GLI STUDI EPIDEMIOLOGICI ANALITICI

GLI STUDI DI COORTE

CLASSIFICAZIONE DEGLI STUDI EPIDEMIOLOGICI

STUDI OSSERVAZIONALI

- DESCRITTIVI
- TRASVERSALI
- CASO-CONTROLLO
- A COORTE

STUDI SPERIMENTALI

- SPERIMENTAZIONI CLINICHE
- SPERIMENTAZIONI SUL CAMPO
- SPERIMENTAZIONI SU COMUNITA'

STUDI OSSERVAZIONALI ANALITICI

- **Uno studio descrittivo può consentire di formulare delle ipotesi sulla possibile associazione tra un fattore ambientale e una determinata patologia, ma non consente di stabilire in via definitiva se l'associazione è causale o spuria.**

- **L'epidemiologia analitica o eziologica costituisce lo strumento indispensabile ad approfondire lo studio dei fenomeni indagati dalla epidemiologia descrittiva.**

STUDI OSSERVAZIONALI
ANALITICI

- **Gli studi analitici, o etiologici, si propongono di investigare le cause dei fenomeni morbosi.**
- **Vi è un'*associazione* di *causa-effetto* quando è possibile dimostrare che la presenza di un fattore, da solo od insieme ad altri, aumenta, o riduce, la probabilità di sviluppare la malattia.**
- **Fattore di rischio/protettivo: fattore che aumenta/ diminuisce la probabilità di ammalarsi ma che non è indispensabile per sviluppare la malattia.**

STUDI OSSERVAZIONALI
ANALITICI

Tipi di indagine epidemiologica analitica:

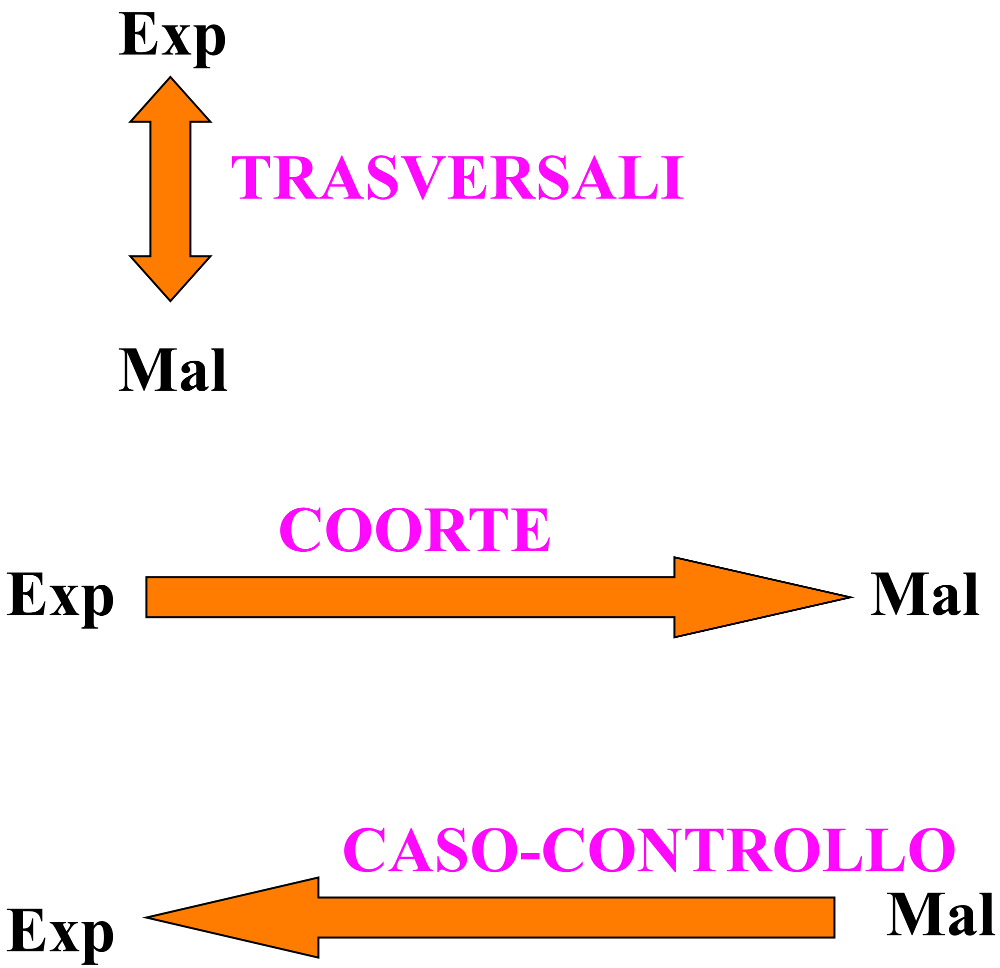
- **studio trasversale o di prevalenza**
- **studio di coorte**
- **studio caso-controllo**

