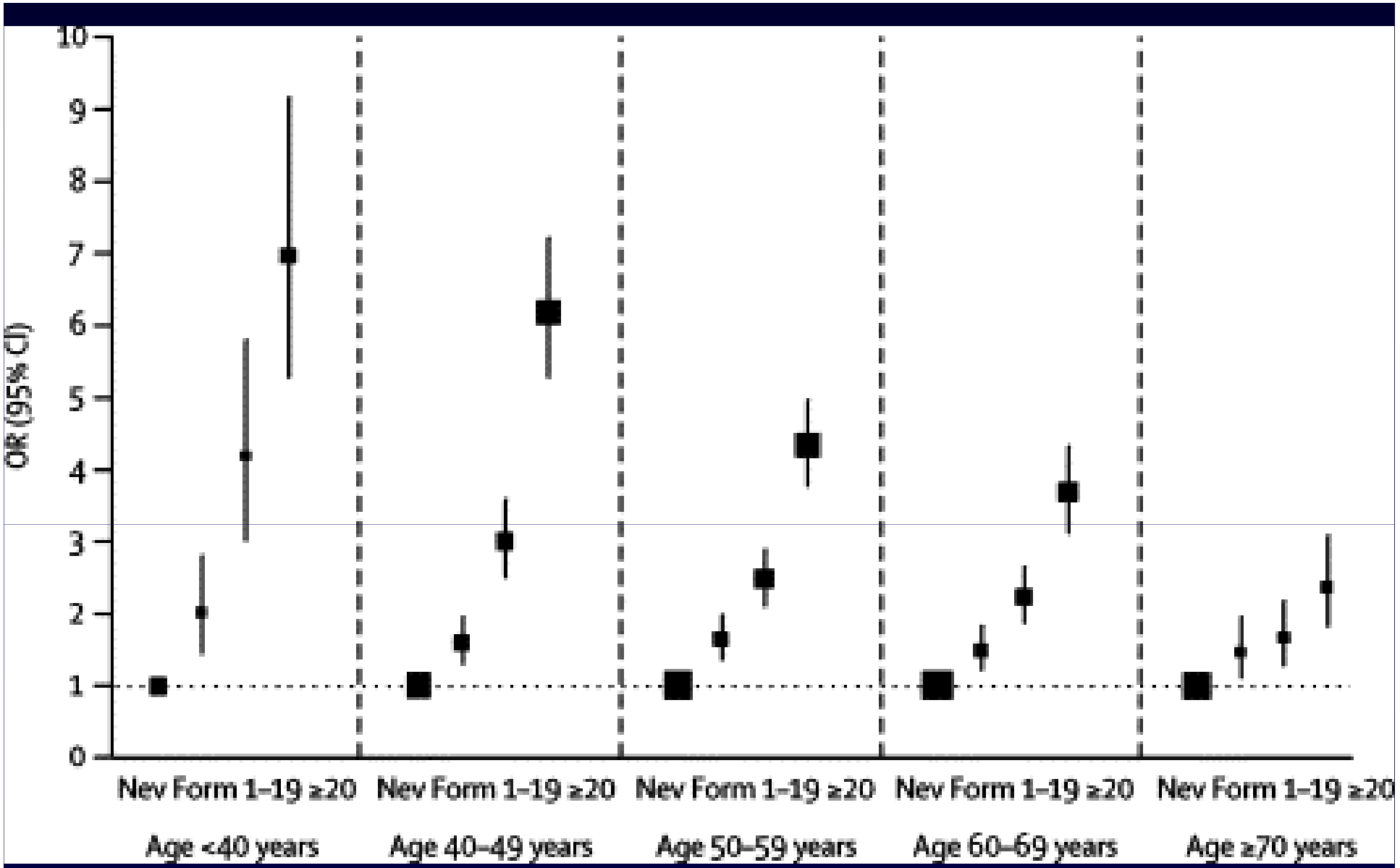


INTERHEART STUDY, Case-Control, 27089 participants (12461 cases, 14637 controls, 52 Countries



Prevalence of smoking by region and sex F=female M=male

Teo KK et al, Lancet, 2006

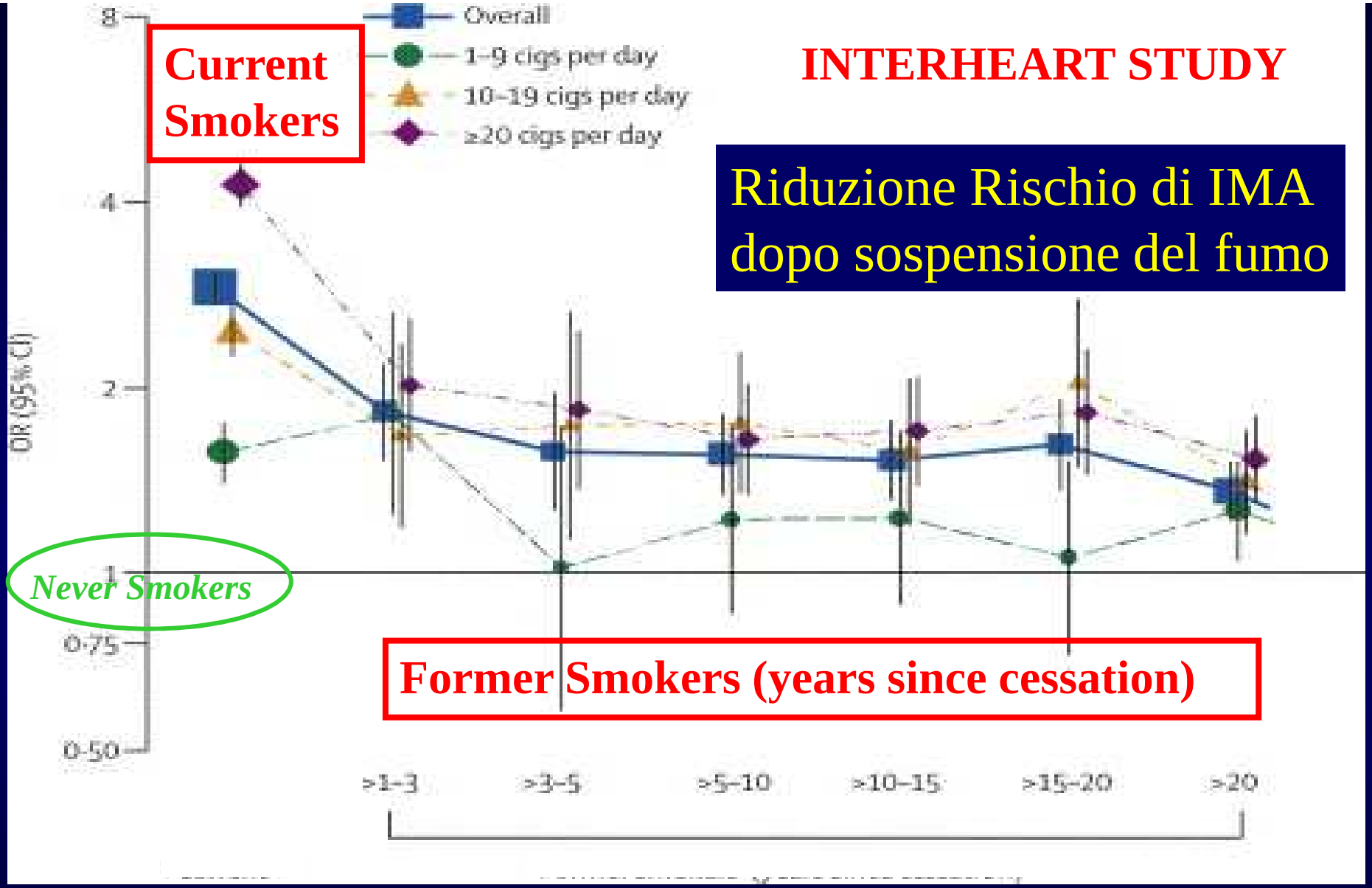


Risk of *Acute Myocardial Infarction* associated with numbers smoked cigarettes, by age group (p for interaction < 0·0001) Nev=Never and For=Former smokers

