

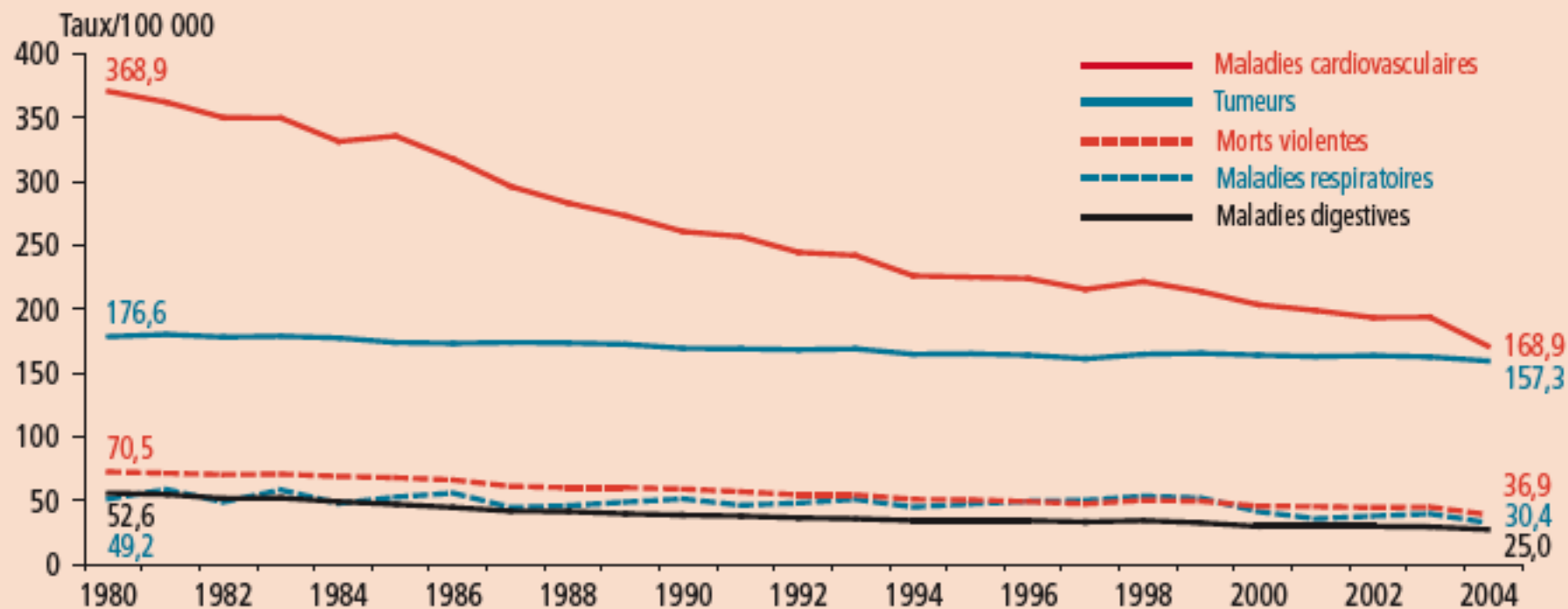
Les cancers bronchiques de la femme : une épidémie

Pr Jean TREDANIEL

Hôpital Saint Joseph

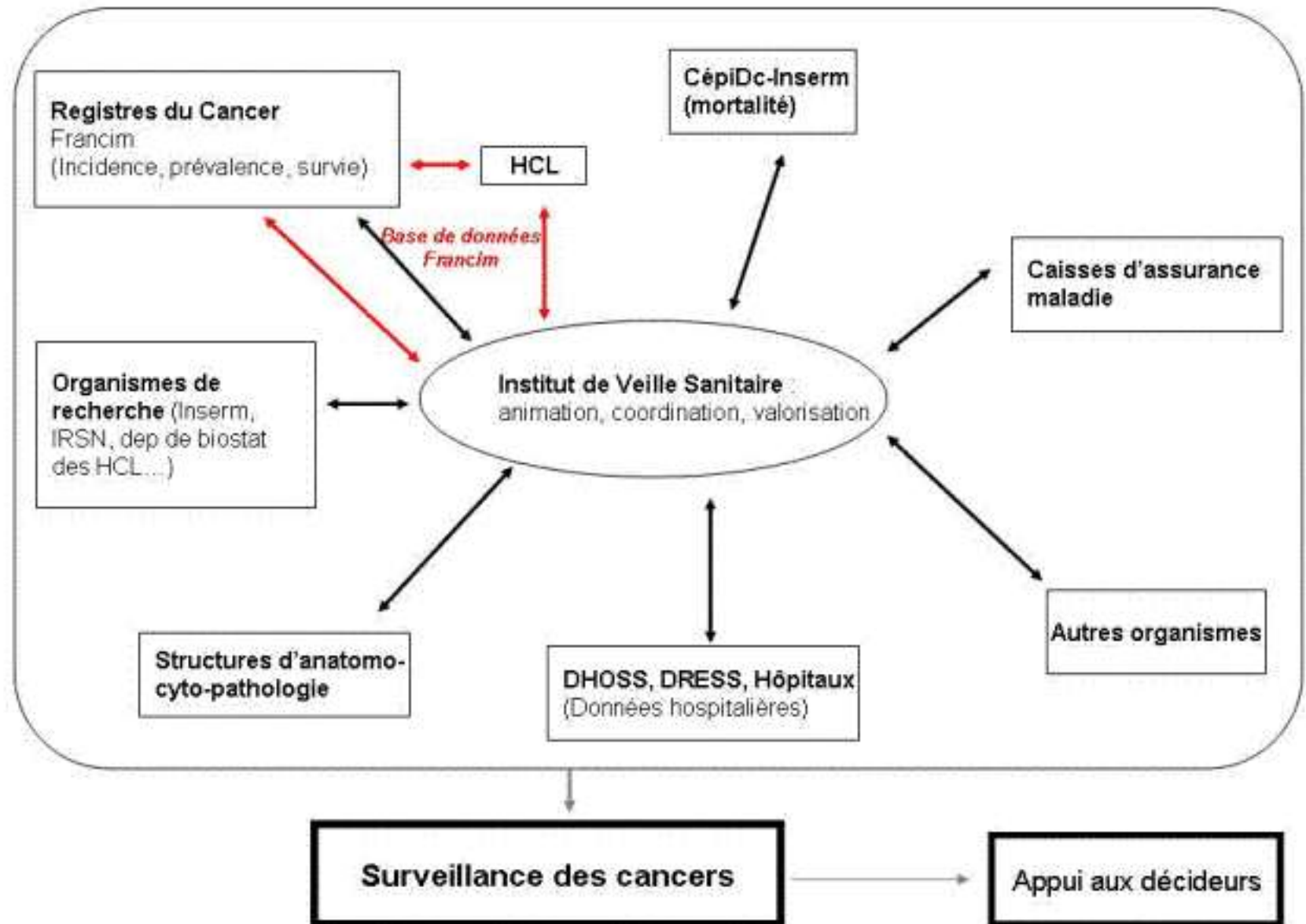
Paris

Figure 4 Evolution des taux* de décès par grande catégorie de causes de décès, 1980-2004, France métropolitaine, femmes / Figure 4 Trends in death rates by main category of causes of death, 1980-2004, metropolitan France, females

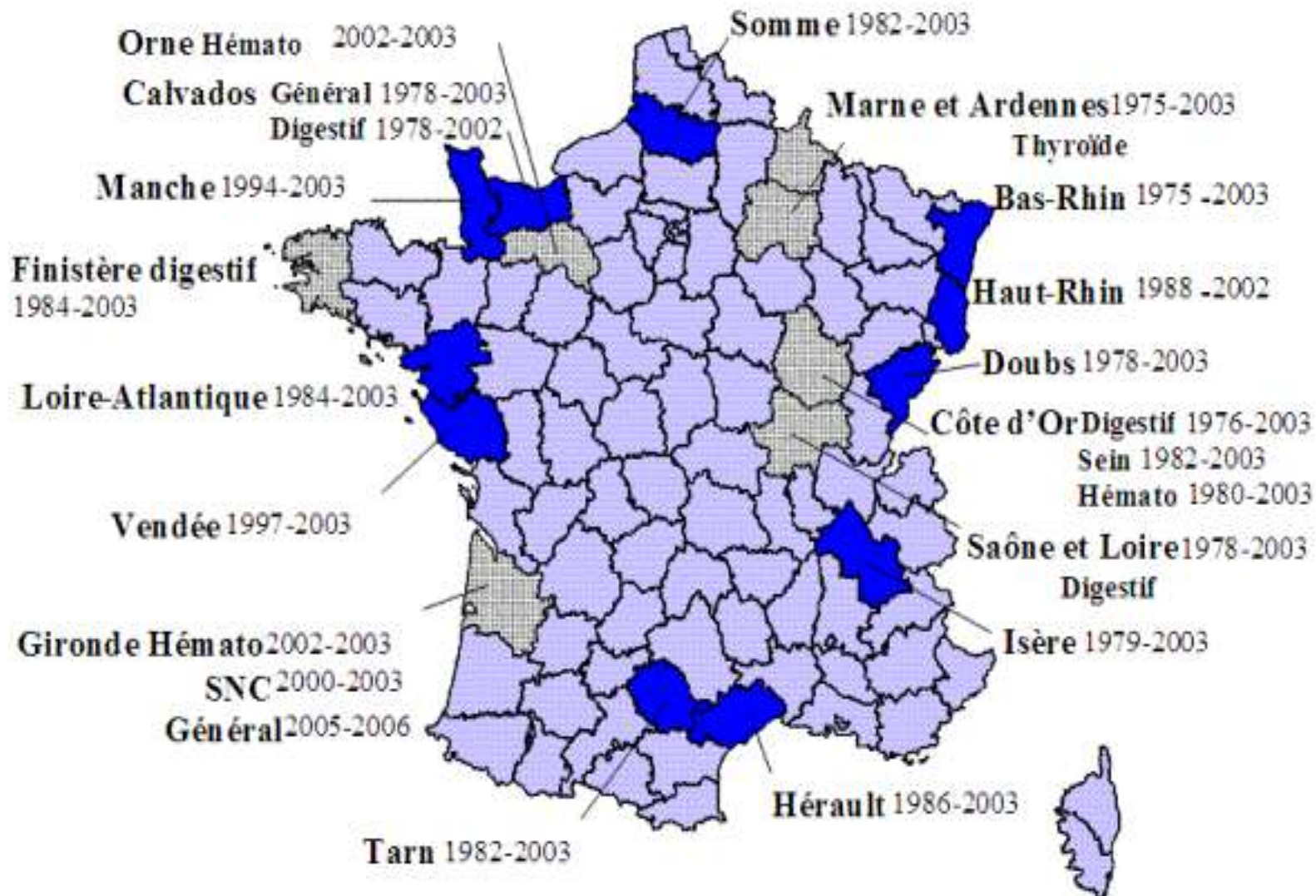


* Taux standardisés pour 100 000.

Le réseau de surveillance épidémiologique nationale des cancers



Situation des registres du cancer en France métropolitaine au 1er janvier 2007



Incidence des cancers à l'échelon national

Elle est modélisée à partir de l'incidence observée par les registres départementaux et la mortalité connue à l'échelon national.



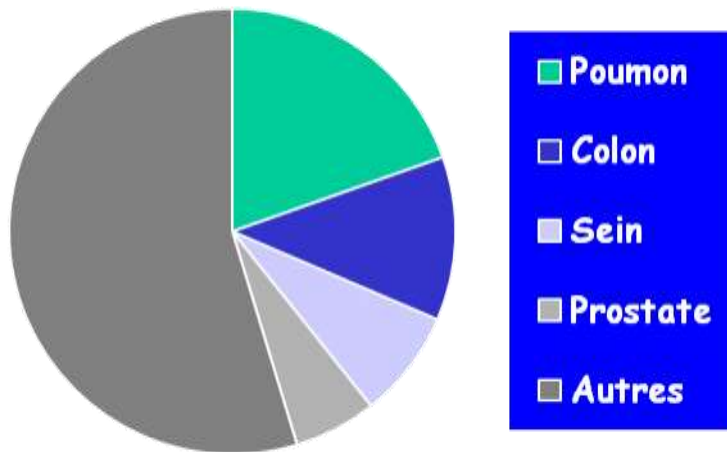
Données projetées de l'incidence des cancers en France, 2010



- Prostate • Prostate: 71 500 cas
- Sein • Sein: 52 200 cas
- Colon • Colon-rectum: 40 000 cas
- Poumon • Poumon: 37 000 cas
- Autres • Autres: 156 700 cas

TOTAL: 357 500 CAS

Nombre projetés des décès par cancer en France, 2010



- Poumon: 28 700
- Colon-rectum: 17 400
- Sein: 11 500
- Prostate: 8 790
- Autres: 80 110

TOTAL: 146 500

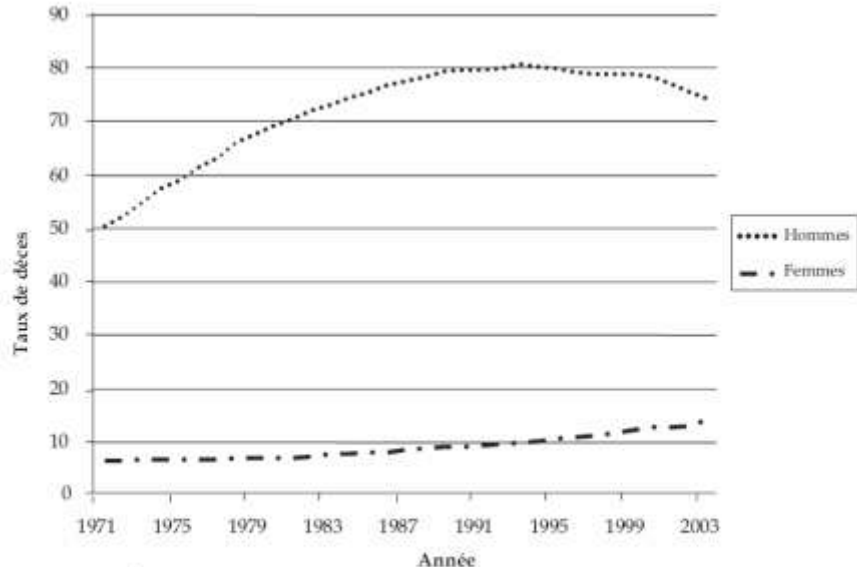


Figure 5.2 : Évolution des taux de décès par cancer du poumon selon le sexe entre 1973 et 2003 en France métropolitaine (d'après CépiDc-Inserm)