STUDI EPIDEMIOLOGICI DI COORTE

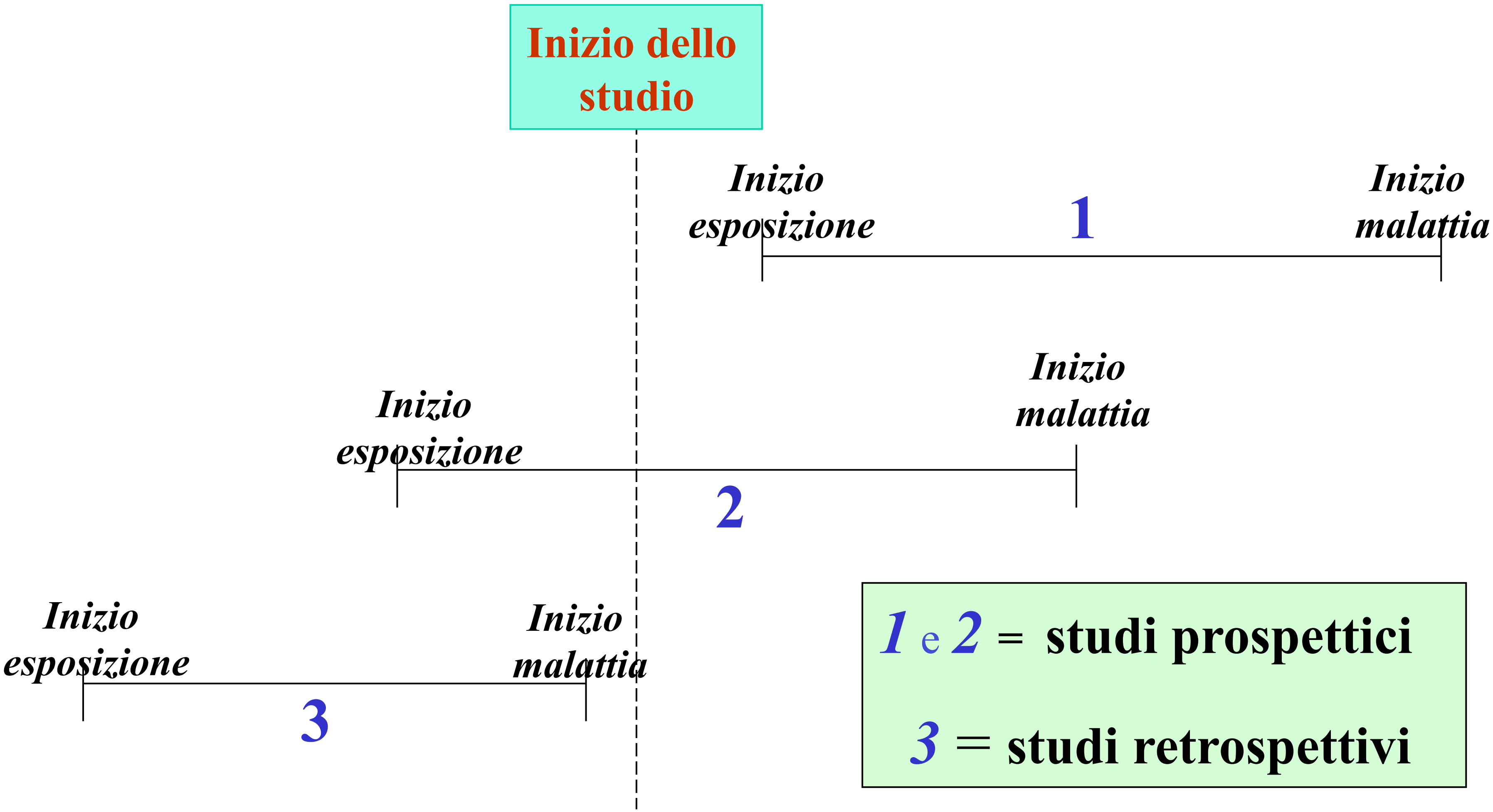
Il disegno di uno studio di coorte prevede che uno o più gruppi di soggetti, esposti e non esposti ai fattori di rischio vengano seguiti nel tempo per valutare l'incidenza di un fenomeno o di una malattia.

DISEGNO DI UNO STUDIO DI COORTE

Direzionalità dei tre più importanti studi osservazionali



TIPI DI STUDI EPIDEMIOLOGICI IN RELAZIONE ALLA CRONOLOGIA DELL'OSSERVAZIONE



1 e 2 = studi prospettici

3 = studi retrospettivi

UN ESEMPIO DI STUDIO DI COORTE: LO STUDIO DI TAIWAN SULL'ASSOCIAZIONE TRA INFEZIONE HBV CRONICA E HCC (Beasley et al., 1988)

22707 soggetti

3454 HBsAg+

19253 HBsAg-

8,9 anni

3302 non HCC

152 HCC

9 HCC

19244 non HCC

$$\text{Rischio relativo (RR)} = \frac{152 \,/\, 3\,454 = 44/\,1\,000}{9 \,/\, 19\,253 = 0{,}47 \,/\, 1\,000} = 93{,}6$$

UN ESEMPIO DI STUDIO DI COORTE
LO STUDIO DI TAIWAN SULL'ASSOCIAZIONE TRA INFEZIONE HBV CRONICA E HCC (Beasley et al., 1988)