Teo KK et al, Lancet, 2006

INTERHEART STUDY

Riduzione Rischio di IMA dopo sospensione del fumo

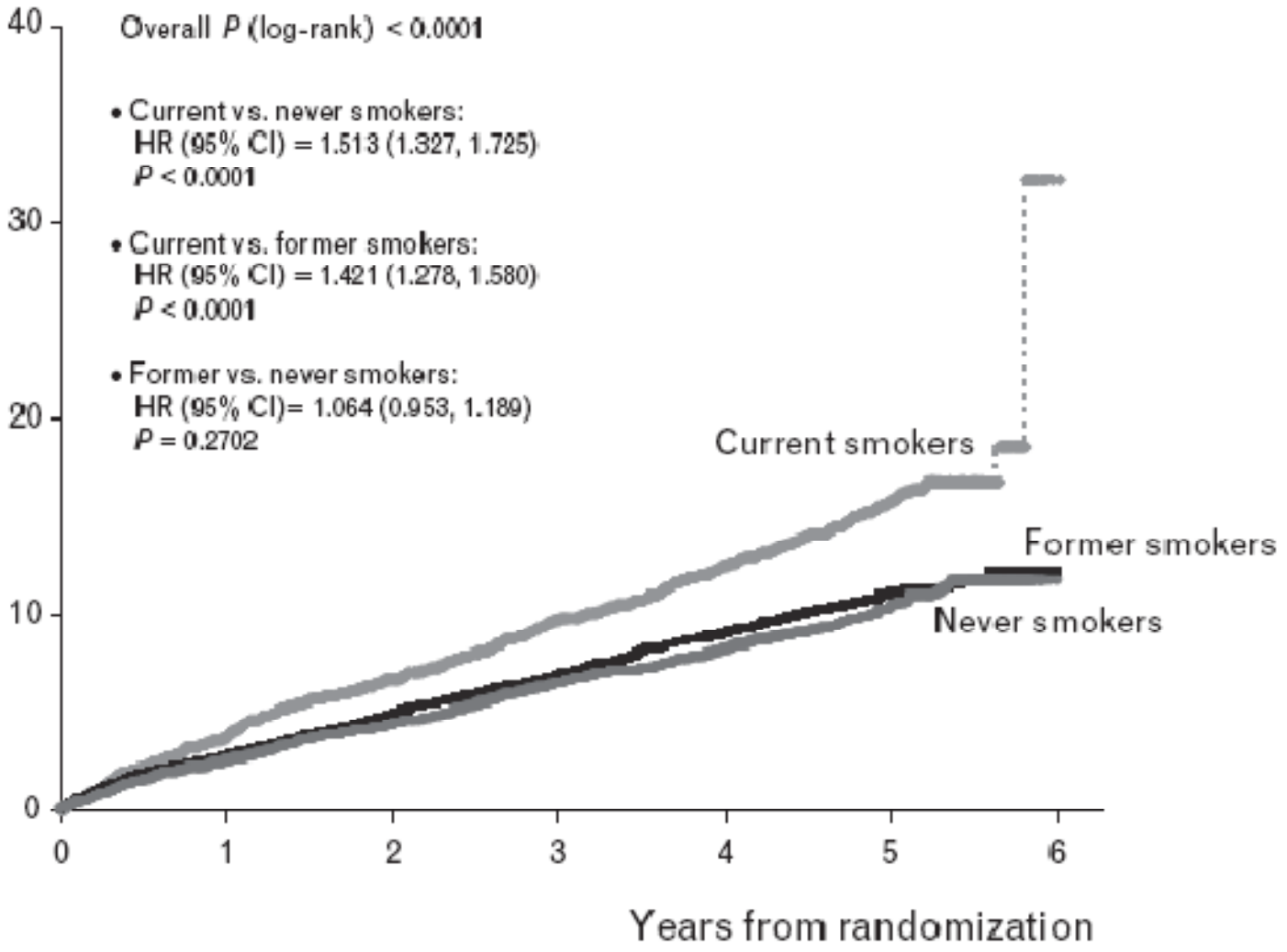


Diminishing risk of AMI associated with quitting in former smokers, with never smokers as reference ORs adjusted for sex, region, diet, alcohol, and physical activity.

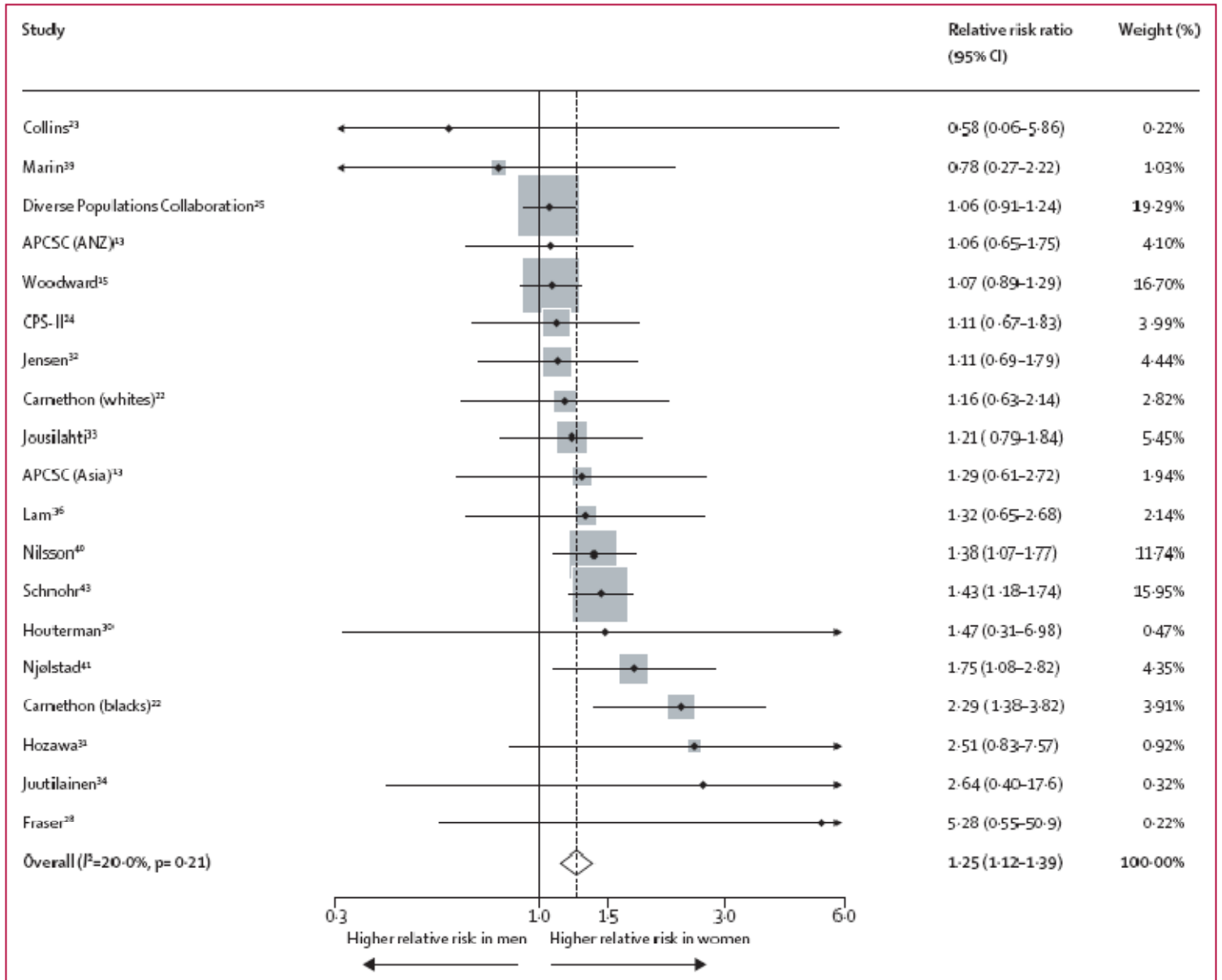
Teo KK et al, Lancet, 2006

Kaplan–Meier curves for major cardiovascular events by smoking status in the pooled post-hoc analysis of the Treating to New Targets and Incremental Decrease in End Points Through **Aggressive Lipid Lowering trials**

This study demonstrates the continued risk of CHD with tobacco use despite contemporary pharmacologic treatment of CHD including intensive lipid-lowering therapy



Frey P et al, Am J Cardiol 2011



Metanalysis

Included 26 articles with data for 3 912 809 individuals and 67 075 coronary heart disease events from 86 prospective trials.

Multiple-adjusted

female-to-male relative risk ratios for Coronary Heart Disease,

smoking compared with not smoking

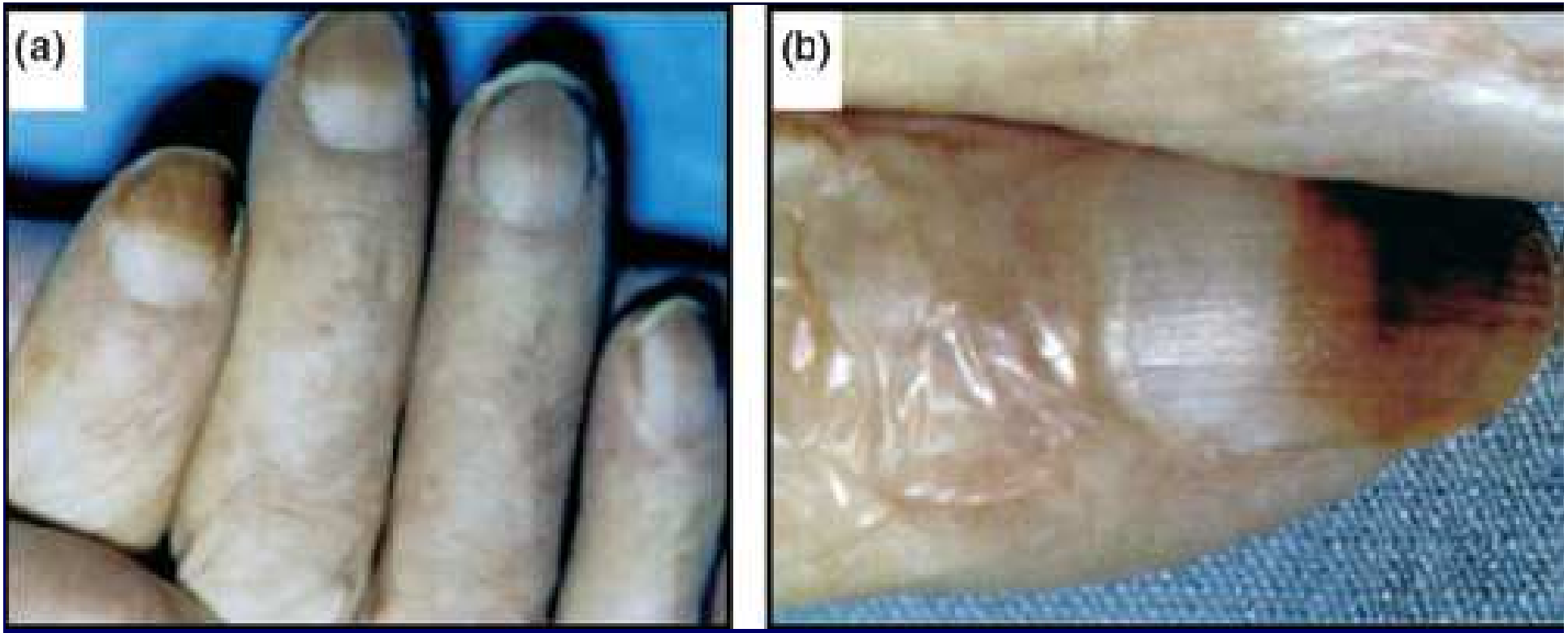
Huxley R R, et al. Lancet 2011

Smoking and stroke: the more you smoke the more you stroke.