Taux pour 100 000 standardisés par âge (population de référence : France 1990), moyenne mobile sur 3 ans

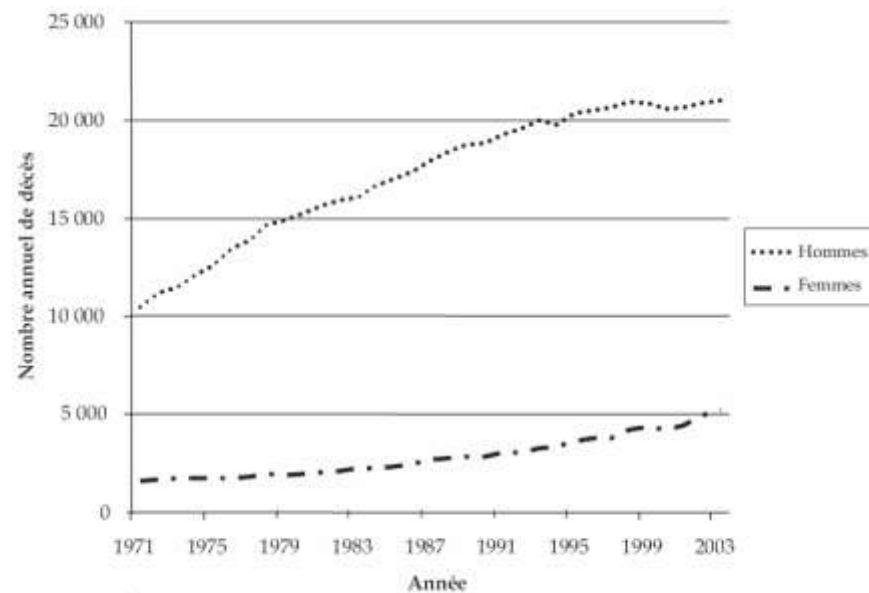
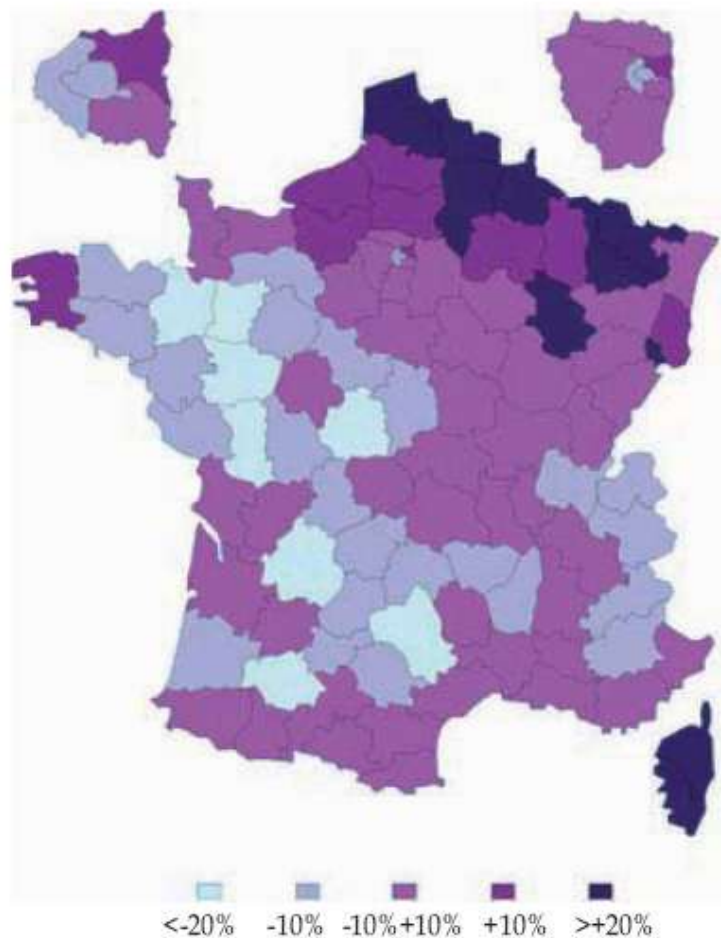


Figure 5.1 : Évolution des effectifs annuels de décès par cancer du poumon selon le sexe entre 1973 et 2003, en France métropolitaine (d'après CépiDc-Inserm)

Incidence et mortalité par cancer en France
(situation en 2005 et tendances évolutives): taux
annuel moyen d'évolution pour le taux standardisé

	Hommes				Femmes			
	Incidence		Mortalité		Incidence		Mortalité	
	1980- 2005	2000- 2005	1980- 2005	2000- 2005	1980- 2005	2000- 2005	1980- 2005	2000- 2005
Tous cancers	+ 1,2	+ 1,7	- 1,1	- 2,5	+ 1,4	+ 1,6	- 0,9	- 1,2
Cancer du poumon	+ 0,2	- 0,5	- 0,1	- 1,7	+ 5,8	+ 5,8	+ 3,5	+ 4,2

Homme



Femme

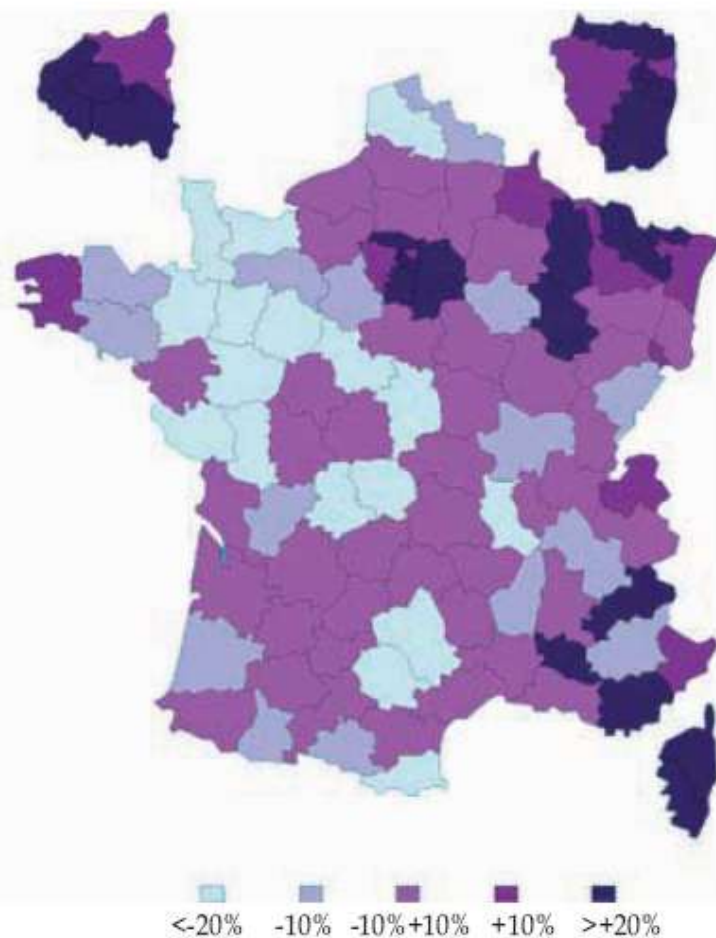
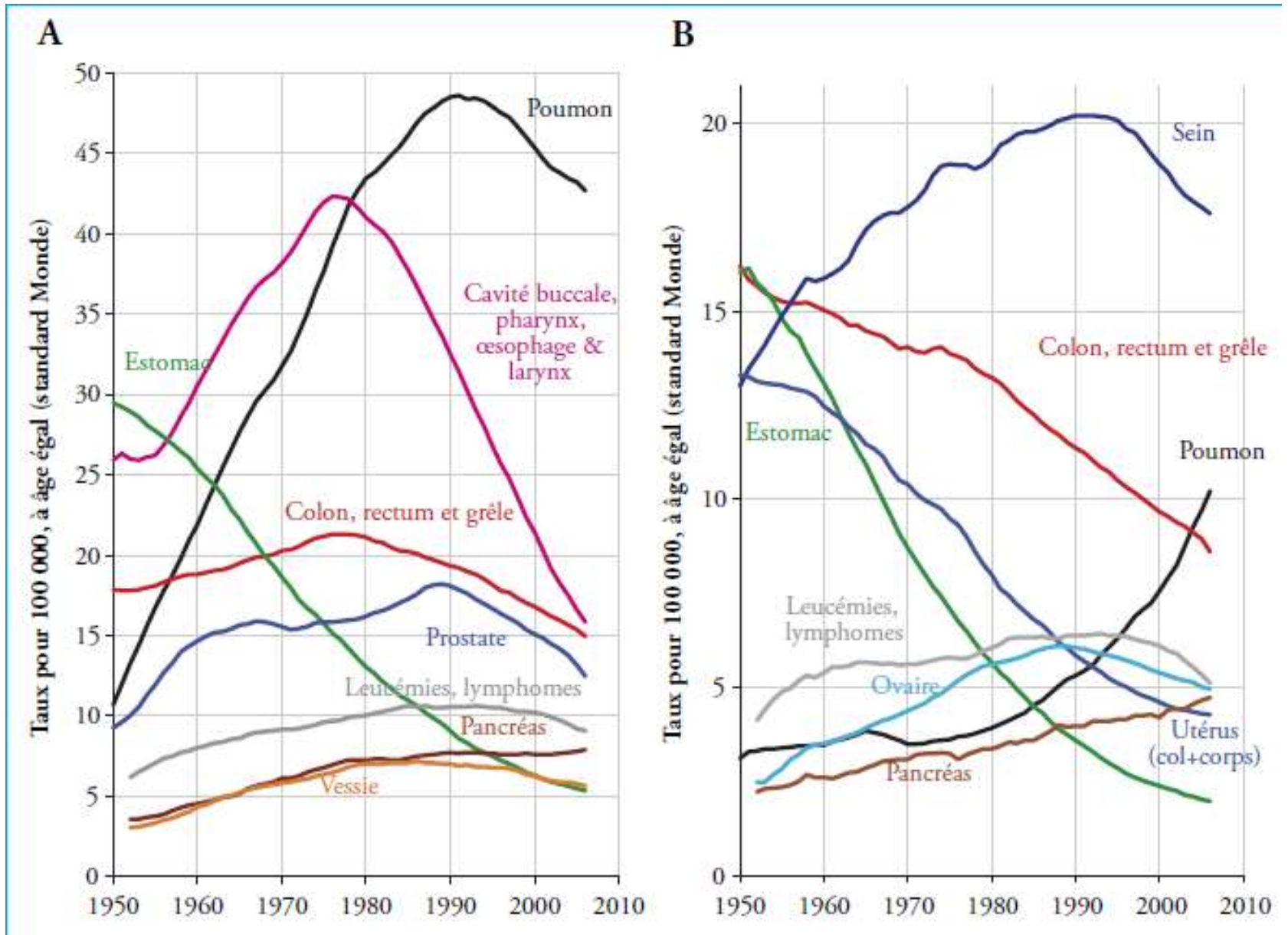


Figure 5.3 : Disparités départementales de mortalité par cancer du poumon (taux standardisés) selon le sexe en France métropolitaine (2000-2002) (d'après CépiDc-Inserm)

Évolution de la mortalité pour les principales localisations de cancer, France, 1950-2006.

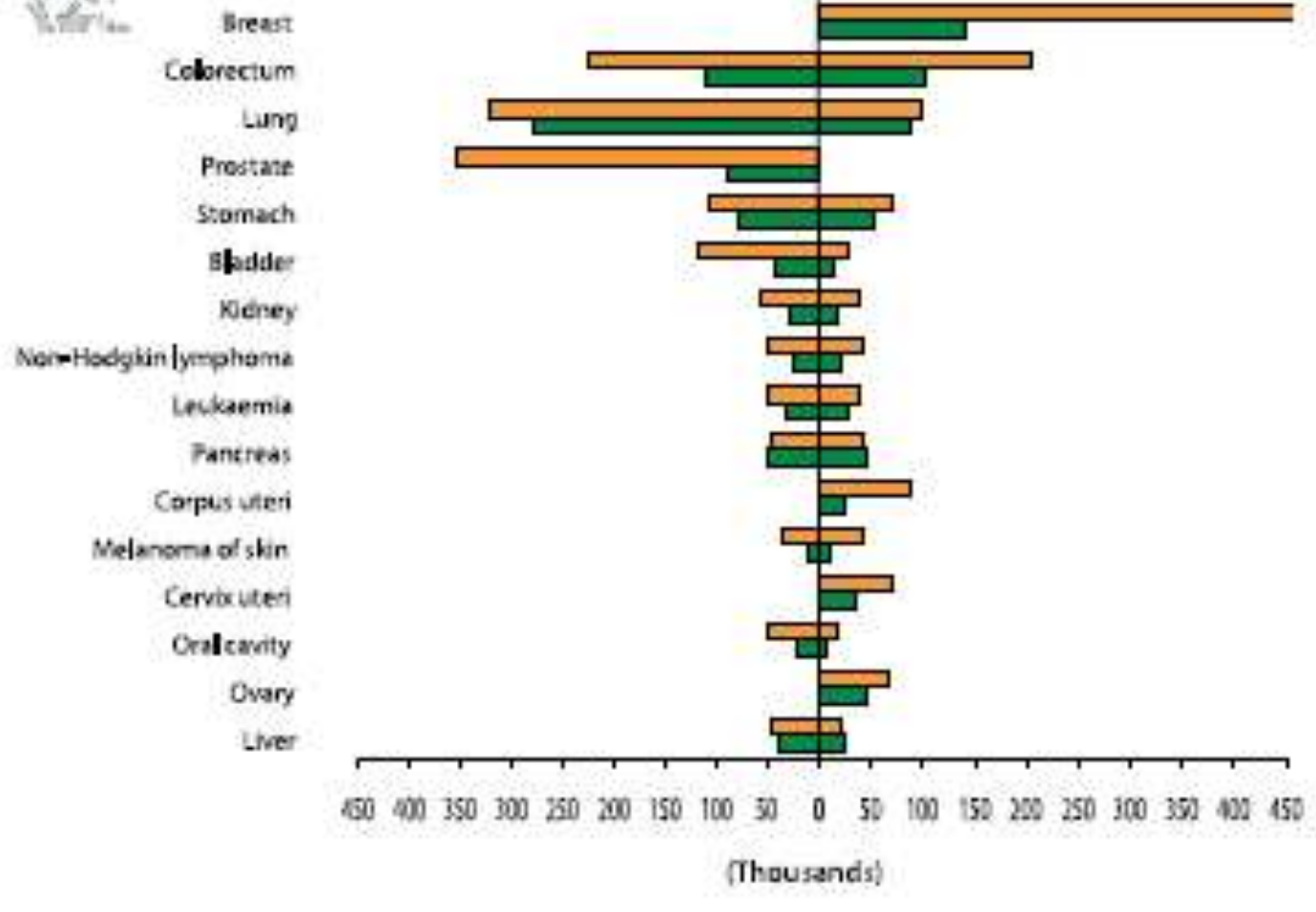


WHO European Region (EURO)