22707 soggetti

3454 HBsAg+ | **19253 HBsAg-**

8,9 anni

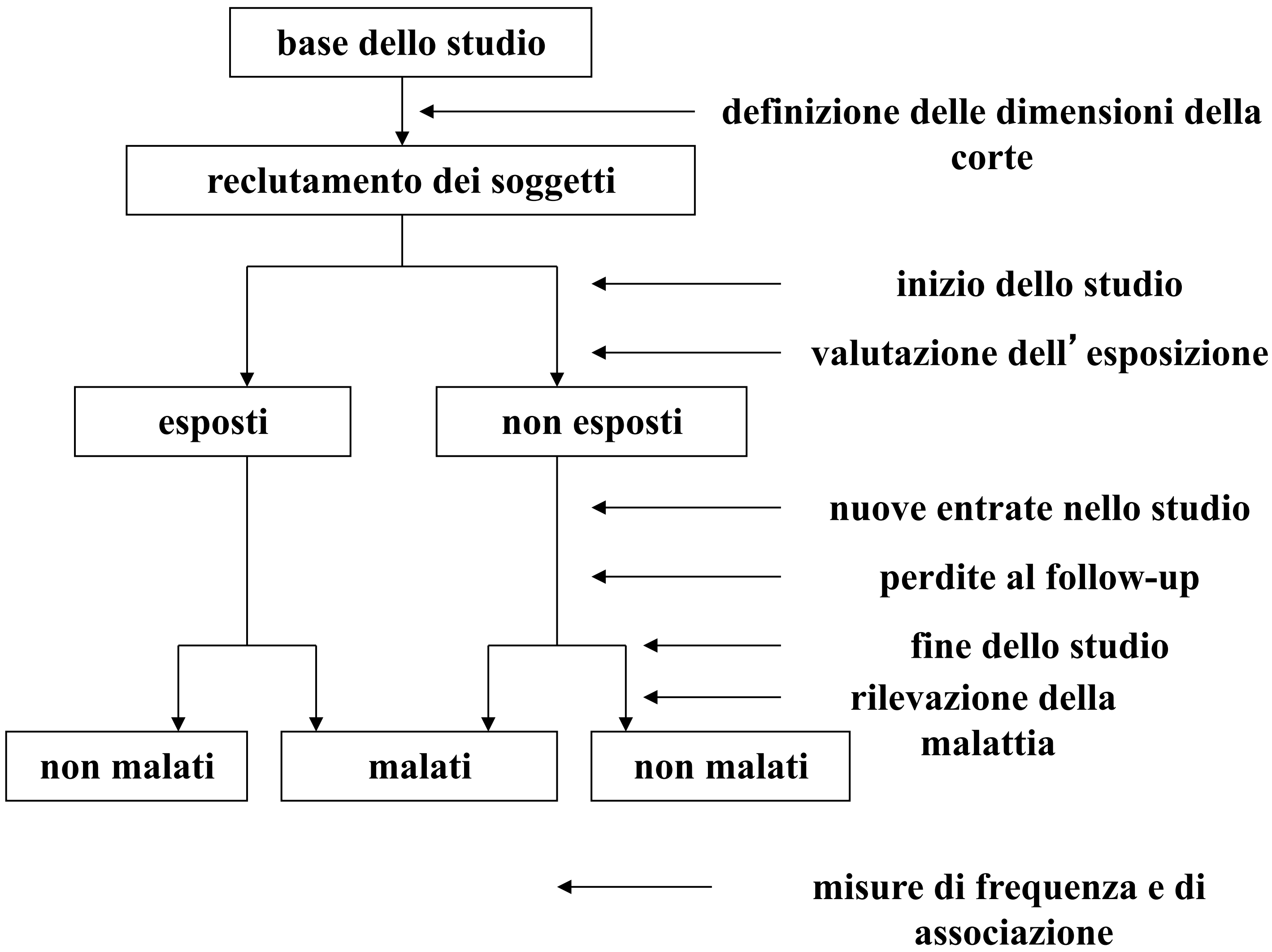
3302 non HCC | **152 HCC** | **9 HCC** | **19244 non HCC**

152 / (30 738 a.p.) = 494,5/ 100 000

Rischio relativo (RR) = -- = 98,4

9 / (169 811 a.p.) = 5,3 / 100 000

DISEGNO DI UNO STUDIO DI COORTE



FUMO DI TABACCO E MALATTIE CRONICO-DEGENERATIVE: LO STUDIO DEI MEDICI INGLESI

(R. Doll e R. Peto)

- **Nel 1951 sono stati arruolati 59.600 medici inglesi che hanno inviato un questionario sulle abitudini fumatorie (risposta: 69%).**
- **Sono stati considerati i soli medici maschi, poiché le donne erano poco numerose e tra di esse poche fumavano.**
- **I questionari sono stati ri-somministrati nel 1966 e 1972.**
- **Gli eventi considerati erano: il decesso e la causa di morte, rilevati mediante la raccolta delle schede di morte a livello nazionale.**
- **Il follow-up è stato aggiornato a 50 anni dall'inizio dello studio.**

BMJ

Mortality in relation to smoking: 50 years' observations on male British doctors

Richard Doll, Richard Peto, Jillian Boreham and Isabelle Sutherland

BMJ 2004;328;1519-; originally published online 22 Jun 2004;
doi:10.1136/bmj.38142.554479.AE

Abstract

Objective To compare the hazards of cigarette smoking in men who formed their habits at different periods, and the extent of the reduction in risk when cigarette smoking is stopped at different ages.
Design Prospective study that has continued from 1951 to 2001.
Setting United Kingdom.
Participants 34 439 male British doctors. Information about their smoking habits was obtained in 1951, and periodically thereafter; cause specific mortality was monitored for 50 years.
Main outcome measures Overall mortality by smoking habit, considering separately men born in different periods.

Results The excess mortality associated with smoking chiefly involved vascular, neoplastic, and respiratory diseases that can be caused by smoking. Men born in 1900-1930 who smoked only cigarettes and continued smoking died on average about 10 years younger than lifelong non-smokers. Cessation at age 60, 50, 40, or 30 years gained, respectively, about 3, 6, 9, or 10 years of life expectancy. The excess mortality associated with cigarette smoking was less for men born in the 19th century and was greatest for men born in the 1920s. The cigarette smoker versus non-smoker probabilities of dying in middle age (35-69) were 42% *v* 24% (a twofold death rate ratio) for those born in 1900-1909, but were 43% *v* 15% (a threefold death rate ratio) for those born in the 1920s. At older ages, the cigarette smoker versus non-smoker probabilities of surviving from age 70 to 90 were 10% *v* 12% at the death rates of the 1950s (that is, among men born around the 1870s) but were 7% *v* 33% (again a threefold death rate ratio) at the death rates of the 1990s (that is, among men born around the 1910s).