Shah RS, Cole JW.

Expert Rev Cardiovasc Ther. 2010 Jul;8(7):917-32.

In this article, we summarize the literature regarding smoking-related stroke risk, the dose-response relationship, and the costs of this detrimental habit to both the individual and society as a whole.



Harlequin or quitter's nail.

(a) Nicotine staining and line of demarcation involving several fingers.

(b) The demarcation line between the distal pigmented yellow nail and a newlydeveloped proximal pink nail appeared after sudden cessation of smoking

Ortiz A, et al. Int J Dermatol, 2012

Smoker's face in a smoker twin. Note significant differences of appearances of the smoking twin 1 and non-smoking twin 2. Twin 1 has a smoking history of approximately 52.5 pack-years.

Both twins have similar cumulative lifetime history of Sun Exposure

Snyder, et al. Int J Dermatol, 2012

Fumo e degenerazione maculare della retina

Fumo di tabacco

- E’ uno dei fattori di rischio accertati
- Riducendo il flusso nei vasi della coroide, accelera la degenerazione maculare, attribuibile all’ invecchiamento dei pigmenti della macula stessa
- Negli ex-fumatori il rischio non è pari a quello dei non-fumatori, ma subisce un decremento significativo

J. Thornton et al. 2005

Fumo e diabete

Fumo di tabacco

- Fattore di rischio indipendente e modificabile per diabete mellito
- Riduce i livelli di insulina a digiuno
- Incrementa transitoriamente la glicemia dopo test da carico con glucosio
- Accelera la comparsa di albuminuria e l'evoluzione verso l'insufficienza renale in soggetti diabetici
- All'inizio aumenta l'insulino- resistenza periferica; poi altera la funzionalità delle cellule β pancreatiche
- L' esposizione ad ETS aumenta il rischio di sviluppare diabete rispetto ai non-fumatori non esposti

Rimm, 1995; Pinto-Sietsma, 2000; K. Tziomalos, 2004, T.Houston, 2006

Fumo e malattie gastroenteriche

Fumo di tabacco

- **Aumentata incidenza di malattia ulcerosa gastro-duodenale e rallentata riparazione delle lesioni**
- **Aumentata incidenza di malattia da reflusso gastro-esofageo**

Watanabe, 2003

Rectal cancer

incidence rates and age-adjusted and multivariate-adjusted relative risks (and 95% confidence intervals) of developing rectal cancer for men and women according to active cigarette smoking (Washington County, Maryland Cohorts, 1963-1978 and 1975-1994)

	1963 Cohort			1975 Cohort		
	No. of cases	Incidence rate/10,000	Relative risk‡ (C.I.)	No. of cases	Incidence rate/10,000	Relative risk ‡ (C.I.)
Men						
Never smoker	5	1.35	1.00	11	1.81	1.00
Former smoker	19	3.42	2.63 (0.98-7.05)	36	3.90	1.98 (0.98-3.78)
Current smoker	42	2.90	3.05 (1.19-7.82)	30	2.51	1.80 (0.88-3.67)
Women						
Never smoker	35	3.60	1.00	41	2.53	1.00
Former smoker	3	1.14	0.62 (0.19-2.08)	15	2.89	1.87 (1.02-3.45)
Current smoker	16	1.70	0.93 (0.48-1.80)	21	2.05	1.57 (0.89-3.76)

‡Poisson regression model adjusted for age (continuous), education (<12 yr/≥ 12 yr) and marital status (married, divorced/separated, widowed, single).

Hooker C.M. et al. – Ann Epidemiol 2008

Bladder cancer

Relative risk of developing bladder cancer according to active cigarette smoking status, Washington County, Maryland, 1963-1978 and 1957-1994

Smoking status	1963 Cohort				1975 Cohort			
	No. of cases	Person years	RR‡	95% CL	No. of cases	Person years	RR‡	95% CL
Never an active smoker, no current secondhand smoke exposure§	20	134,243	1.0		40	223,063	1.0	
Current secondhand smoke exposure only	14	84,119	1.4	0.7, 2.7	8	73,183	0.8	0.4,1.7
Former smoker	11	81,852	1.2	0.5, 2.5	57	144,156	2.3	1.5, 3.4
Current smoker	48	239,377	2.7	1.6, 4.7	67	221,944	2.6	1.7, 3.9
Current amount smoked (cigarettes/day)								
≤10	7	47,111	1.7	0.7, 4.1	11	22,878	2.2	1.4, 3.6
11-20	28	119,803	3.2	1.7, 5.9	34	125,638	3.3	1.7, 6.7
>20	12	68,480	2.9	1.4, 6.1	20	66,384	3.3	1.9, 1.7

‡Adjusted for age, education, and marital status.

§Referent categry

Alberg AJ et al., Am J Epidemiol 2007

Fumo e sesso maschile

Fumo di tabacco

- **Responsabile della disfunzione endoteliale dei vasi penieni**
- **Aumenta il rischio di disfunzioni erettili (riduzione della velocità di picco sistolica e diastolica all'eco-color-doppler dei vasi penieni)**
- **La cessazione dell'abitudine tabagica comporta un miglioramento della sintomatologia e la normalizzazione dei parametri ecografici**
- **Aumento dei livelli di SHBG e consensuale riduzione della frazione libera di testosterone**

Il SHBG (sex hormone binding globulin) è una beta-globulina prodotta dal fegato che lega tutti gli ormoni sessuali che non possono entrare nelle cellule e legarsi allo specifico recettore ormonale.
La produzione del SHBG e' aumentata dagli estrogeni e ridotta dagli androgeni

M.C. Sighinolfi et al 2006; D. Kapoor and T.H. Jones 2005

Fumo e sesso femminile

Apparato riproduttivo

Nelle fumatrici maggiore incidenza di:

- **disfunzioni mestruali**
- **menorragie**
- **menopausa precoce e sintomi post-menopausali (Flushing, cardiopalmo ecc...)**
- **riduzione della densità minerale ossea ed osteoporosi**
- **effetti collaterali cardiovascolari in corso di terapia contraccettiva orale**
- **gravidanza ectopica**
- **aborti spontanei**

Fumo e sesso femminile

Gravidanza

Il fumo di tabacco è associato a maggiore incidenza di patologie della gravidanza e del prodotto del concepimento:

- **placenta previa**
- **distacco prematuro di placenta**
- **rottura prematura delle membrane**
- **parto pretermine**
- **neonati piccoli per l'età gestazionale**
- **asma bronchiale**

Lannero E et al. 2006

Spontaneous preterm birth and small for gestational age infants in women who stop smoking early in pregnancy: prospective cohort study

Table 2 | Pregnancy outcomes

	Non-smokers (n=1992)	Stopped smokers (n=261)	Mean difference (95% CI) *	P value*	Current smokers (n=251)	Mean difference (95% CI)†	P value†
Spontaneous preterm birth	88 (4)	10 (4)	-0.6% (-2.6 to 2.6)	0.66	25 (10)	6.1% (1.7 to 10.8)	0.006
Small for gestational age	195 (10)	27 (10)	-0.5% (-5.0 to 2.9)	0.80	42 (17)	6.4% (0.4 to 12.4	0.03
Birth weight (g)	3409 (592)	3479 (560)	-70 (-146 to 6)	0.09	3139 (751)	270 (190 to 350)	<0.001
Delivery gestation (weeks)	39.5 (2.3)	39.7 (2.4)	-0.2 (-0.5 to 0.1)	0.11	38.6 (3.6)	0.9 (0.6 to 1.2)	<0.001
Customised centile	48.9 (28.7)	49.3 (28.5)	-0.4 (-4.1 to 3.3)	0.88	41.3 (29.7)	7.6 (3.8 to 11.4)	0.002
Uncomplicated pregnancy	1192 (60)	162 (62)	-2.2% (-8.3 to 4.2)	0.49	111 (44)	-17.8% (-26.1 to -9.2)	<0.001

Data are mean (SD) or number (%). P values are for χ^2 or Student's *t* test.
*Comparison between stopped smokers and non-smokers.
†Comparison between stopped smokers and current smokers.