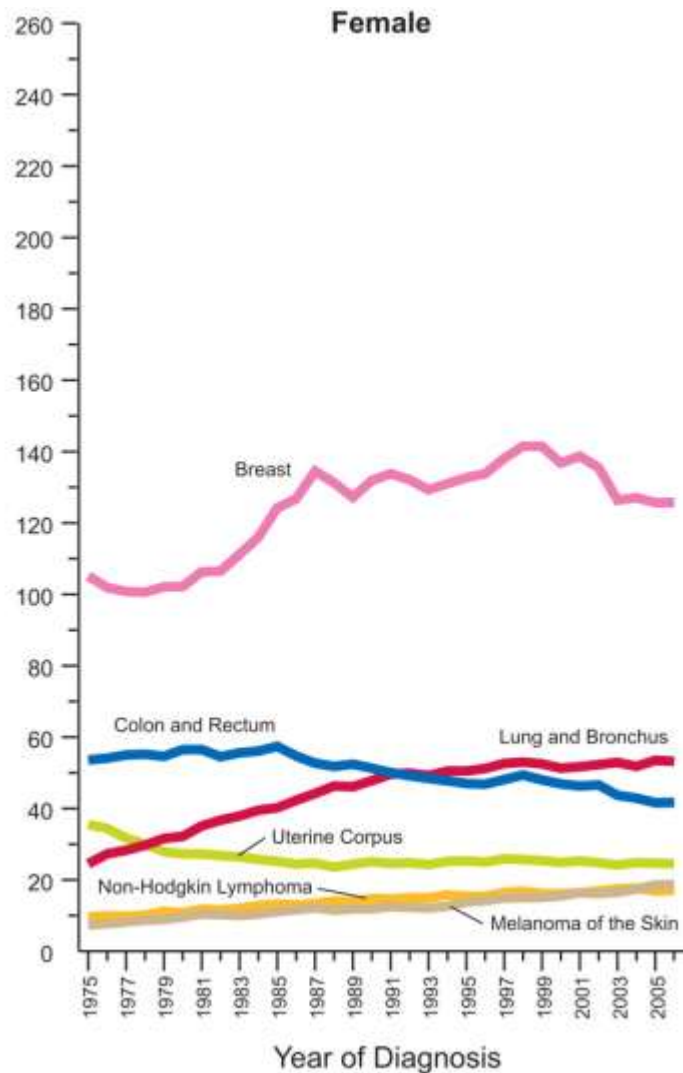
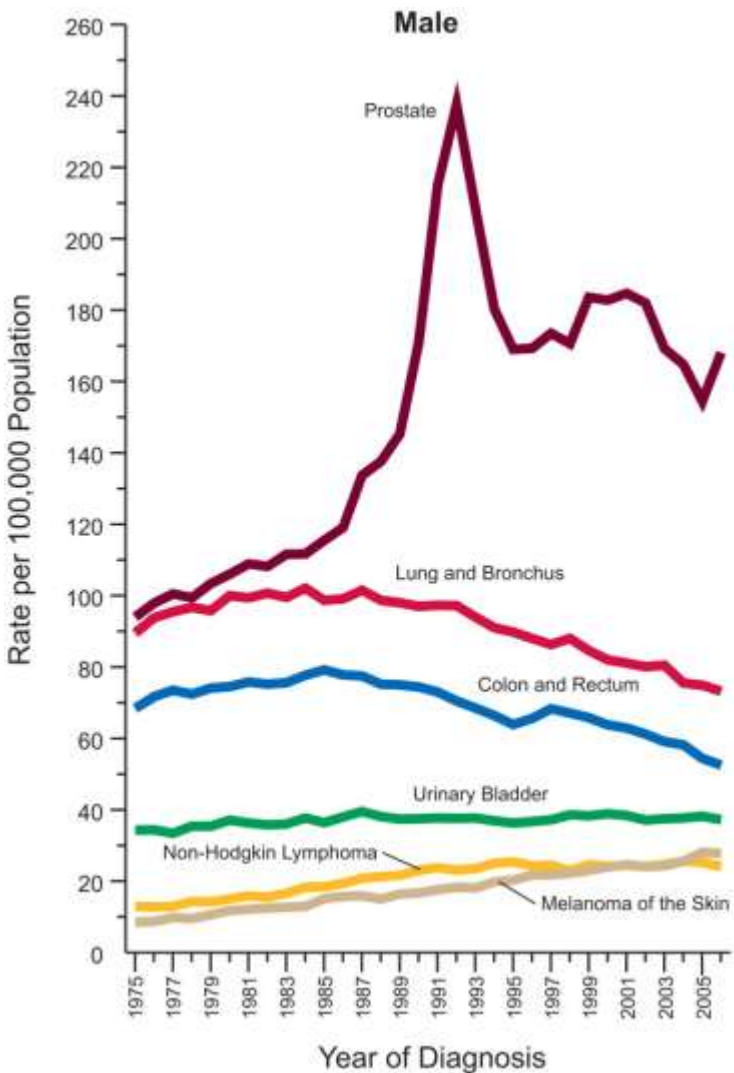


Males
1,821,000 cases
1,034,000 deaths

Females
1,601,000 cases
813,000 deaths



Annual Age-adjusted Cancer Incidence Rates Among Males and Females for Selected Cancers, US, 1975 to 2006.



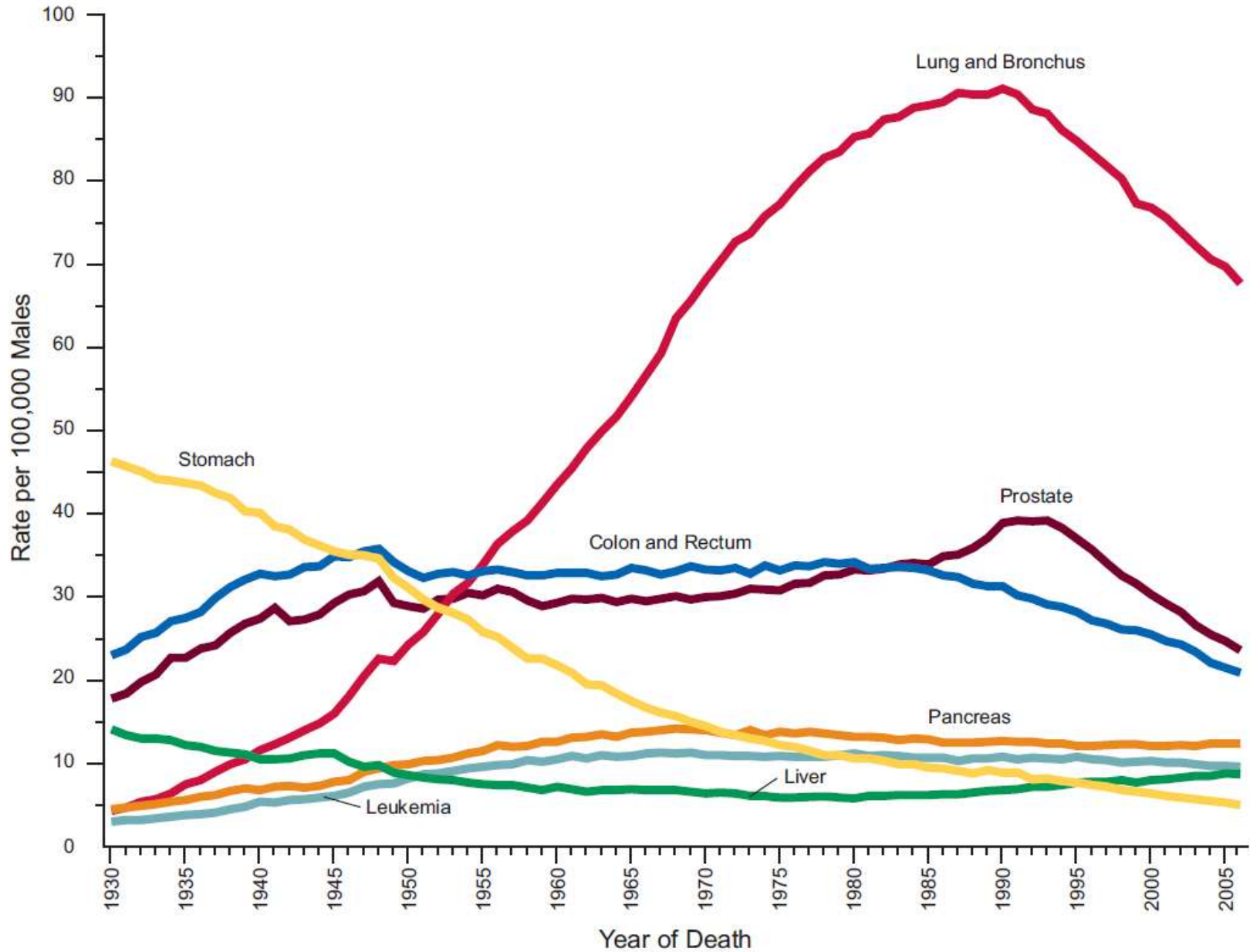


FIGURE 4. Annual Age-Adjusted Cancer Death Rates* Among Males for Selected Cancers, United States, 1930 to 2006.

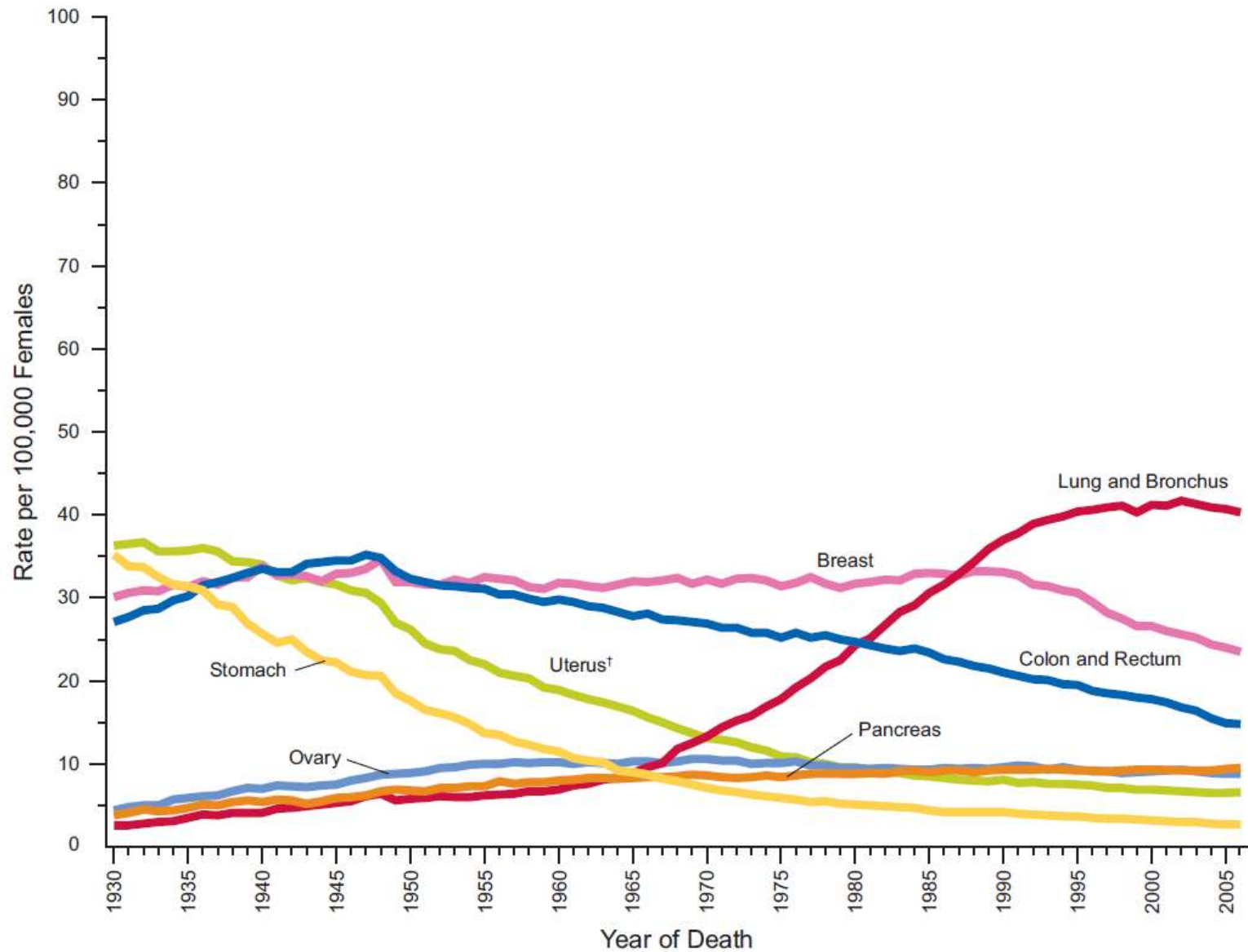
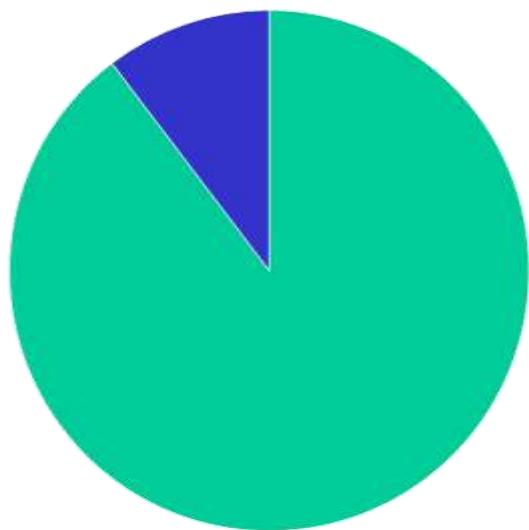


FIGURE 5. Annual Age-Adjusted Cancer Death Rates* Among Females for Selected Cancers, United States, 1930 to 2006.

*Rates are age adjusted to the 2000 US standard population.