Conclusion A substantial progressive decrease in the mortality rates among non-smokers over the past half century (due to prevention and improved treatment of disease) has been wholly outweighed, among cigarette smokers, by a progressive increase in the smoker *v* non-smoker death rate ratio due to earlier and more intensive use of cigarettes. Among the men born around 1920, prolonged cigarette smoking from early adult life tripled age specific mortality rates, but cessation at age 50 halved the hazard, and cessation at age 30 avoided almost all of it.

Table 1 Cause specific mortality by smoking habit, standardised indirectly for age and study year, for all 34 439 men born in 19th or 20th century (1851-1930) and observed 1951-2001

		Age standardised mortality rate per 1000 men/year								Standardised tests for trend (χ^2 on 1 df)*	
			Cigarette smokers (no other smoking habit previously reported)								
					Current (cigarettes/day)			Other smokers			
Cause of death	No of deaths 1951-2001	Lifelong non-smokers	Former	Current	1-14	15-24	≥25	Former	Current	N/X/C†	Amount†
Cancer of lung	1052	0.17	0.68	2.49	1.31	2.33	4.17	0.71	1.30	394	452
Cancers of mouth, pharynx, larynx, oesophagus	340	0.09	0.26	0.60	0.36	0.47	1.06	0.30	0.47	68	83
All other neoplasms	3893	3.34	3.72	4.69	4.21	4.67	5.38	3.66	4.22	32	36
Chronic obstructive pulmonary disease	640	0.11	0.64	1.56	1.04	1.41	2.61	0.45	0.64	212	258
Other respiratory disease	1701	1.27	1.70	2.39	1.76	2.65	3.11	1.69	1.67	44	70
Ischaemic heart disease	7628	6.19	7.61	10.01	9.10	10.07	11.11	7.24	7.39	138	133
Cerebrovascular disease	3307	2.75	3.18	4.32	3.76	4.35	5.23	3.24	3.28	48	65
Other vascular (including respiratory heart) disease	3052	2.28	2.83	4.15	3.37	4.40	5.33	2.99	3.08	77	94
Other medical conditions	2565	2.26	2.47	3.49	2.94	3.33	4.60	2.49	2.44	34	54
External causes	891	0.71	0.75	1.13	1.08	0.79	1.76	0.89	0.92	17	27
Cause unknown	277	0.17	0.28	0.52	0.39	0.57	0.59	0.25	0.31	16	24
All cause (No of deaths)	25 346	19.38 (2917)	24.15 (5354)	35.40 (4680)	29.34 (1450)	34.79 (1725)	45.34 (1505)	23.96 (5713)	25.70 (6682)	699	869

*Values of χ^2 on one degree of freedom for trend between three or four groups: values ≥15 correspond to $P<0.0001$.

†N/X/C compares three groups: lifelong non-smokers, former cigarette smokers, and current cigarette smokers. Amount compares four groups: never smoked regularly, and current cigarette smokers consuming 1-14, 15-24 or ≥25 cigarettes/day when last asked.

LO STUDIO DEI MEDICI INGLESI:
risultati a 50 anni di follow-up *(Doll et al, 2004)*

Cause di morte	Misura	Non fum.	Ex fum.	Fum.	Fum. 1-14 sig/die	Fum. 15-24 sig/die	Fum. 25 + sig/die
Tumori del polmone	Tassi per 100.000	17	68	249	31	233	417
	Rischi relativi	1 (Rif.)	4	14,6	7,7	13,7	24,5
Mal. Resp. croniche	Tassi per 100.000	11	64	156	104	141	261
	Rischi relativi	1 (Rif.)	5,8	14,2	9,5	12,8	23,7
Mal. Cardio-vasc. ischemiche	Tassi per 100.000	619	761	1001	910	1007	1111
	Rischi relativi	1 (Rif.)	1,2	1,6	1,5	1,6	1,8
Tutte le cause	Tassi per 100.000	1938	2415	3540	2934	3479	4534
	Rischi relativi	1 (Rif.)	1,2	1,8	1,5	1,8	2,3

Table 2 Characteristics in 1978 of smokers, ex-smokers, and smokers born in 20th century (aged 48-78 at 1978 survey). Means and prevalences are standardised to age distribution of all 12 669 respondents to 1978 questionnaire

	Current smoker (n=3866)	Ex-smoker for <10 years (n=1787)	Ex-smoker for ≥10 years (n=4074)	Never smoker (n=2942)
Means of some vascular risk factors				
Alcohol consumption (units/week)	19.0	18.1	14.8	8.3
Body mass index*	24.5	24.7	24.3	24.1
Blood pressure, systolic (mm Hg)	136.9	137.6	137.2	135.6
Blood pressure diastolic (mm Hg)	83.1	84.3	83.5	83.1
Prevalences (%) of various replies				
Quit for vascular disease	NA	12.2	3.9	NA
Quit for respiratory disease	NA	14.0	8.3	NA
Any vascular disease	18.6	29.2	20.8	15.7
Short of breath hurrying†	17.2	20.2	13.8	9.1
Phlegm in winter†	25.5	12.4	8.6	5.5

NA=not applicable.

*Body mass index=weight (kg)/(height(m)^2).

†Are you short of breath when hurrying; and, do you usually bring up phlegm from your chest during the winter?