In women who stopped smoking before 15 weeks' gestation (differently from current smokers), rates of spontaneous preterm birth and small for gestational age infants did not differ from those in non-smokers

McCowan L ME et al, BMJ 2009;

Fumo e sesso femminile

Carcinoma mammario

- Il fumo contiene sostanze potenzialmente cancerogene per la mammella
- Aumentata prevalenza di addotti al DNA legati al fumo e mutazioni del gene *p53* in fumatori
- Da studi epidemiologici **non** emerge un **incremento del rischio** per cr. mammario nella maggior parte delle fumatrici
- Recenti evidenze sull'incremento del rischio legato alla *durata dell'abitudine* al fumo, in particolare prima della gravidanza, all'*esposizione a fumo passivo e a certi genotipi* necessitano di ulteriori conferme

Terry, Rohan, 2002

Active smoking and secondhand smoke increase breast cancer risk: the report of the Canadian Expert Panel on Tobacco Smoke and Breast Cancer Risk (2009)

…to comprehensively examine the weight of evidence from epidemiological and toxicological studies and understanding of biological mechanisms regarding the relationship between tobacco smoke and breast cancer

The Panel concluded that:

1) the association between active smoking and breast cancer is consistent with causality and

2) the association between SHS and breast cancer among younger, primarily premenopausal women who have never smoked is consistent with causality

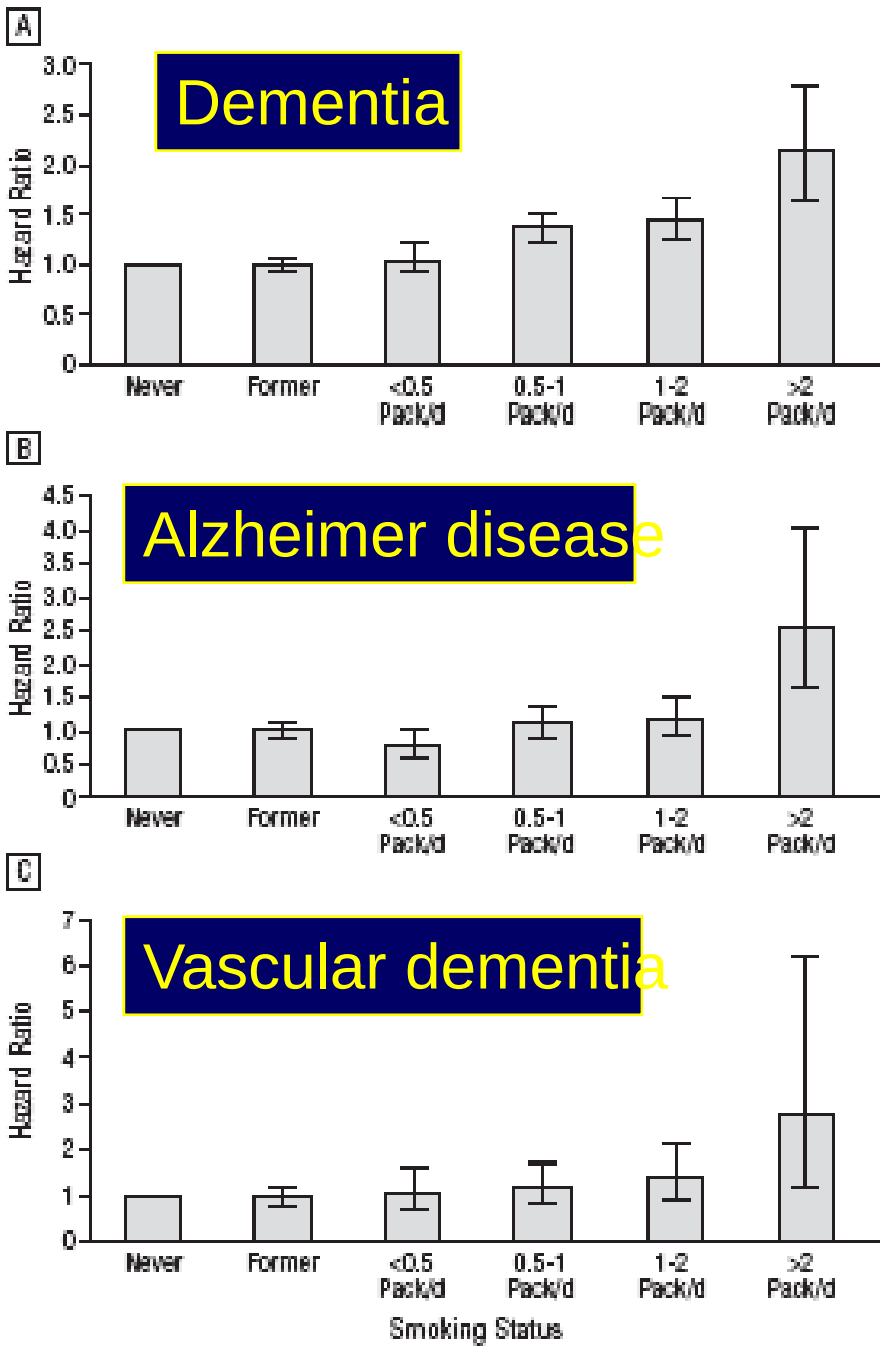
***Johnson KC et al, Tob Control* 2011**

Heavy Smoking in Midlife and Long-term Risk of Alzheimer Disease and Vascular Dementia

Methods: …multiethnic **population-based cohort of 21 123 members** …participated in a survey between 1978 and 1985. Diagnoses of dementia, AD, and VaD made in internal medicine, neurology, and neuropsychology were **collected from January 1, 1994, to July 31, 2008.**

Conclusions: In this large cohort, **heavy smoking in midlife** was associated with a greater than 100% increase in risk of **dementia**, **AD**, and **VaD** more than 2 decades later. These results suggest that the brain is not immune to long-term consequences of heavy smoking.

Rusanen M et al, Arch Intern Med, 2010



The risk of dementia (A), Alzheimer disease (B), and vascular dementia (C) according to **smoking amount (*Packs/day*)** in midlife Values. are hazard ratios from Cox proportional hazards model adjusted for age, sex, education, race, marital status, hypertension, high cholesterol, body mass index, diabetes, heart disease, stroke, and alcohol drinking. Error bars indicate 95% confidence intervals.

Rusanen M et al, Arch Intern Med, 20

Fumo passivo

Involontaria inalazione da parte di un non fumatore del fumo di sigaretta, sigaro o pipa prodotto nelle sue vicinanze

Fumo di tabacco

Inspirato ed espirato dal fumatore

Emesso dalla sigaretta durante la combustione

95% del fumo di tabacco ambientale

Componente diretta

"mainstream smoke"

Componente indiretta

"sidestream smoke"

Maggiore concentrazione di alcuni tossici

(> potere cancerogeno (*IPA, amine*), mutageno e genotossico

(*nitrosamine, nicotina, ammoniaca, monossido di carbonio*)

Fumo passivo ed effetti sulla salute

Il fumo passivo è considerato la *3ª causa prevenibile di malattia, disabilità e morte*

Chi è a rischio?

- **Tutti sono a rischio in quanto non esiste una soglia di esposizione al di sotto della quale il fumo passivo possa essere considerato privo di effetti tossici**
- **Maggior rischio per i conviventi dei fumatori e coloro che lavorano in ambienti dove l'abitudine al fumo è permessa**
- **Maggior suscettibilità per malati cronici (cardiopatici, bronchitici, asmatici) e bambini**

Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries

Mattias Öberg, Maritta S Jaakkola, Alistair Woodward, Armando Peruga, Annette Prüss-Ustün

Oberg M et al, Lancet 2010

Background

We aimed to estimate the worldwide exposure to second-hand smoke and its burden of disease in children and adult non-smokers in 2004

Methods

The burden of disease estimated as **deaths** and **disability-adjusted life-years (DALYs)** for children and adult non-smokers. The calculations were based on disease-specific relative risk estimates and area-specific estimates of the proportion of people exposed to second-hand smoke, by comparative risk assessment methods, with data from **192 countries during 2004**

Worldwide, 40% of children, 33% of male non-smokers, and 35% of female non-smokers were exposed to second-hand smoke in 2004

This exposure caused 603.000 deaths (about 1% of worlwide mortality) from

- 379 000 ischaemic heart disease
- 165 000 lower respiratory infections
- 36 900 asthma
- 21 400 lung cancer

DALYs lost amounted to 10·9 million (about 0·7% of total worldwide burden)

The largest disease burdens were from

- lower respiratory infections in children younger than 5 years (5 939 000)
- ischaemic heart disease in adults (2 836 000)
- asthma in adults (1 246 000) and children (651 000)

Oberg M et al, Lancet 2010

Fumo passivo ed effetti sulla salute

Effetti acuti

- Fastidio/disturbo ("annoyance")
- Irritazione nasale ed oculare, raucedine
- Tosse, dispnea e sibili
- Disturbi gastrici
- Vertigini, cefalea

Reardon JZ, Clin Chest Med, 2007

Fumo passivo ed effetti sulla salute

Effetti cronici

Adulti:

- ridotta funzione polmonare
- tumore polmonare, tumore del colon, tumore della vescica
- malattie cardiovascolari

Bambini:

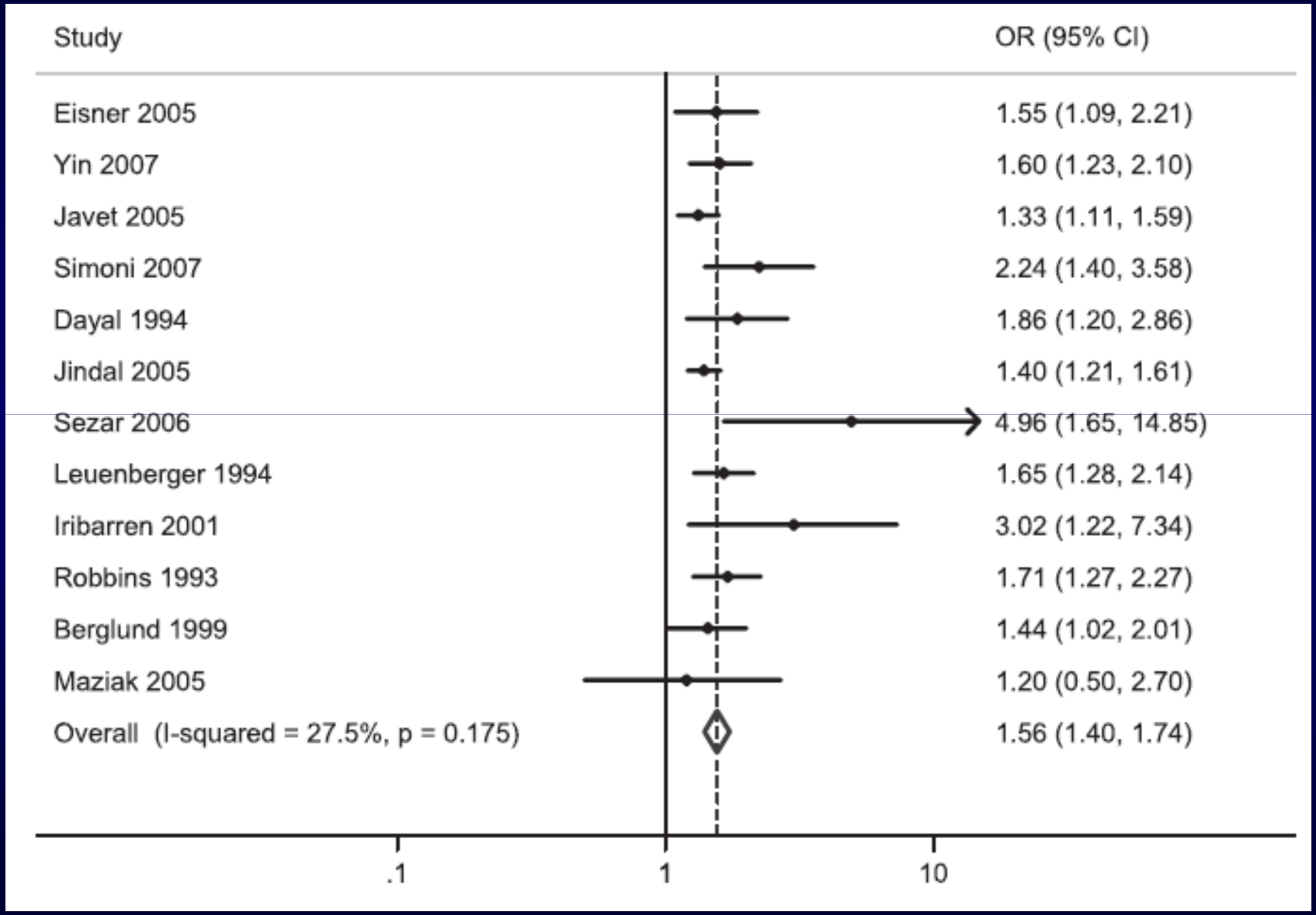
- infezioni respiratorie (tracheo-bronchiti, polmoniti)
- asma bronchiale, otite media

Feti e neonati:

- ritardo nello sviluppo, basso peso alla nascita, parto pretermine, aborto spontaneo
- morte improvvisa neonatale

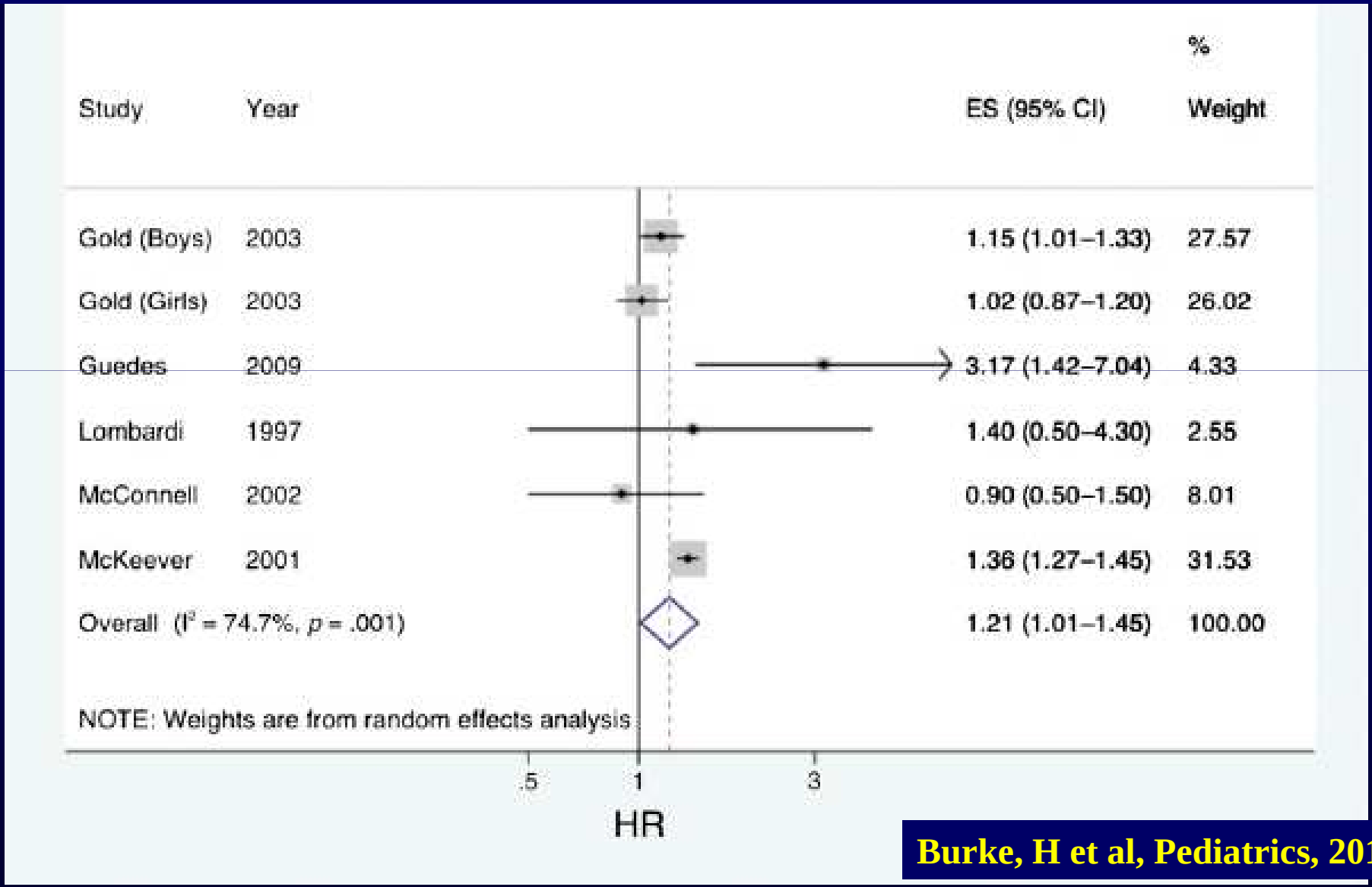
Reardon JZ, Clin Chest Med, 2007

Secondhand smoke (SHS) and the risk of COPD. **Forest plot shows studies of SHS exposure and the risk of chronic obstructive pulmonary disease. Summary odds ratio was derived from meta-analysis with random effects model. CI: confidence interval; OR: odds ratio**



Eisner MD et al, Am J Respir Crit Care Med , 2010

Exposure to postnatal maternal smoking and incidence of asthma



Burke, H et al, Pediatrics, 2012

Fumo passivo e tumore polmonare

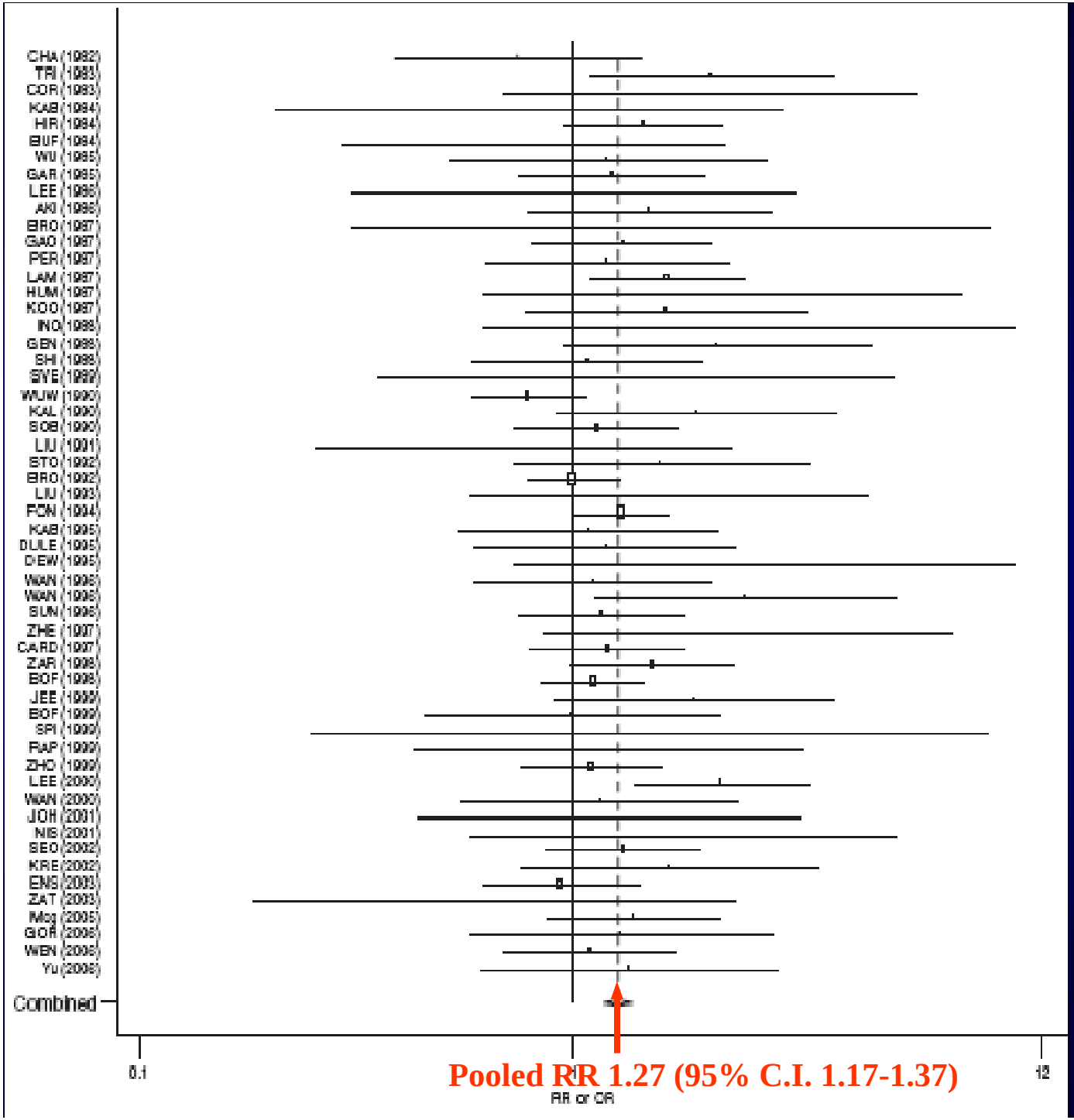
1981: primi rapporti scientifici (Hirayama)