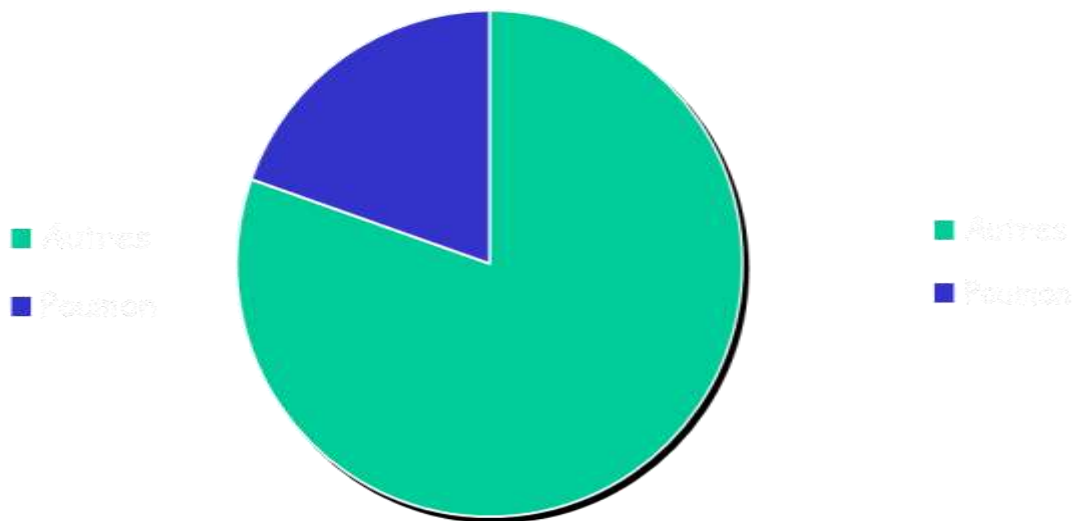
Part relative des cancers du poumon parmi les autres cancers, France, 2010

10 %



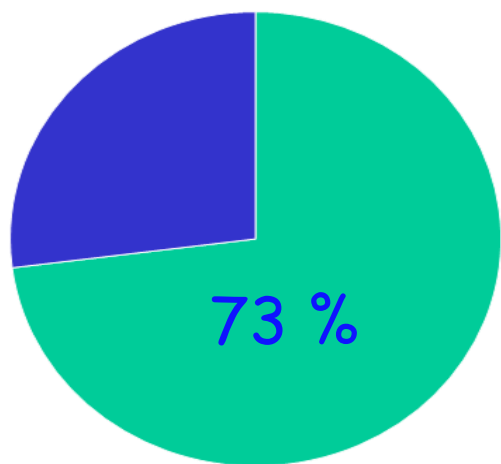
INCIDENCE

19,6 %



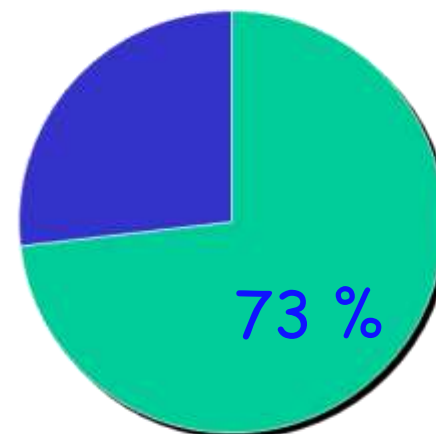
MORTALITÉ

Cancer du poumon en France en 2010 : sexe ratio



INCIDENCE
(37 000 cas)

=

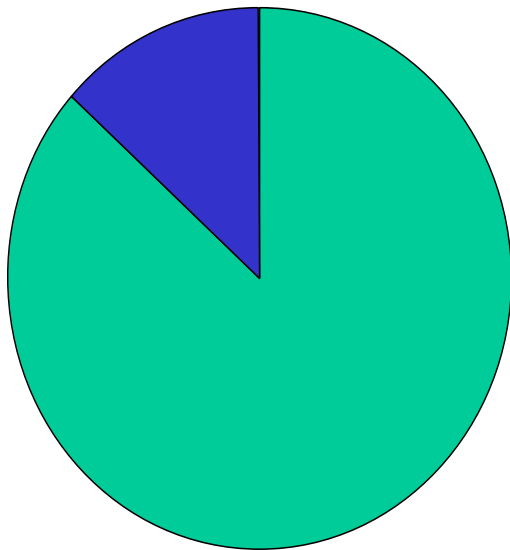


MORTALITÉ
(28 700 décès)

■ Hommes
■ Femmes

Part relative des cancers du poumon parmi les autres cancers chez l'homme, France, 2010

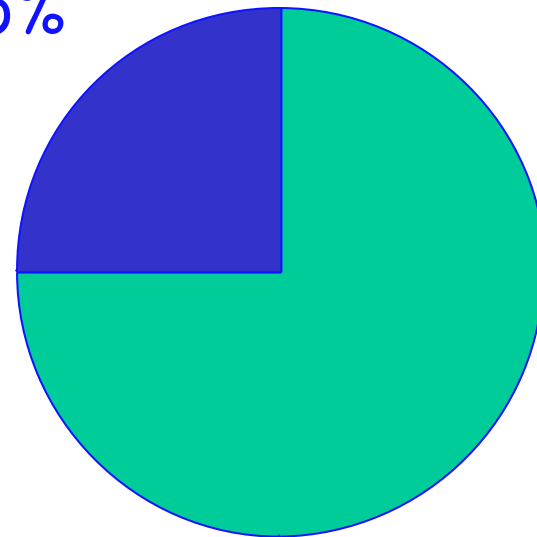
13.3%



INCIDENCE

■ Autres
■ Poumon

25%

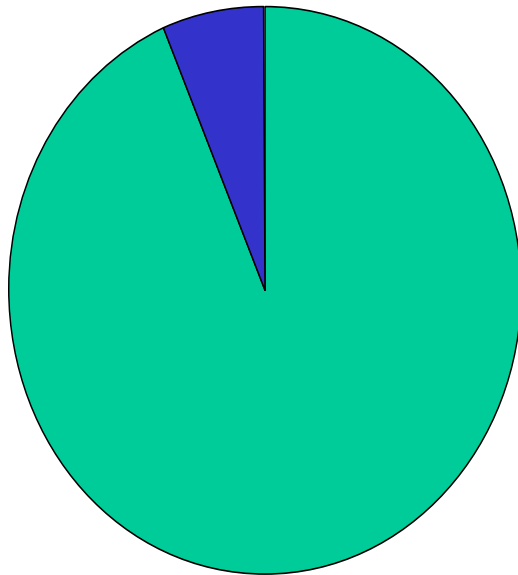


■ Autres
■ Poumon

MORTALITÉ

Part relative des cancers du poumon parmi les autres cancers chez la femme, France, 2010

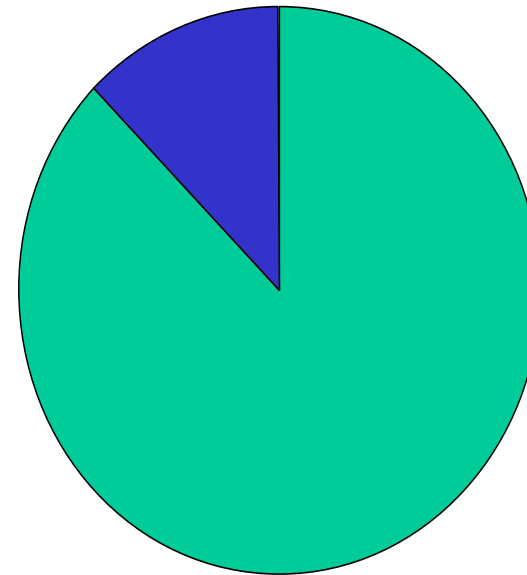
6.5%



INCIDENCE

■ Autres
■ Poumon

12.5%



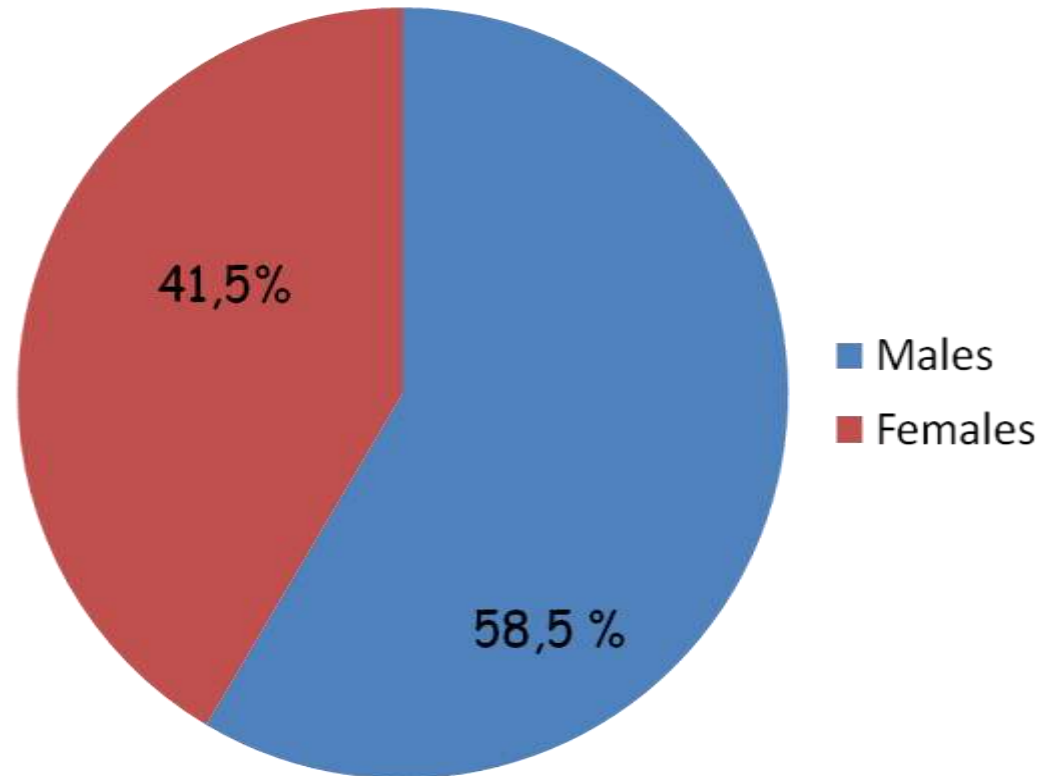
MORTALITÉ

■ Autres
■ Poumon

National survey of non-small cell lung cancer in the United States

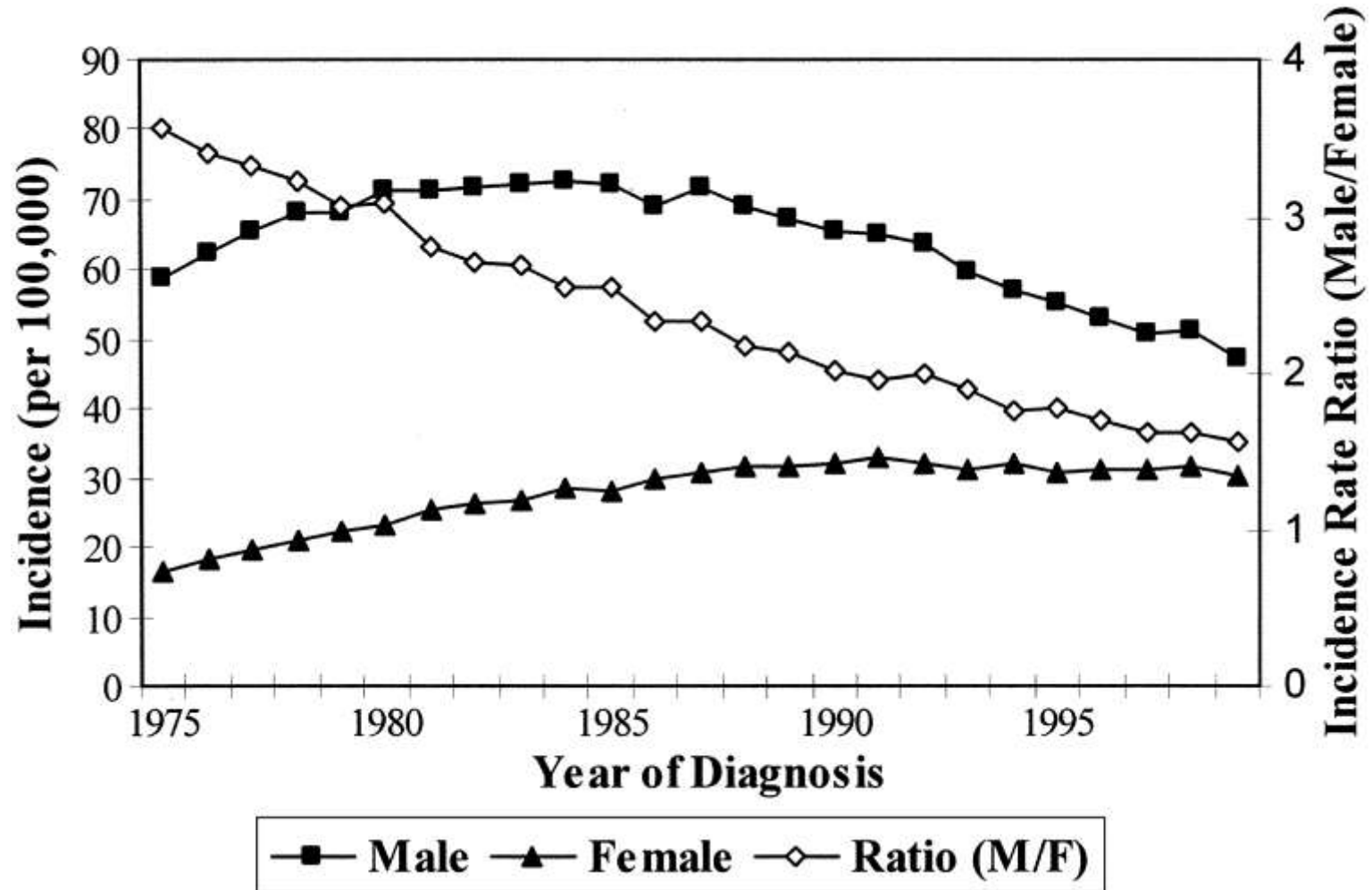
National Cancer Database: patient care evaluation study in 719 hospitals.

Information was obtained on 40 909 patients



Lung Cancer in Women.