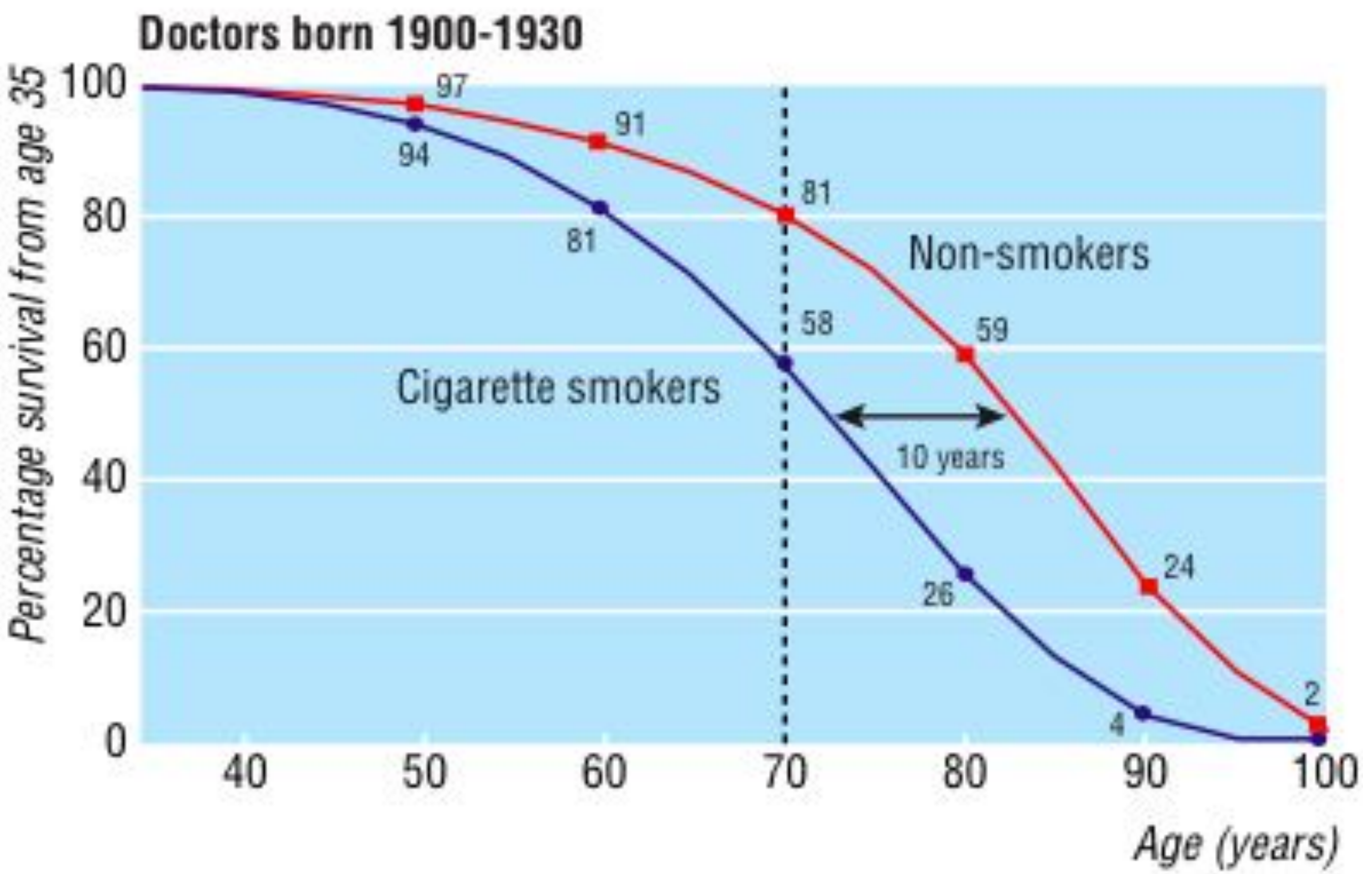


Fig 3 Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1930, with percentages alive at each decade of age