1986: IARC, National Research Council e Surgeon General classificano il fumo passivo come cancerogeno umano

1992: EPA (Environmental Protecion Agency) classifica il fumo passivo come cancerogeno di classe A

1997: eccesso di rischio per tumore polmonare in non fumatori conviventi con fumatori è pari a 24% (Hackshaw et al.)

2000: eccesso di rischio ridimensionato al 15% (Copas et al.)



Forest plot of odds ratios and relative risks of lung cancer (and 95% CI) from 55 studies (7 cohort, 48 case-control) of never smoking women exposed to smoking spouses, 1981–2006

Taylor R et al, Int J Epidemiol, 2007

Bladder cancer

relative risk according to secondhand exposure to household cigarette smoke among women who were never active smokers, Washington County, Maryland, 1963-1978 and 1975-1994

SHS* Exposure	1963 Cohort				1975 Cohort			
	No. of cases	Person years	RR‡	95% CL	No. of cases	Person years	RR‡	95% CL
Current SHS exposure versus noncurrent SHS exposure								
No current SHS exposure§	10	97,221	1.0		24	162,130	1.0	
Current SHS exposure	13	73,506	2.3	1.0, 5.4	6	61,194	0.9	0.4, 2.3
Current and former SHS expsure versus never SHS exposure								
Never SHS exposure§	9	66,576	1.0		17	107,375	1.0	
Former SHS exposure	1	30,645	0.3	0.1, 2.5	7	54,756	0.8	0.3, 2.0
Current SHS exposure	13	73,506	1.8	0.8, 4.5	6	61,194	0.9	0.3, 2.2
Source of SHS exposure								
Spouse only	5	45,318	1.1	0.3, 3.8	5	40,369	1.2	0.4, 36
Other household member only	8	19,682	3.0	1.2, 7.9	1	15,603	0.4	0.1, 3.3

*SHS, secondhand smoke; RR, relative risk; CL, confidence limits.

‡Adjusted for age, education, and marital status.

§Referent category

Alberg A.J. et al. - Am J Epidemiol 2007

Rectal cancer

incidence rates and age-adjusted and multivariate-adjusted relative risks (and 95% confidence intervals) for men and women according to household passive smoke exposure (Washington County, Maryland Cohorts, 1963-1978 and 1975-1994)

	1963 Cohort			1975 Cohort		
	No. of cases	Incidence rate/10,000	Relative risk‡ (C.I.)	No. of cases	Incidence rate/10,000	Relative risk ‡ (C.I.)
Men						
Never smoker	5	1.35	1.00	11	1.81	1.00
Passive smoker	7	6.60	5.81 (1.84-18.36)	2	1.67	1.10 (0.24-4.97)
Women						
Never smoker	35	3.60	1.00	41	2.53	1.00
Passive smoker	21	2.86	1.03 (0.58-1.81)	13	2.12	1.04 (0.54-1.98)

‡Poisson regression model adjusted for age (continuous), education (<12 yr/≥ 12 yr) and marital status (married, divorced/separated, widowed, single).

Hooker C.M. et al. – Ann Epidemiol 2008

Fumo passivo e cardiopatie

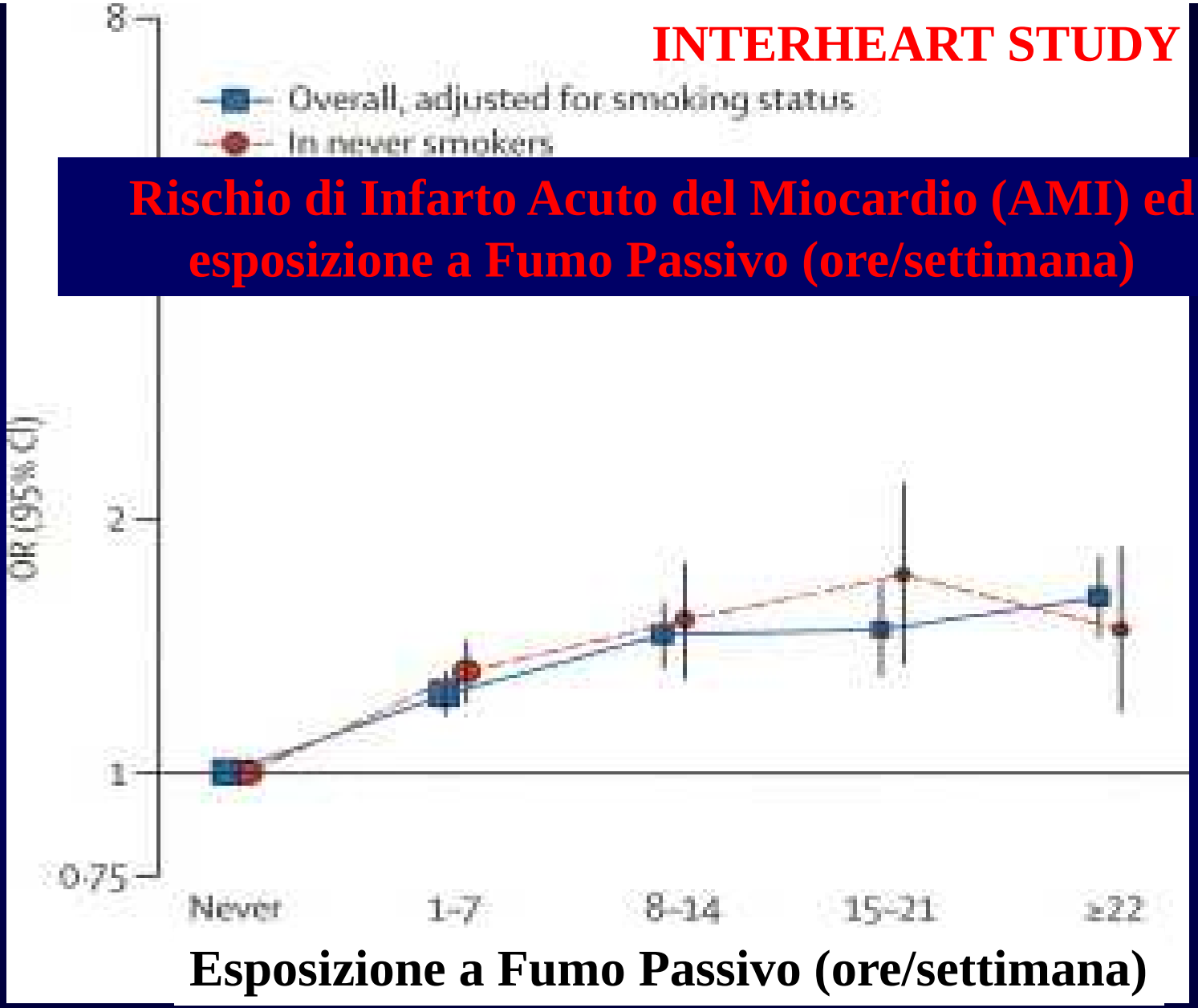
Rischio di coronaropatia:

- **aumentato del 25-30%** (EPA, 1997)
- **relazione dose-effetto con il numero di sigarette/die fumate dal coniuge e durata dell'esposizione** (He, 1999)
- **aumentato del 25-35% per eventi acuti** (Jousilahti, 2002)