Analysis of the National SEER Database, 1975-1999



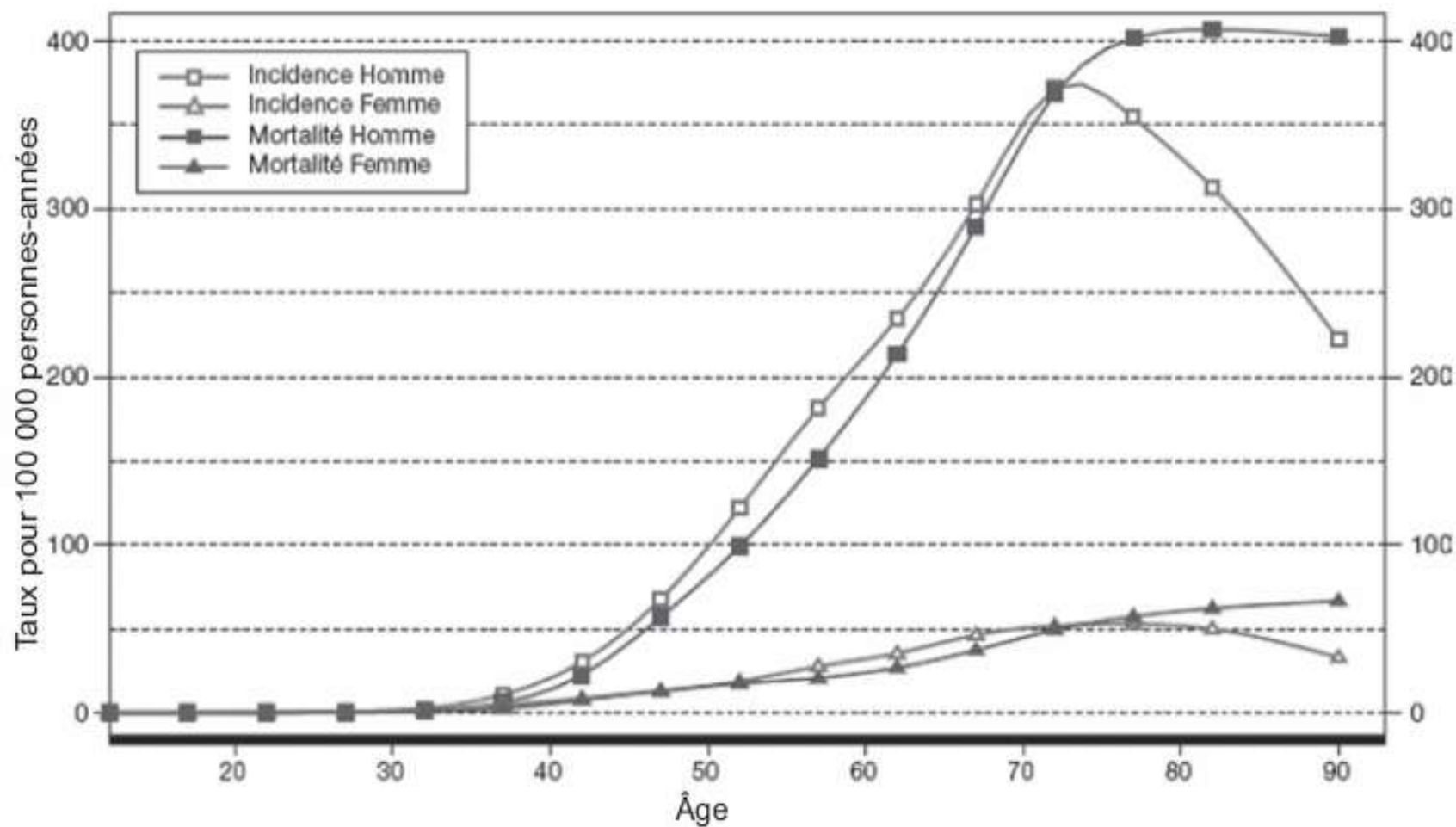
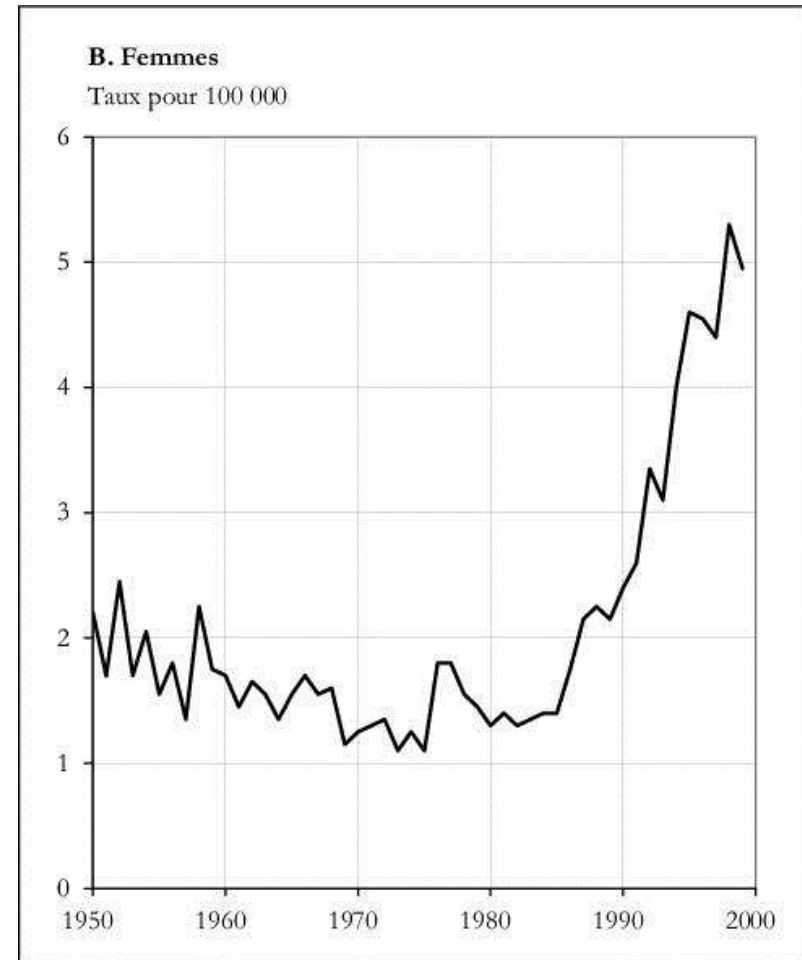
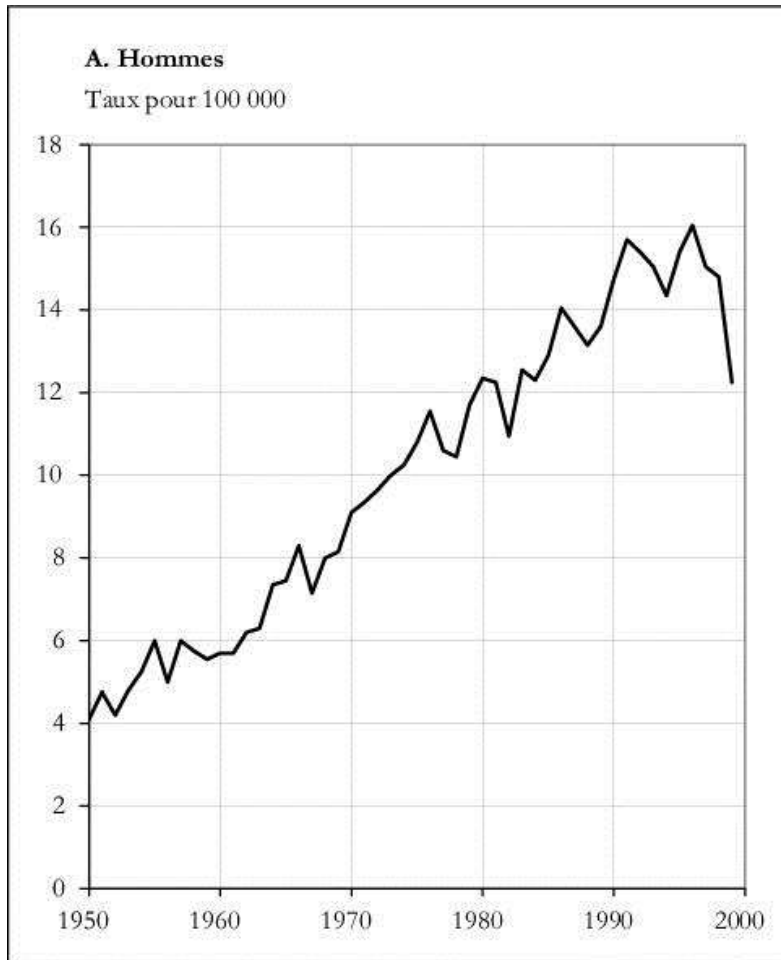
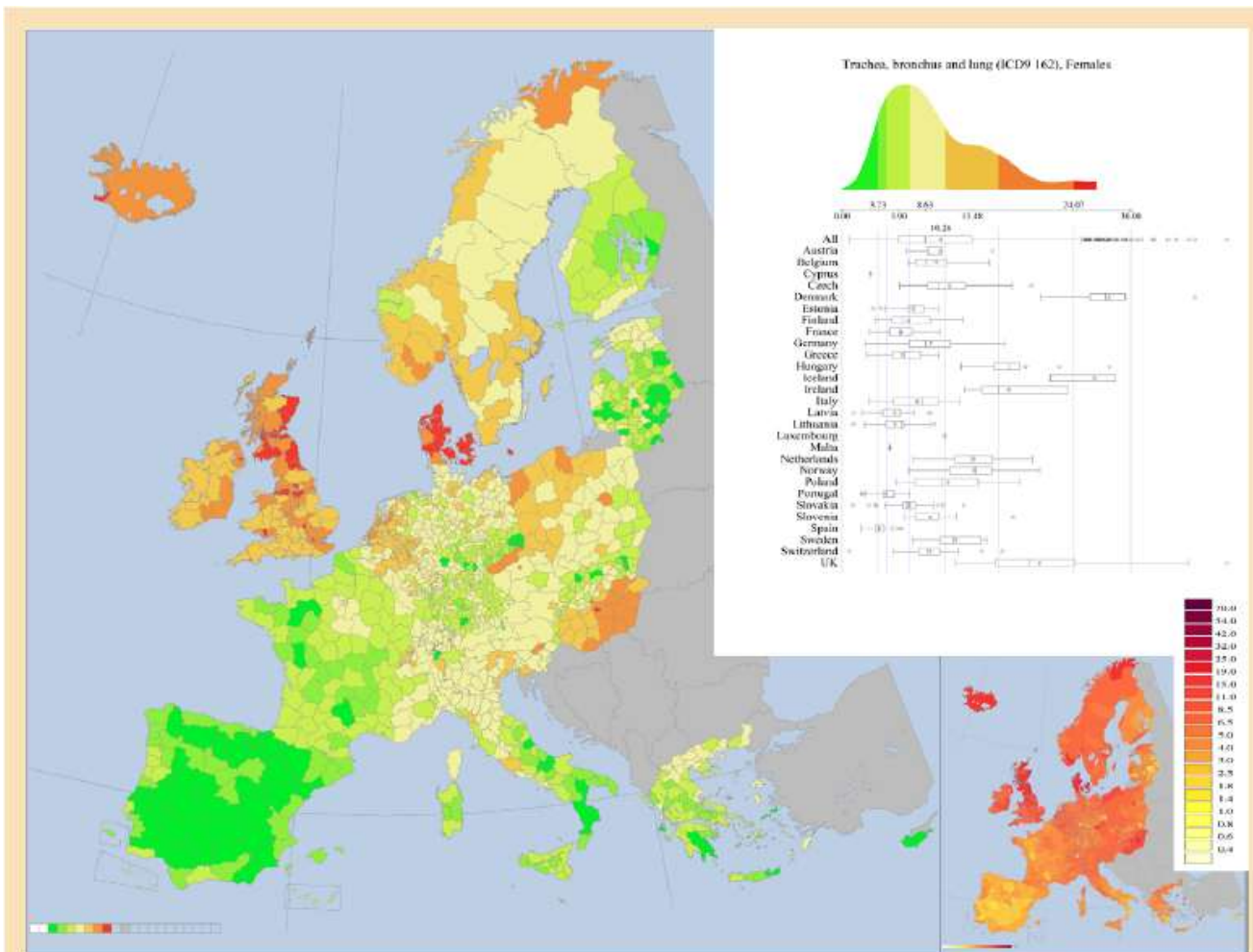


Figure 4.1 : Incidence (taux brut) et mortalité estimées par âge pour l'année 2000 (d'après Remontet et coll., 2003)

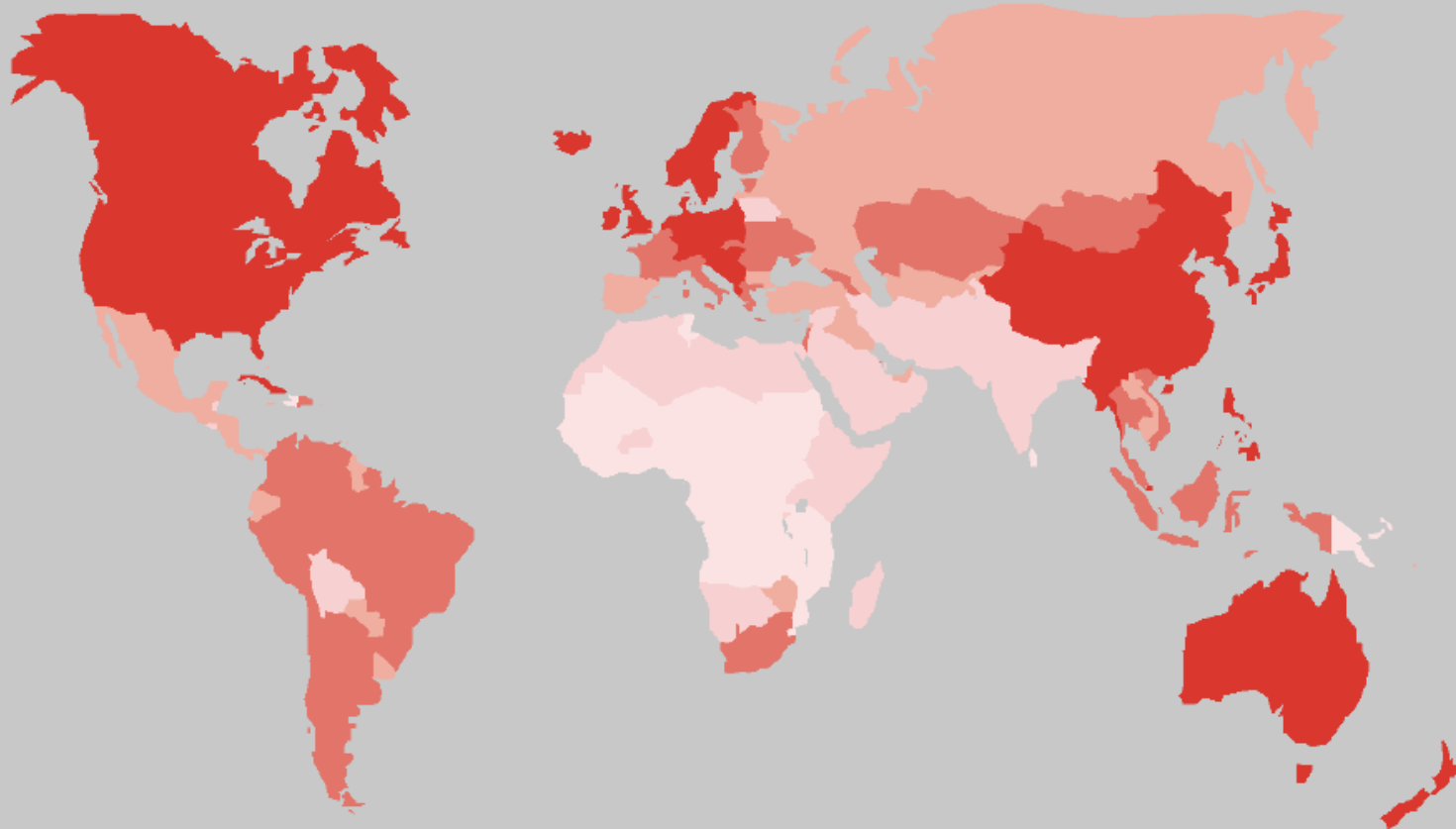
Évolution de la mortalité par cancer du poumon entre 35 et 44 ans.