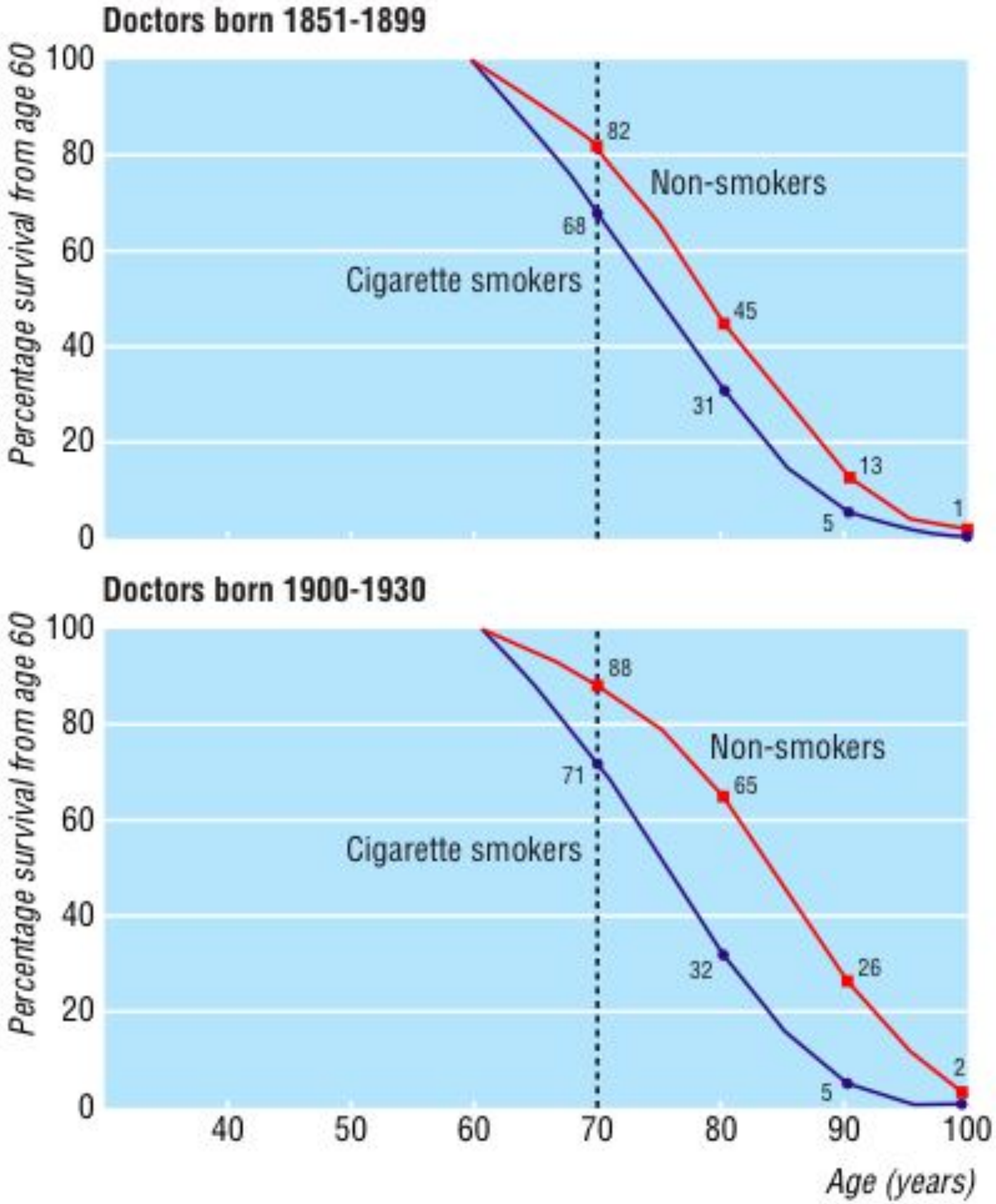


Fig 1 Survival from age 60 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1851-1899 (median 1889) and 