Reardon JZ, Clin Chest Med, 2007

INTERHEART STUDY

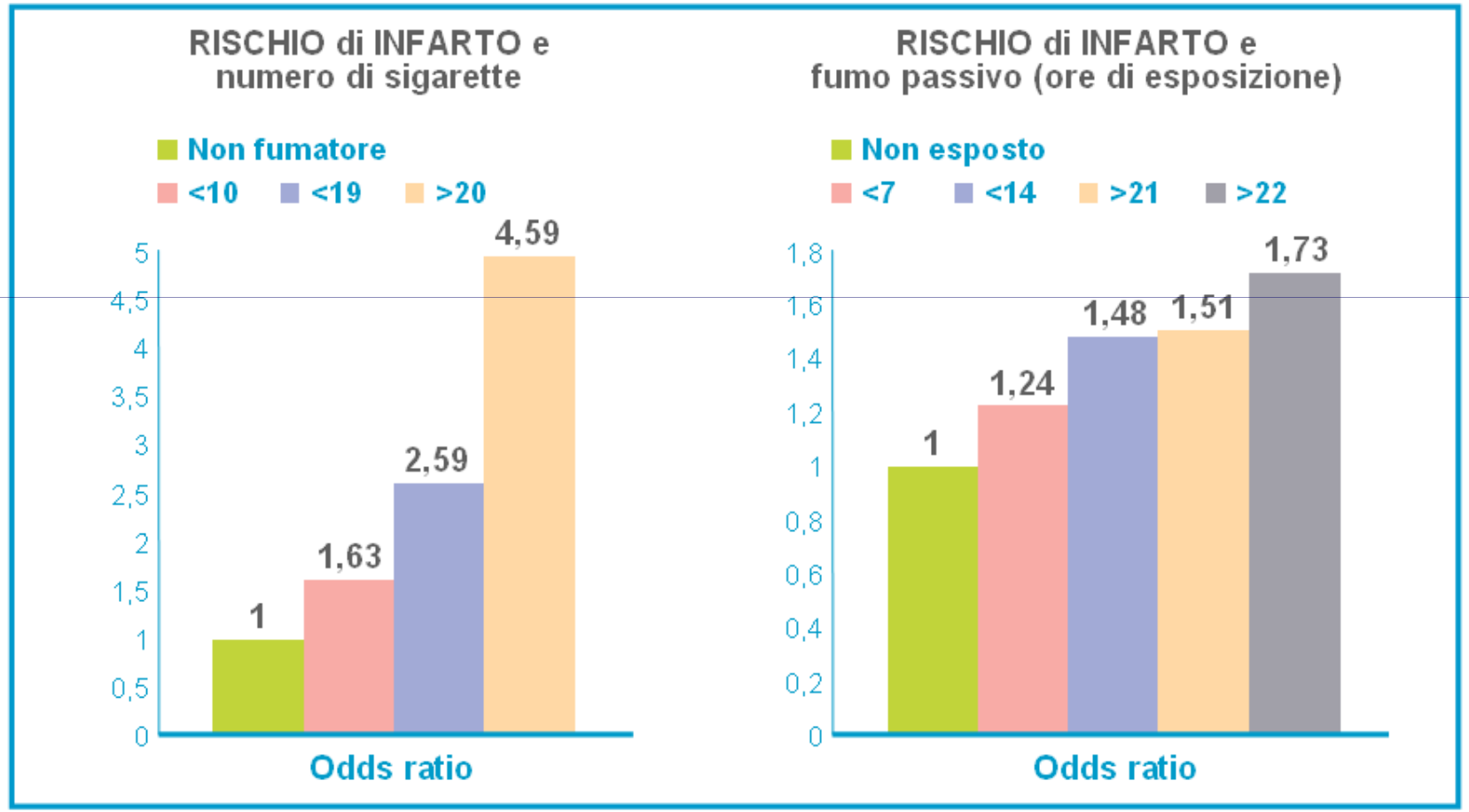
Rischio di Infarto Acuto del Miocardio (AMI) ed esposizione a Fumo Passivo (ore/settimana)



Adjusted for smoking status in all individuals and in never smokers. Graded increase in risk occurs with increasing exposure

Teo KK et al, Lancet, 2006

Lo studio INTERHEART



Teo KK, et al. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *Lancet*. 2006; 368:647-58.

Odds ratios of STROKE for women non-smokers, 1997-2000

Husbands' smoking	Cases	Age-adj OR	Multivar OR*
Never smoked (ref.) (N=22983)	213	1.00	1.00
Formerly smoke (N= 5108)	74	1.03 (0.79-1.35)	0.94 (0.71-1.24)
Currently smoke (N= 32287)	239	1.47(1.22-1.78)	1.41(1.16-1.72)

*Adjusted for age, education, occupation, income, alcohol, exercise, BMI, menopausal, hormone therapy, contraceptive, hypertension, diabetes, antihypert. med., aspirin

Zhang x, et al., Am J Epidemiol, 2005

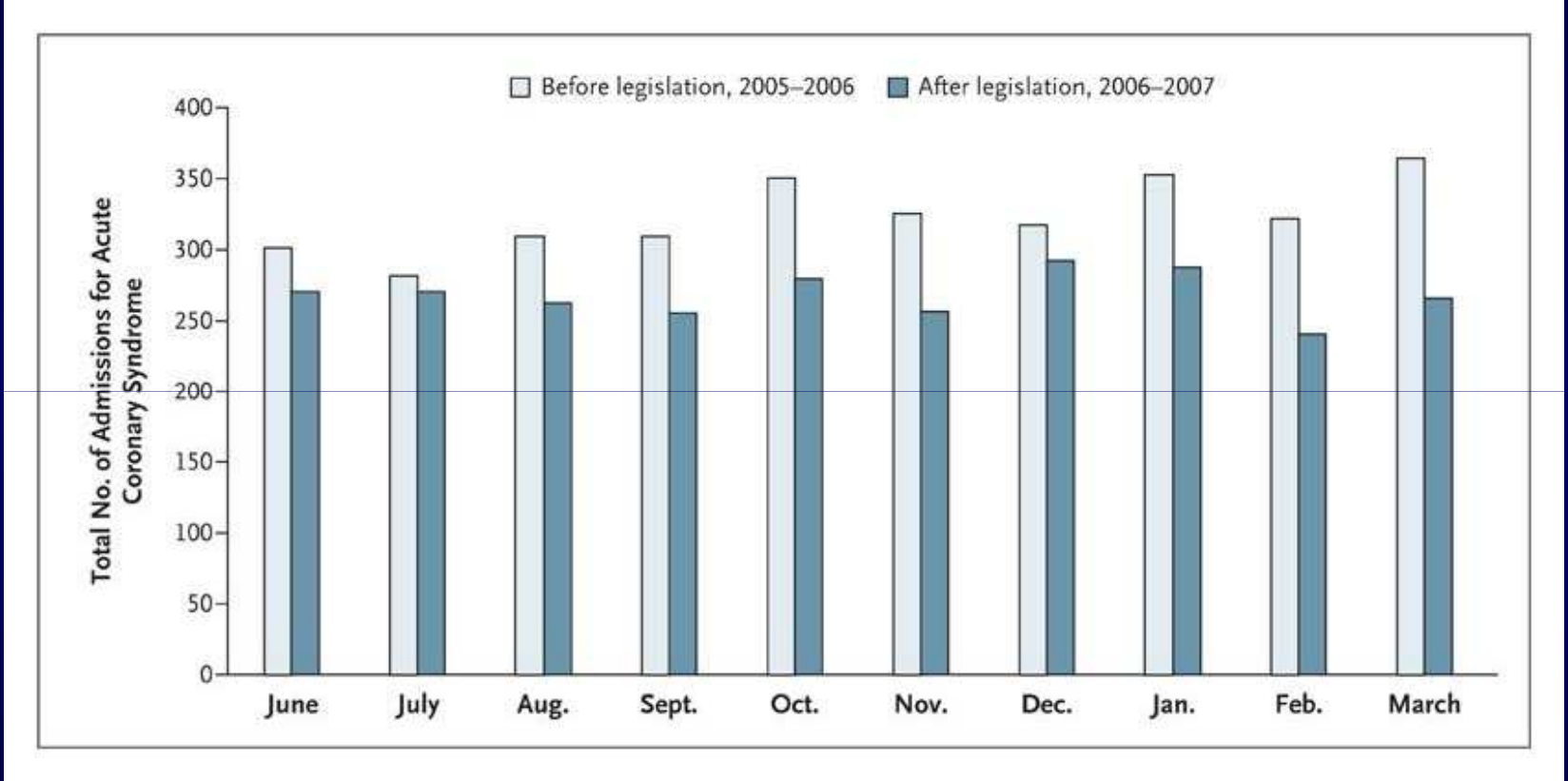
Odds ratios of STROKE for women non-smokers, 1997-2000

Husbands' smoking	Cases	Age-adj OR	Multivar OR*
Never smoked (ref.)	213	1.00	1.00
No of cigarettes/day			
1-9	46	1.30 (0.95, 1.79)	1.28 (0.92,1.77)
10-19	77	1.36 (1.05, 1.76)	1.32 (1.01,1.72)
>20	116	1.62 (1.30, 2.02)	1.62 (1.28,2.05)
P for trend		< 0.0001	< 0.0002
Duration of smoking (ys)			
< 17	25	1.18 (0.74, 1.88)	1.13 (0.70,1.82)
> 17	214	1.49 (1.25, 1.79)	1.47 (1.22,1.78)
P for trend		< 0.0001	< 0.0004

* Adjusted for age, education, occupation, income, alcohol, exercise, BMI, menopausal, hormone therapy, contraceptive, hypertension, diabetes, antihypert. med., aspirin

Zhang x. et al., Am J Epidemiol. 2005

Admissions for Acute Coronary Syndrome According to Month before and after Smoke-free Legislation (Scotland, 2006)