European Map 5.10.2 The pattern of lung cancer mortality in women was quite different from that observed in males. The highest rates were in the United Kingdom (particularly the north), Ireland, Denmark and Iceland, and parts of Norway and Sweden, all of which had generally lower-than-average lung cancer mortality rates in males. There were, however, similar areas of higher-than-average rates in females as in males in Belgium and The Netherlands, in north and west Poland, and in Hungary. Low rates aggregated particularly in Portugal and Spain, but also in France, Greece, southern Italy and Finland. In terms of our understanding of lung cancer etiology, the current geographical patterns better represent the smoking habits in the various countries 20–30 years ago than those of today. In particular, the high mortality from lung cancer in women in Denmark and the United Kingdom reflects the early uptake of the smoking habit by large portions of females in those countries. An epidemic of tobacco-related lung cancer in women throughout Europe has yet to materialise (as it has previously in men) and effective intervention is now needed urgently to avoid this catastrophe [1].

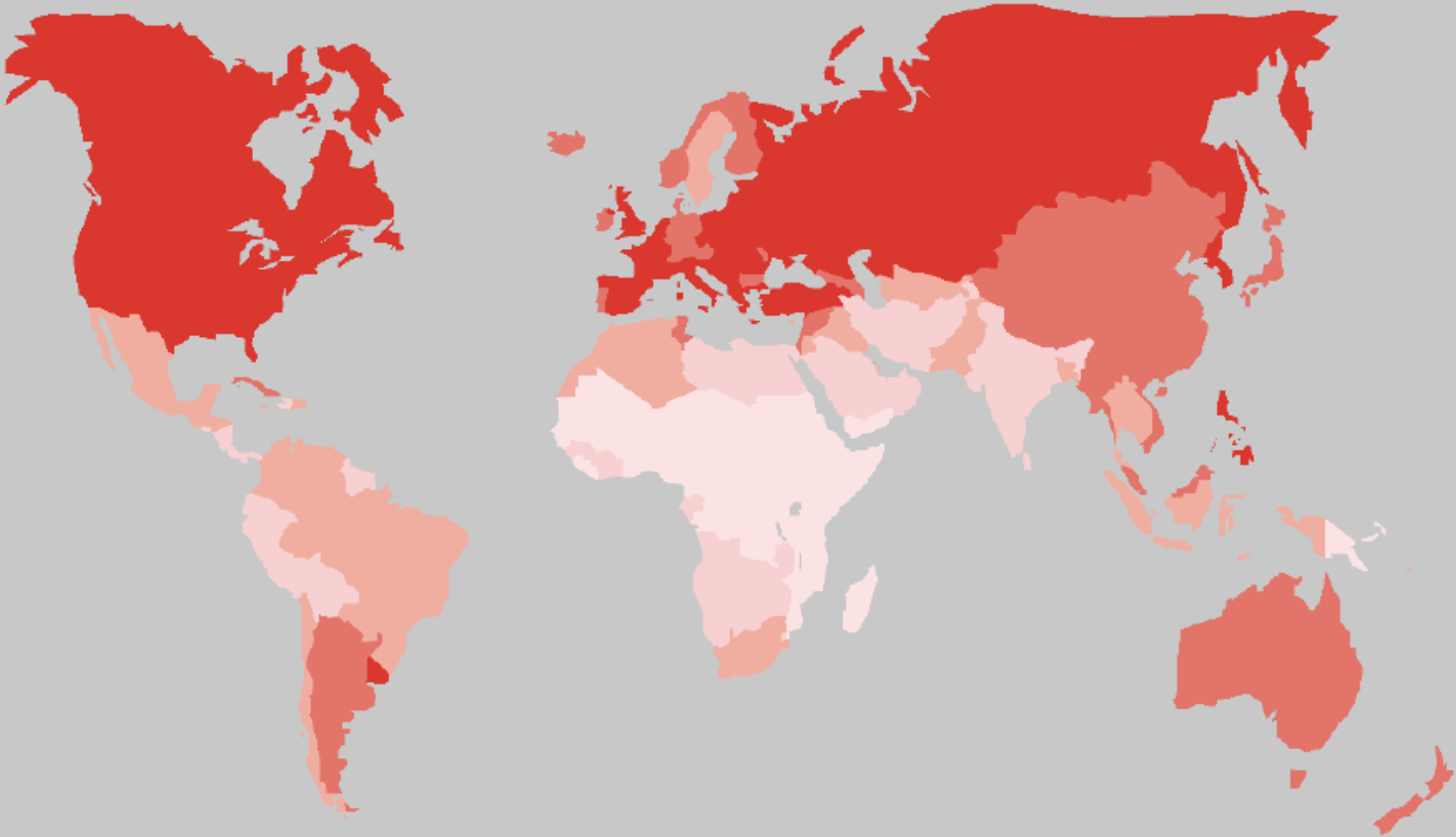
Incidence of Lung cancer: ASR (World)-Female (All ages)



< 1.9 < 4.6 < 6.7 < 12.2 < 36.1

GLOBALCAN 2002

Incidence of Lung cancer: ASR (World)-Male (All ages)



< 5.0 < 15.7 < 27.1 < 46.7 < 94.6

GLOBOCAN 2002

GLOBOCAN: age-standardized incidence rates for lung cancer.

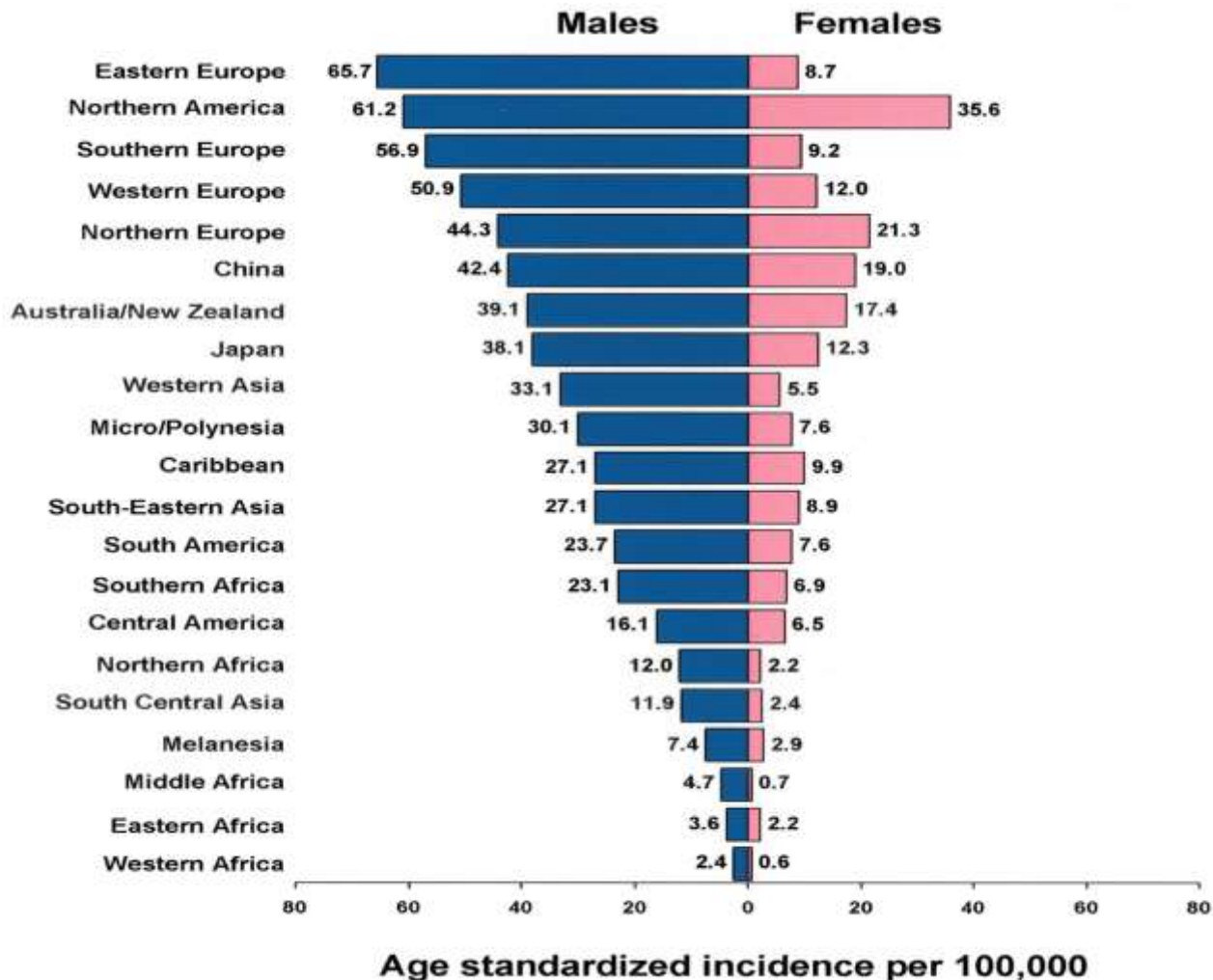


Figure 1a Survie relative à 5 ans standardisée pour l'âge, chez l'homme

Figure 1a Age-standardized five-year relative survival in men

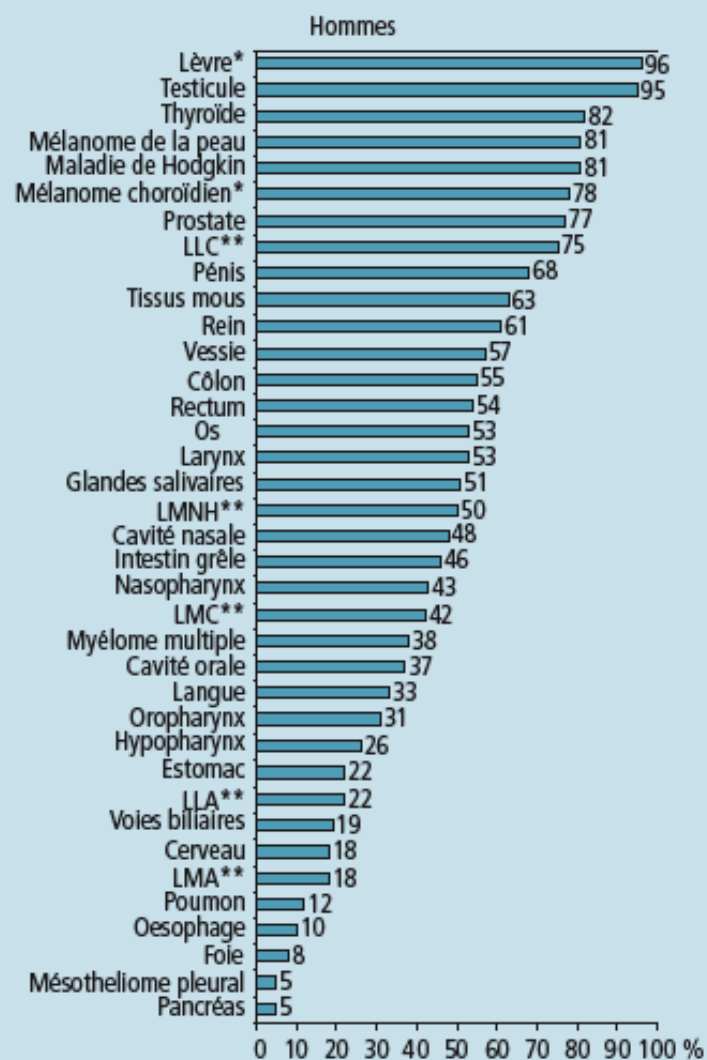


Figure 1b Survie relative à 5 ans standardisée pour l'âge, chez la femme

Figure 1b Age-standardized five-year relative survival in women

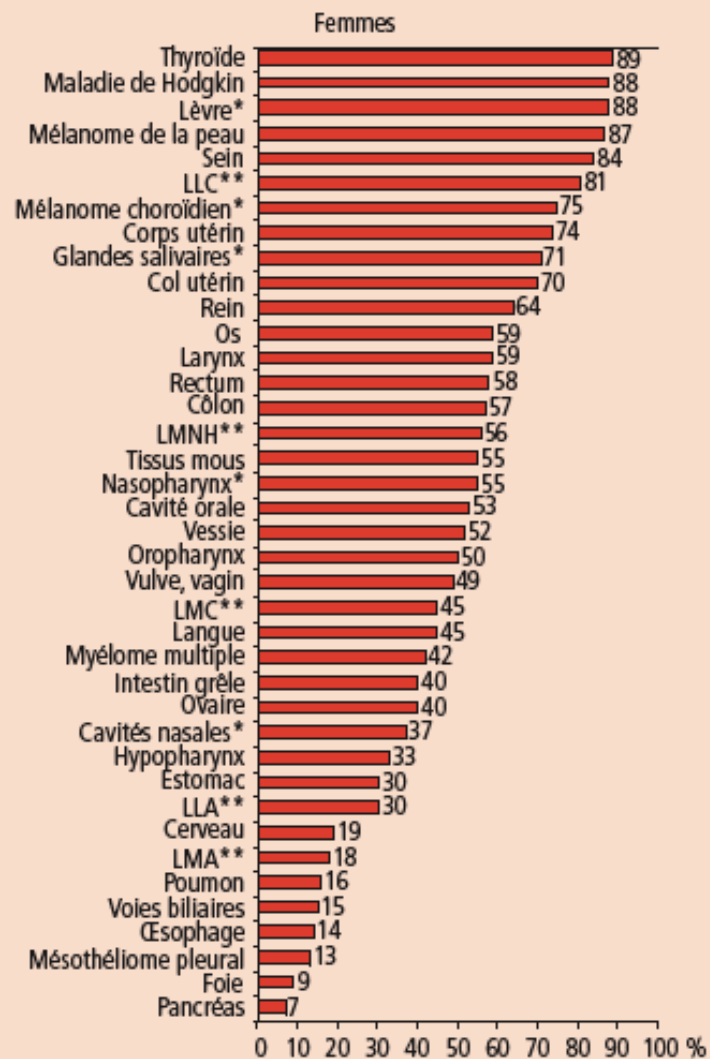


Tableau 1 Impact pronostique du sexe sur le taux de mortalité supplémentaire : taux relatif et intervalle de confiance [IC] à 95 %