1900-1930 (median 1915), with percentages alive at each decade of age

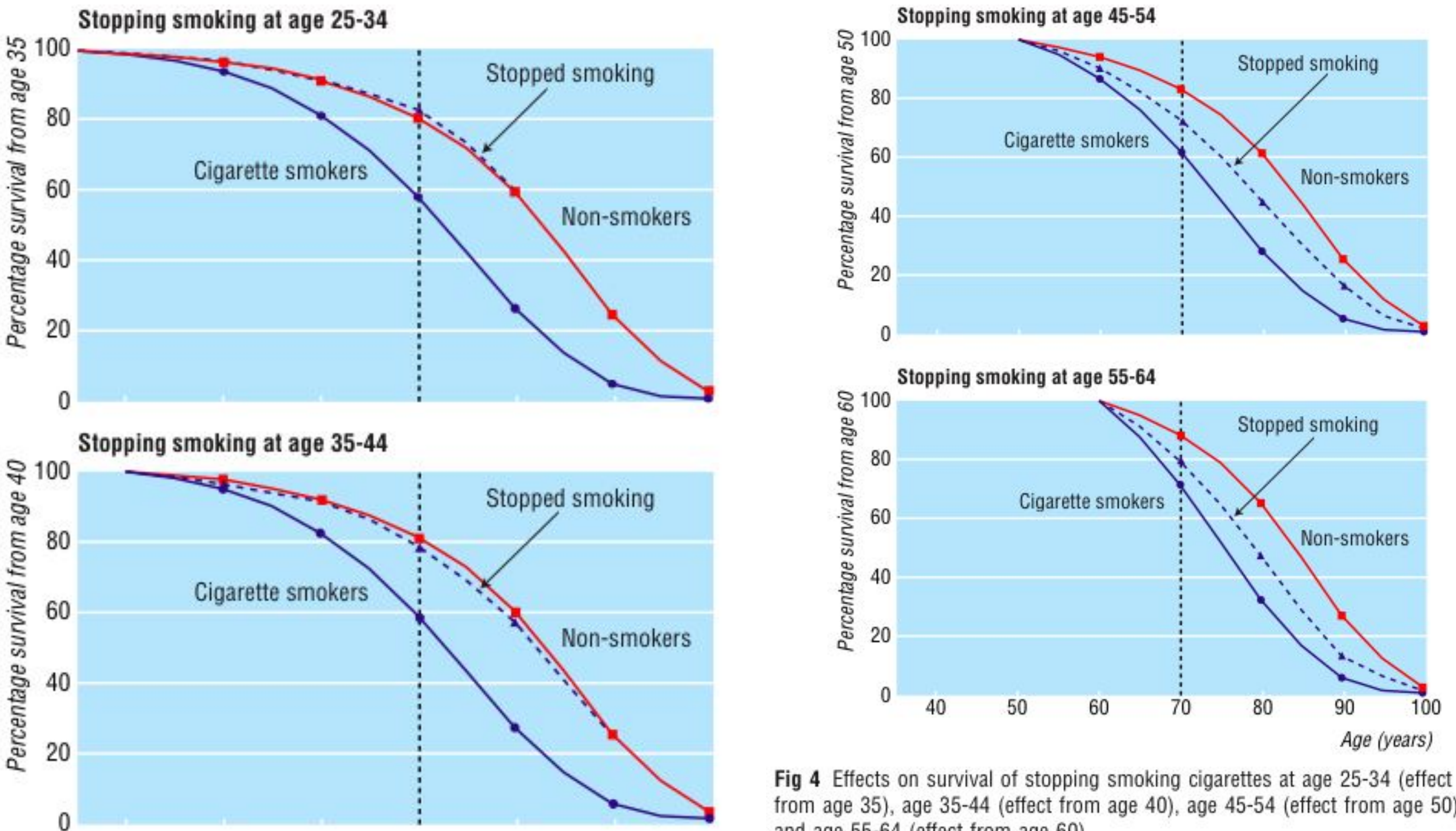
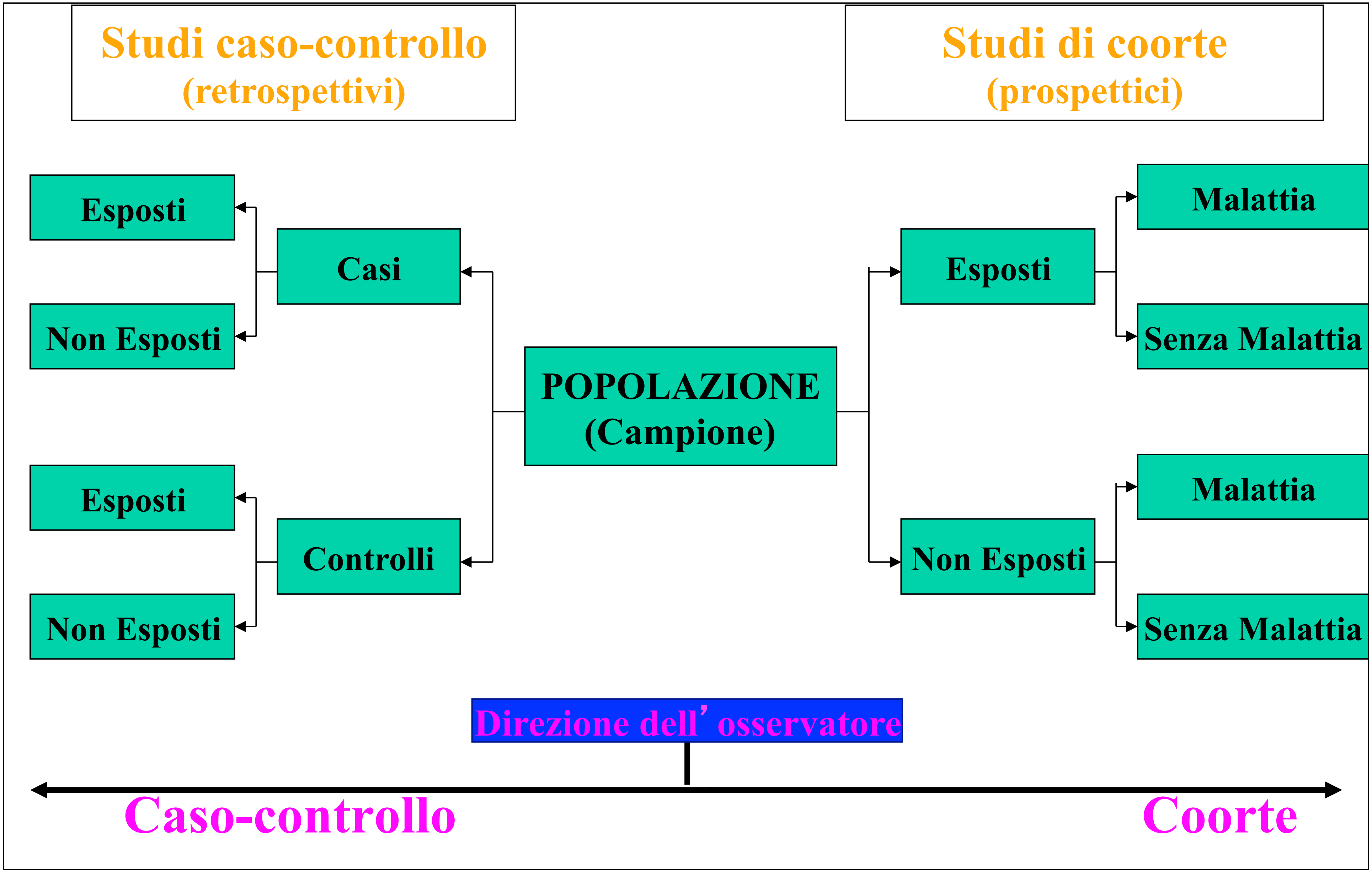