Pell JP et al. N Engl J Med 2008; 359:482-491

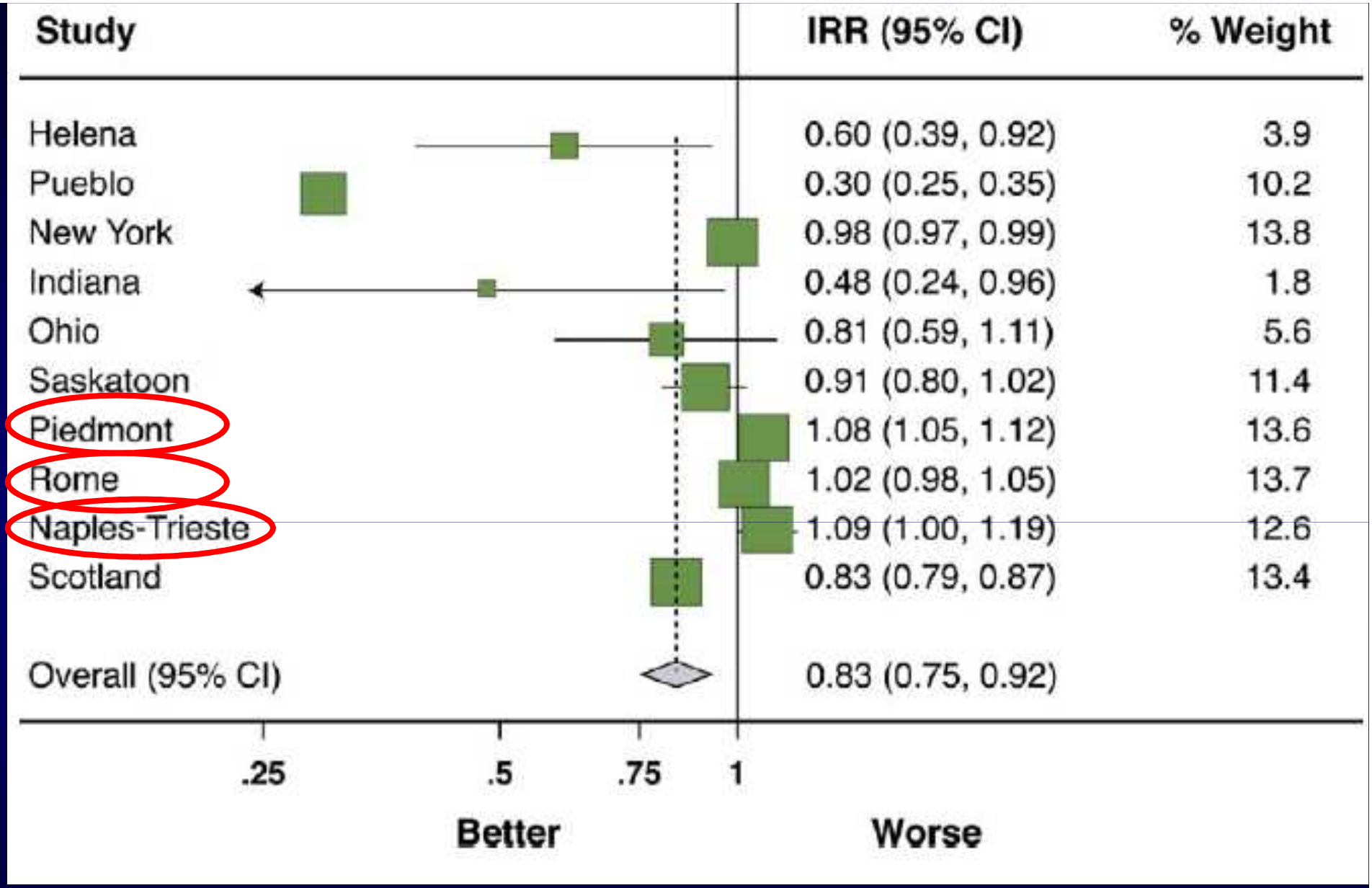
Cardiovascular Effect of Bans on Smoking in Public Places

Systematic review and Meta-analysis to determine the association between public smoking bans and risk for hospital admission for acute myocardial infarction (AMI)

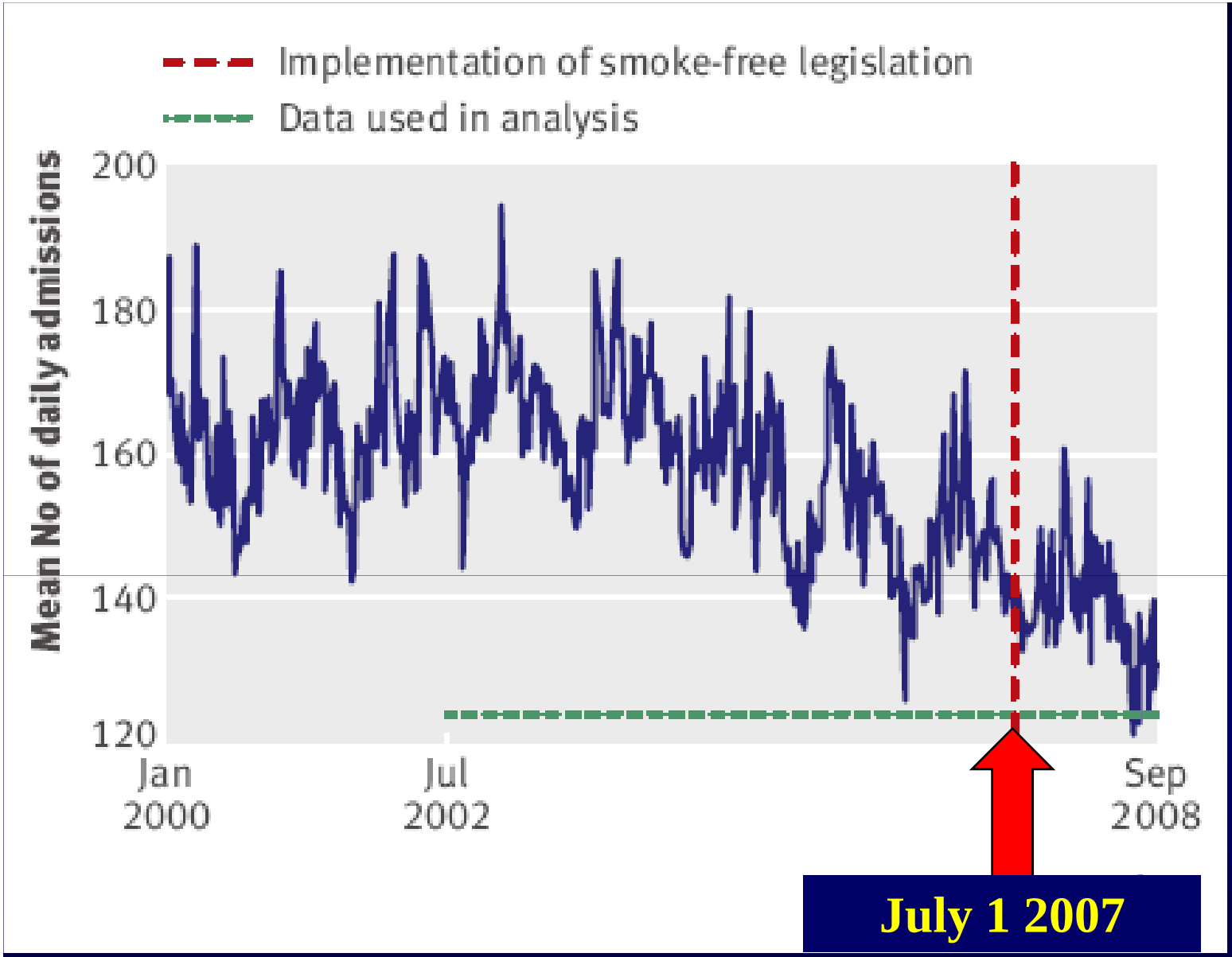
11 reports from 10 study locations; AMI risk decreased by 17% overall (IRR: 0.83, 95% CI: 0.75 to 0.92); greatest effect among younger individuals and nonsmokers. The incidence rate ratios (IRRs) incrementally decreased 26% for each year of observation after ban implementation

Smoking bans in public places and workplaces are significantly associated with a reduction in AMI incidence, particularly if enforced over several years

Meyers DG, et al (J Am Coll Cardiol 2009;54:1249–55)



Meyers DG, et al (J Am Coll Cardiol 2009;54:1249–55)



England: Trends in overall weekly number of emergency admissions for myocardial infarction (average daily count) from January 2000 to September 2008.

Sims M, et al BMJ 2010

Exposure to secondhand smoke and cognitive impairment in non-smokers: national cross sectional study with cotinine measurement

Objective: To examine the association between a biomarker of exposure to secondhand smoke (salivary cotinine concentration) and cognitive impairment.

Participants: 4809 non-smoking adults aged 50 years or more from the 1998, 1999, and 2001 waves of the Health Survey for England

Main outcome measure: **Cognitive impairment** as defined by the lowest 10% of scores on a battery of neuropsychological tests (attenzione, velocità di analisi, orientamento nel tempo, memoria verbale immediata e tardiva, memoria prospettica, capacità di calcolo, fluidità del linguaggio)

Lleewllyn JD et al, BMJ 2009;338:b462

Benefici nel tempo dopo la cessazione del fumo

Ore:	**Livelli di CO come non fumatori**
Giorni:	**Migliorano il gusto e l'olfatto**
1-2 mesi:	**Migliorano sintomi di BPCO (tosse, espettorato, resp. sibilante)**
1 anno:	**BPCO lieve-moderata: miglioramento PF Respiratoria**
2-4 anni:	**Non CHD: riduzione rischio Vs fumatori** **CHD: riduzione 35% rischio di re-infarto o morte**
5 anni:	**Declino funzione respiratoria vicina ai non fumatori**
	Cancro cervice uterina come non fumatori
5-9 anni:	**Evidenza riduzione rischio di Cr polmone rispetto ai persistenti**
10-15 anni:	**Riduzione rischio Cr laringe del 60% rispetto a persistenti**
	Rischio CHD come non fumatori (dati non univoci)
10-19 anni:	**Rischio Cr polmone inferiore di oltre il 70% Vs persistenti**
20 anni:	**Rischio Cr orofaringe come non fumatori**

IARC 2007

Conclusioni

- Il **fumo di tabacco** è causa certa di riduzione dell'aspettativa di vita, di aumento della mortalità e del rischio per malattie croniche
- Il **fumo passivo** è ritenuto causa certa della maggior parte delle stesse malattie
- La **nicotina** è confermata **agente causale** di malattie cardiovascolari oltre che di dubbi effetti positivi
- **L'abolizione del fumo** è l'unico rimedio di dimostrata efficacia