Table 1 Prognostic impact of sex on the excess mortality rate: relative rates and 95% confidence intervals [CI]

Localisation	Effet du sexe Taux relatif^a [IC 95 %]
Thyroïde	0,60 [0,45-0,82] ^b
Mélanome de la peau	0,60 [0,50-0,73] ^b
Tête et cou	0,65 [0,60-0,72] ^b
Leucémie lymphoïde chronique	0,69 [0,53-0,89] ^c
Lymphome hodgkinien	0,70 [0,51-0,98] ^c
Leucémie lymphoïde aigue	0,75 [0,57-0,99] ^c
Estomac	0,82 [0,78-0,88] ^b
Lymphome malin non hodgkinien	0,83 [0,77-0,90] ^b
Poumon	0,87 [0,83-0,91] ^b
Myelome	0,88 [0,78-1,00] ^c
Rein	0,90 [0,81-1,00] ^c
Côlon-rectum	0,90 [0,87-0,93] ^b

a Femmes versus hommes

b p < 0,001

c p < 0,05

Some carcinogen identification programmes

International Agency for Research on Cancer
*IARC Monographs on the Evaluation of
Carcinogenic Risks to Humans*
<http://monographs.iarc.fr/>

U.S. National Toxicology Program
Report on Carcinogens
<http://ntp.niehs.nih.gov/>

U.S. Environmental Protection Agency
Integrated Risk Information System (IRIS)
<http://cfpub.epa.gov/ncea/iris/>

German Research Foundation (Deutsche
Forschungsgemeinschaft, DFG)
Maximum Allowable Concentrations
(Maximale Arbeitsplatzkonzentrationen, MAK)
and Biological Tolerance Values (Biologische
Arbeitsstofftoleranzwerte, BAT)
<http://www.dfg.de/>

California Environmental Protection Agency
List of chemicals known to the State to cause
cancer
<http://www.oehha.ca.gov/prop65.html>

- Group 1: Carcinogenic to humans
- Group 2A: Probably carcinogenic to humans
- Group 2B: Possibly carcinogenic to humans
- Group 3: Unclassifiable as to carcinogenicity in humans
- Group 4: Probably not carcinogenic to humans

WHO Region*	Smoking-Attributable Cancer Mortality					
	Male		Female		Total	
	N	%	N	%	N	%
Europe C	133 000	49	11 000	5	144 000	29
Europe B	72 000	44	9 000	8	81 000	29
Southeast Asia (India and others)	174 000	43	16 000	4	190 000	24
Southeast Asia B	45 000	43	2 000	4	47 000	24
North America	131 000	42	80 000	26	211 000	34
Western Europe	225 000	40	47 000	10	272 000	27
Western Pacific A	69 000	36	18 000	13	87 000	27
Eastern Mediterranean B	12 000	30	2 000	7	14 000	21
Eastern Mediterranean B	26 000	28	3 000	3	29 000	16
Americas B	48 000	27	12 000	6	60 000	17
Western Pacific (China and others)	209 000	20	35 000	5	244 000	14
Africa E	23 000	17	5 000	4	28 000	10
Africa D	5 000	9	400	1	5 400	5
Americas D	2 000	6	300	1	2 300	3

Table 2.2.1 Estimated cancer mortality attributable to smoking by WHO Region in 2000

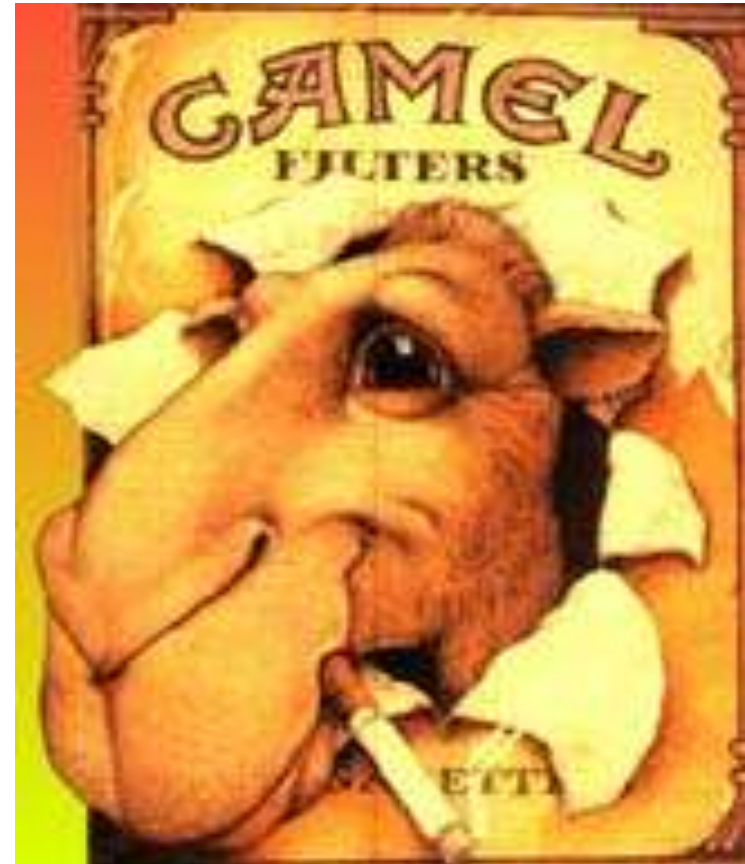
TABAC ET CANCERS

- Associé aux cancers:
 - Du poumon°
 - Des VADS°
 - Du pancréas°
 - De la vessie°
 - *Du rein**
 - *Du foie**
 - *De l'estomac**
 - *Du col de l'utérus**
 - *Et aux leucémies myéloïdes**

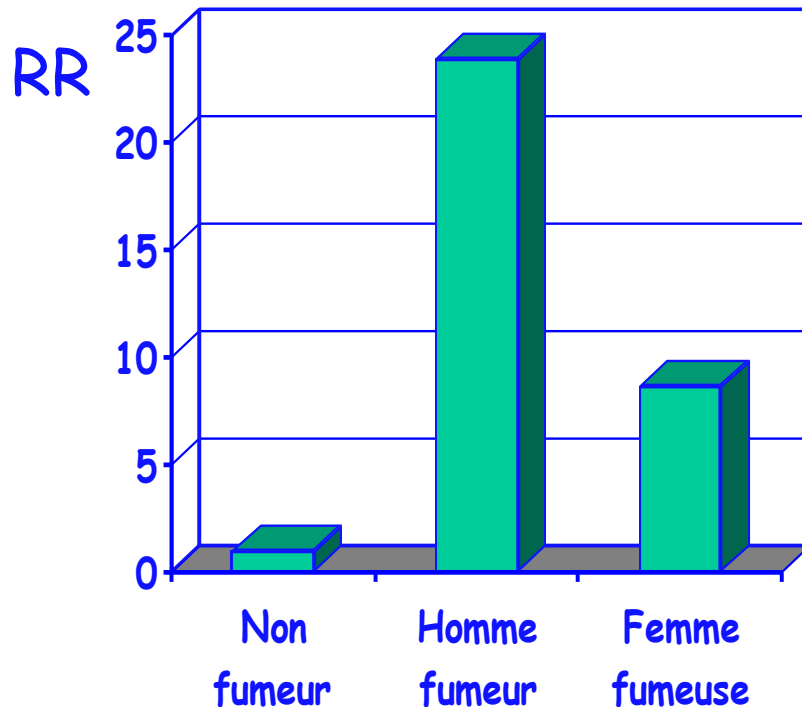
°: IARC, 1986, vol 38

*: IARC: 2002, vol 83

Vineis et al. JNCI 2004; 96: 99-106



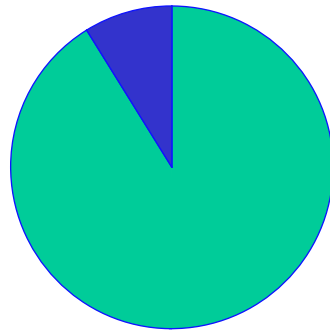
Lung cancer and cigarette smoking in Europe: an update of risk estimates and an assesment of inter-country heterogeneity.



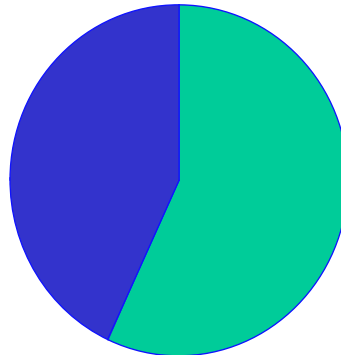
- 10 études cas-témoins, conduites dans 6 pays européens,
- 7609 cancers et 10431 témoins,
- Risque relatif de cancer du poumon chez les fumeurs par rapport aux non fumeurs:
 - Chez l'homme: 23,9
 - Chez la femme: 8,7

Lung cancer and cigarette smoking in Europe: an update of risk estimates and an assessment of inter-country heterogeneity.

Chez l'homme



Chez la femme

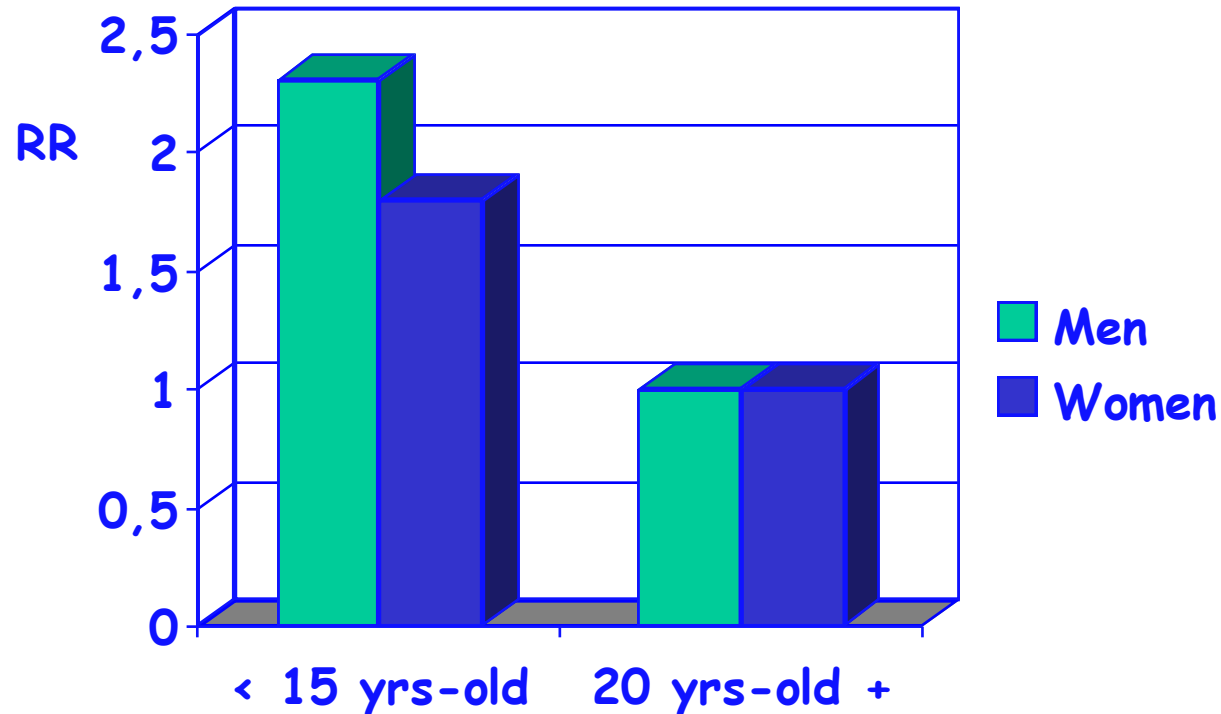


- 10 études cas-témoins, conduites dans 6 pays européens,
- 7609 cancers et 10431 témoins,
- Fraction des cancers du poumon attribuables au tabagisme:
 - Chez l'homme: 91%
 - Chez la femme: 57%

Tabac et cancer du poumon: effet de la durée

- Doubler la dose de cigarettes (quotidienne ou cumulée) double le risque
- Doubler la durée du tabagisme revient à augmenter le risque d'un facteur 2^4 (16) à 2^5 (32), disons 20 fois !