Fig 4 Effects on survival of stopping smoking cigarettes at age 25-34 (effect from age 35), age 35-44 (effect from age 40), age 45-54 (effect from age 50), and age 55-64 (effect from age 60)

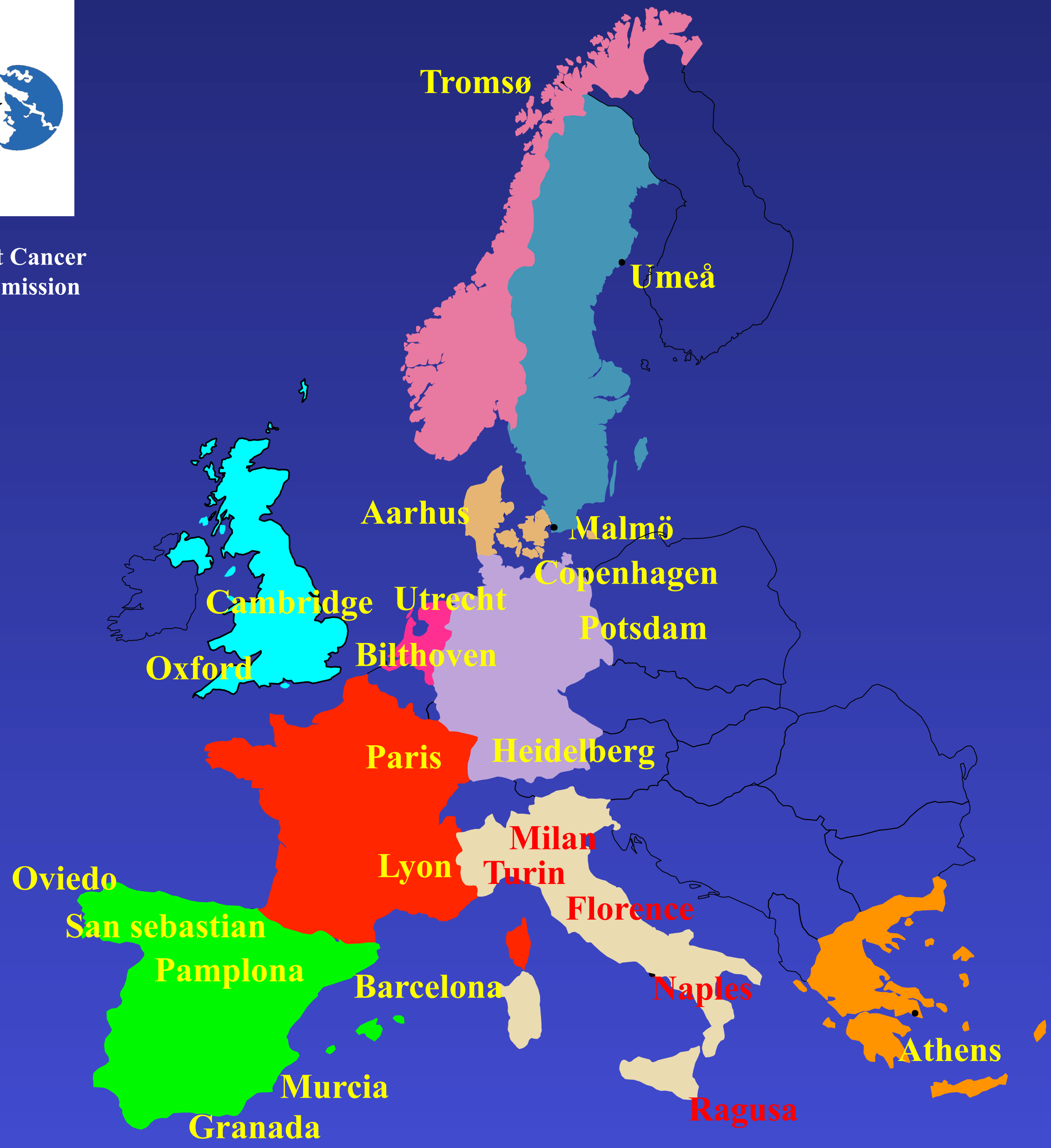
STUDI ANALITICI



I.A.R.C
W.H.O

Europe Against Cancer
European Commission

European Prospective Investigation into Nutrition and Cancer (EPIC)



Lancet 2003; **361:** 1496–501

Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study

Sheila A Bingham, Nicholas E Day, Robert Luben, Pietro Ferrari, Nadia Slimani, Teresa Norat, Françoise Clavel-Chapelon, Emmanuelle Kesse, Alexandra Nieters, Heiner Boeing, Anne Tjønneland, Kim Overvad, Carmen Martinez, Miren Dorronsoro, Carlos A Gonzalez, Timothy J Key, Antonia Trichopoulou, Androniki Naska, Paolo Vineis, Rosario Tumino, Vittorio Krogh, H Bas Bueno-de-Mesquita, Petra HM Peeters, Göran Berglund, Göran Hallmans, Eiliv Lund, Guri Skeie, Rudolf Kaaks, Elio Riboli

Summary

Background Dietary fibre is thought to protect against colorectal cancer but this view has been challenged by recent prospective and intervention studies that showed no protective effect.

Methods We prospectively examined the association between dietary fibre intake and incidence of colorectal cancer in 519 978 individuals aged 25–70 years taking part in the EPIC study, recruited from ten European countries. Participants completed a dietary questionnaire in 1992–98 and were followed up for cancer incidence. Relative risk estimates were obtained from fibre intake, categorised by sex-specific, cohort-wide quintiles, and from linear models relating the hazard ratio to fibre intake expressed as a continuous variable.

Findings Follow-up consisted of 1 939 011 person-years, and data for 1065 reported cases of colorectal cancer were included in the analysis. Dietary fibre in foods was inversely related to incidence of large bowel cancer (adjusted relative risk 0·75 [95% CI 0·59–0·95] for the highest versus lowest quintile of intake), the protective effect being greatest for the left side of the colon, and least for the rectum. After calibration with more detailed dietary data, the adjusted relative risk for the highest versus lowest quintile of fibre from food intake was 0·58 (0·41–0·85). No food source of fibre was significantly more protective than others, and non-food supplement sources of fibre were not investigated.

Interpretation In populations with low average intake of dietary fibre, an approximate doubling of total fibre intake from foods could reduce the risk of colorectal cancer by 40%.

Lancet 2003; **361:** 1496–501
See Commentary page 1487

STUDI EPIDEMIOLOGICI DI COORTE

OBIETTIVI

- **Calcolare tassi di incidenza, tassi di mortalità, rischi, sopravvivenza, frequenza di recidive, ecc.**
- **Calcolare il rischio relativo e il rischio attribuibile per ciascun fattore di rischio indagato**

VANTAGGI

- **Conservazione della corretta relazione temporale tra esposizione e malattia**
- **In genere una discreta/buona qualità della rilevazione dell'esposizione e della malattia**
- **Possibilità di esaminare più fattori di rischio e più malattie nello stesso studio**
- **Possibilità di effettuare studi caso-controllo innestati nello studio di coorte (nested) o studi caso-coorte**

STUDI EPIDEMIOLOGICI DI COORTE

SVANTAGGI

Necessità di arruolare un numero elevato di soggetti

- **Lunga durata, disegno complesso e costoso**
- **Non indicato per malattie rare nella coorte in esame**
- **Difficoltà a mantenere costanti nel tempo le modalità di rilevazione**

BIAS

Perdite al follow-up

- **Cambiamenti nel tempo delle rilevazioni**

N.B: In genere non è soggetto a bias di selezione o di informazione