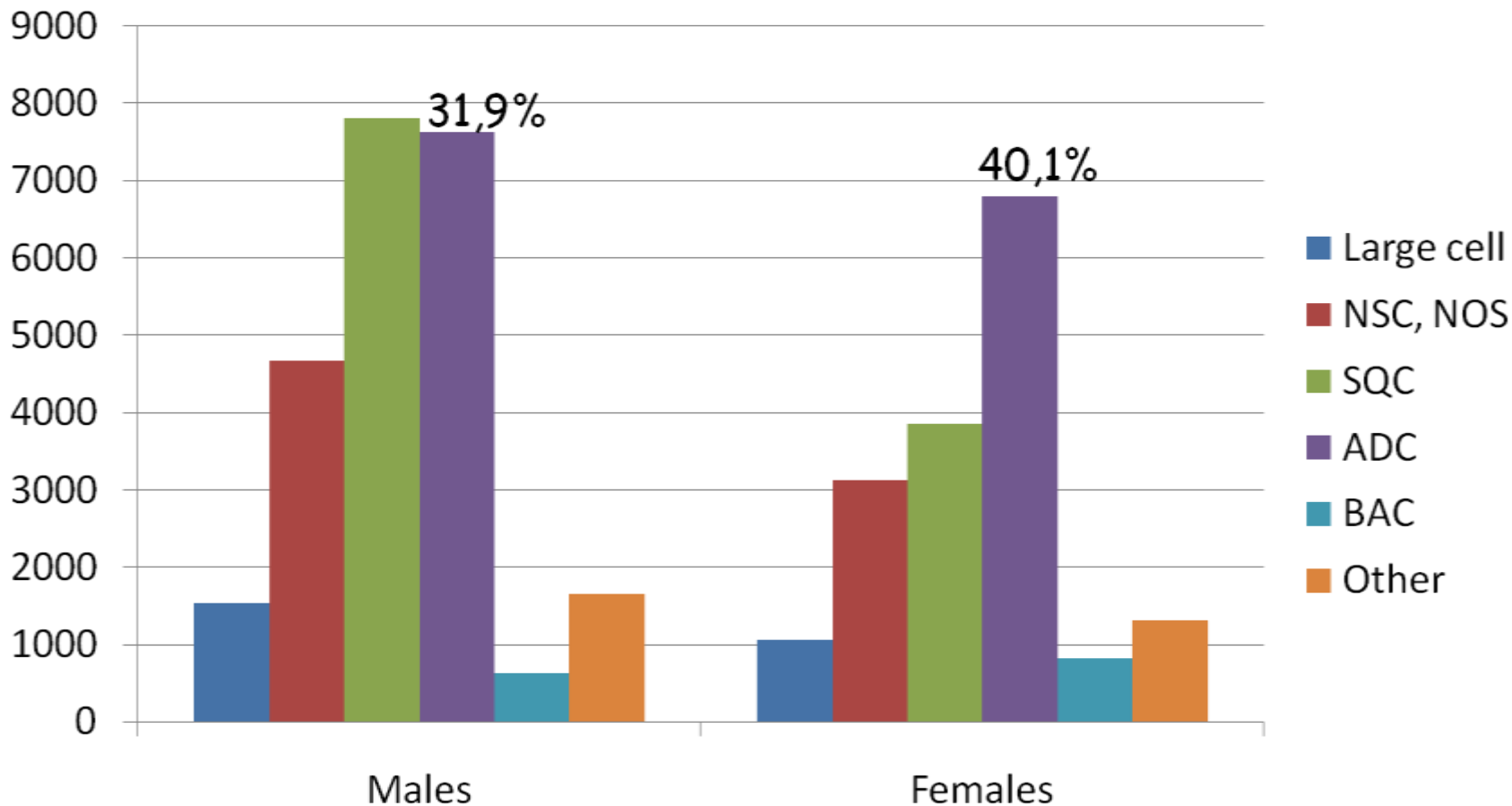
Effet de l'âge d'initiation du tabagisme sur le risque relatif de cancer du poumon.



TABAC ET CANCERS

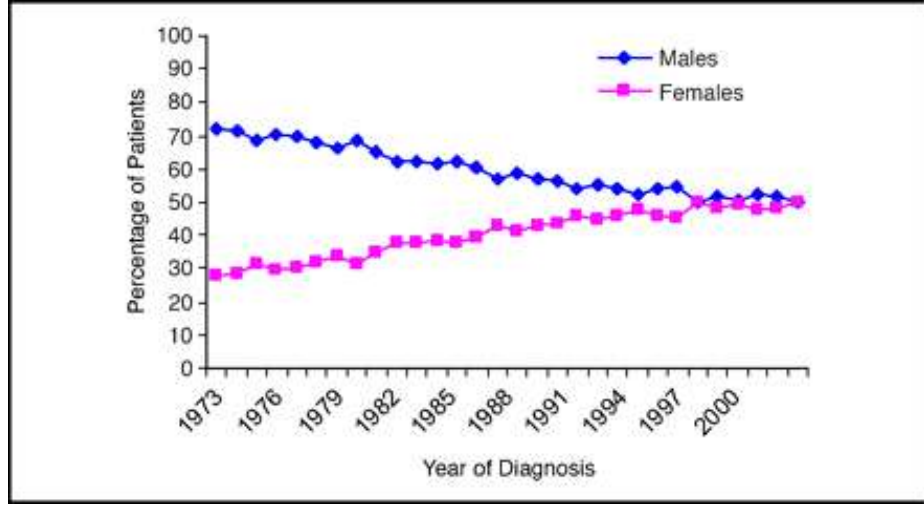
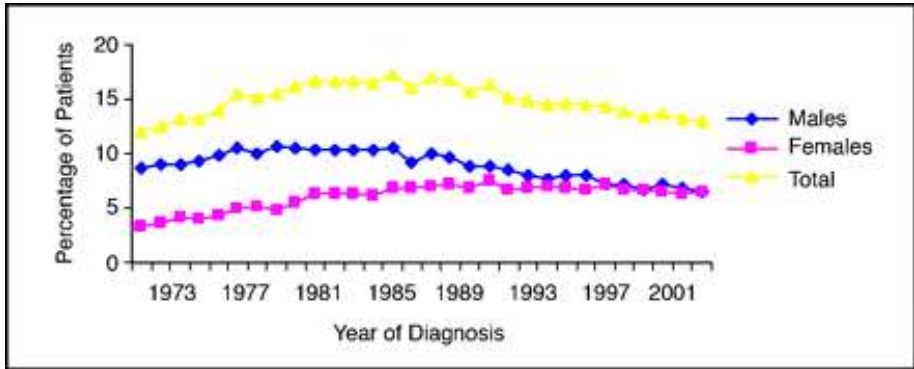
- Présence d'au moins une cinquantaine de carcinogènes dans la fumée de tabac: hydrocarbures polycycliques aromatiques - HPA, (benzopyrène), nitrosamines, etc
- Les cigarettes dites légères ne diminuent pas le risque de cancer mais ont modifié sa présentation anatomo-clinique:
 - diminution des cancers centraux au profit des cancers périphériques: le fumeur, qui a besoin de sa dose de nicotine, inhale plus souvent et plus profondément,
 - diminution des épidermoïdes au profit des adénocarcinomes, par modification des carcinogènes présents dans la fumée (augmentation des nitrosamines aux dépens des HPA).

National survey of non-small cell lung cancer in the United States



Lung Cancer 2007; 57: 253-260

Changing Epidemiology of Small-Cell Lung Cancer in the United States Over the Last 30 Years: Analysis of the Surveillance, Epidemiologic, and End Results Database



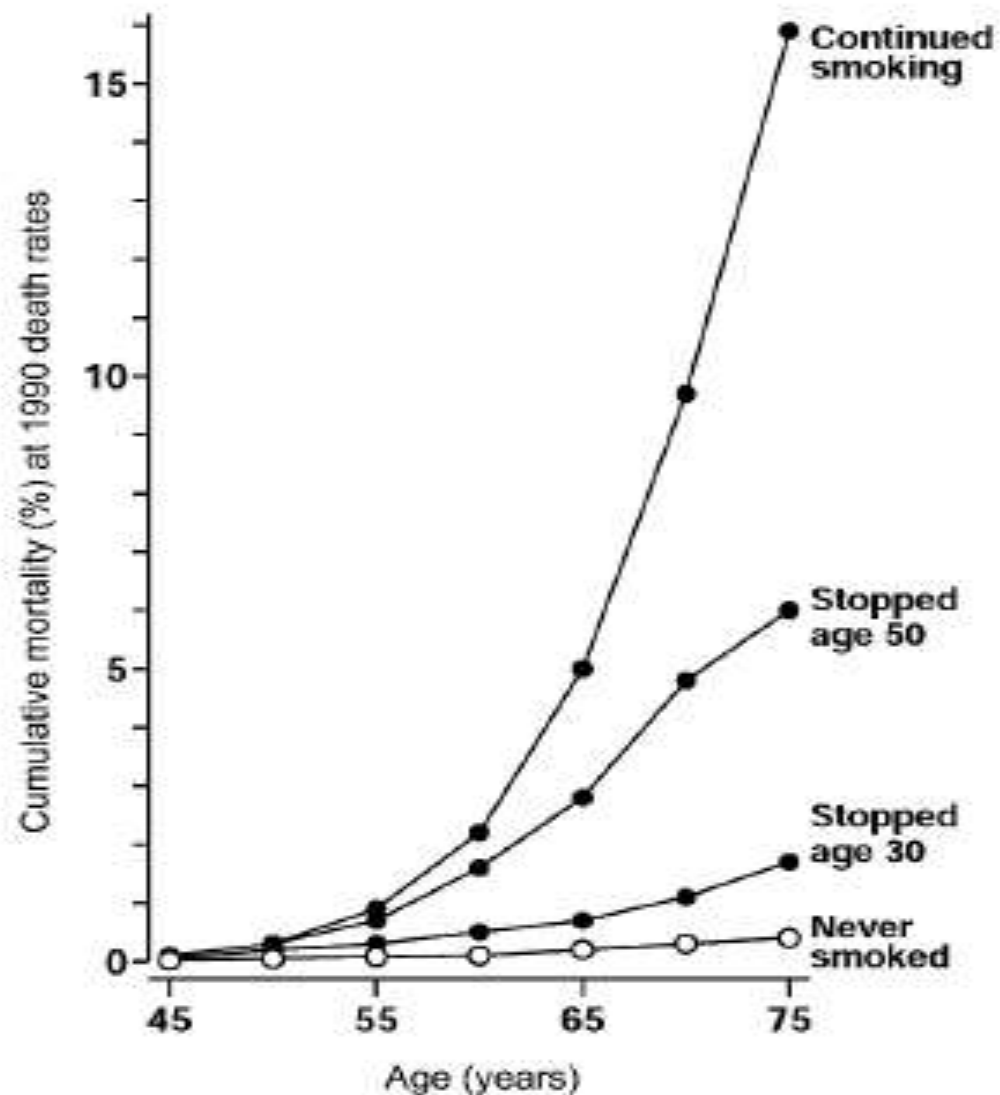
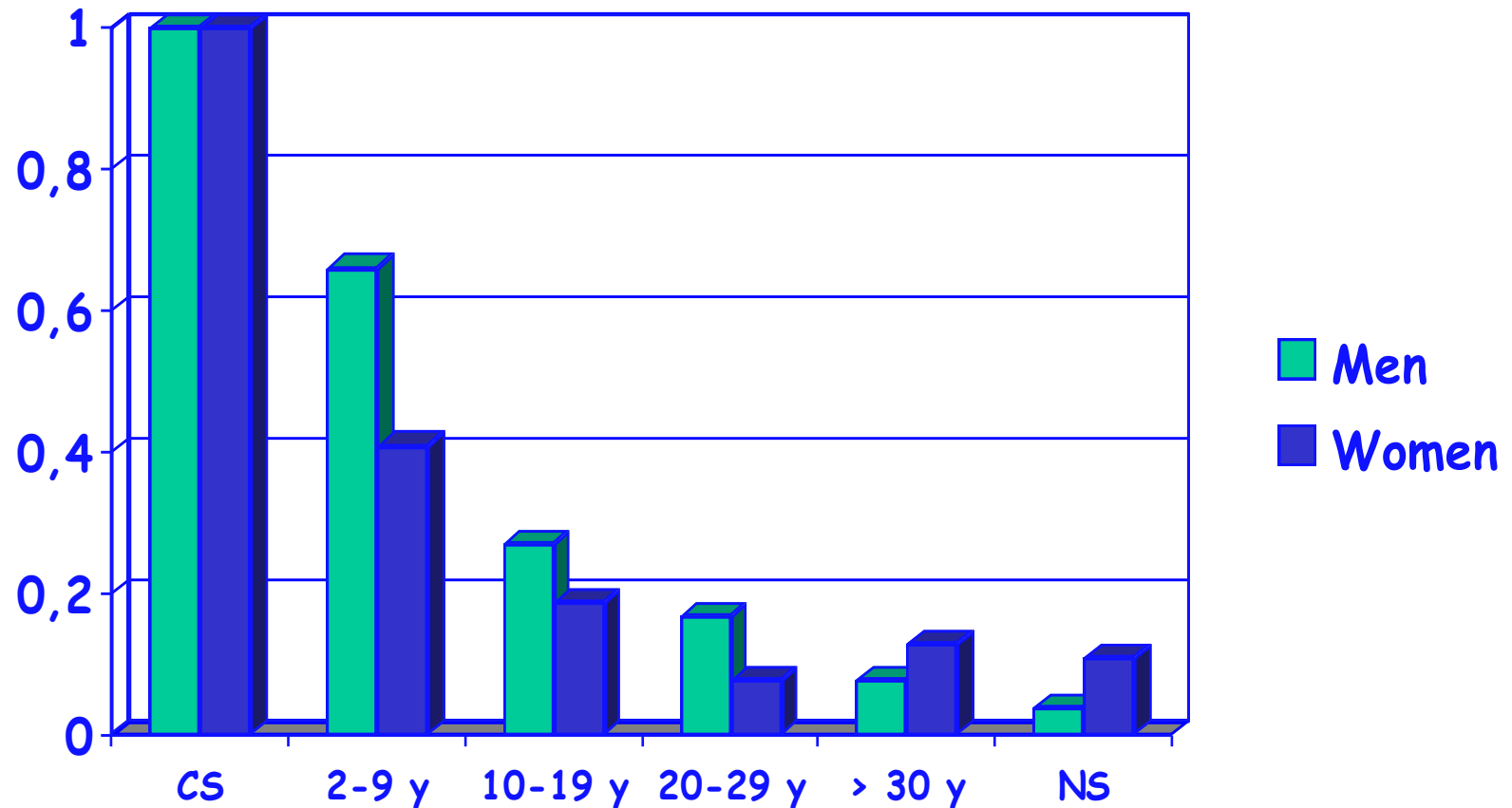


Fig. 2.2.3 Lung cancer mortality in UK current and former male smokers by age at quitting

Effect of smoking cessation on lung cancer risk



Simonato et al. Int J Cancer 2001;91:876-87.

En juin 2002, l'OMS déclare
que l'exposition passive à la
fumée de tabac est
cancérogène pour le poumon !

Le risque relatif pour
un fumeur passif de
développer un cancer du
poumon est de 1,25 (soit
25% d'augmentation du
risque par comparaison avec
un non fumeur non enfumé).



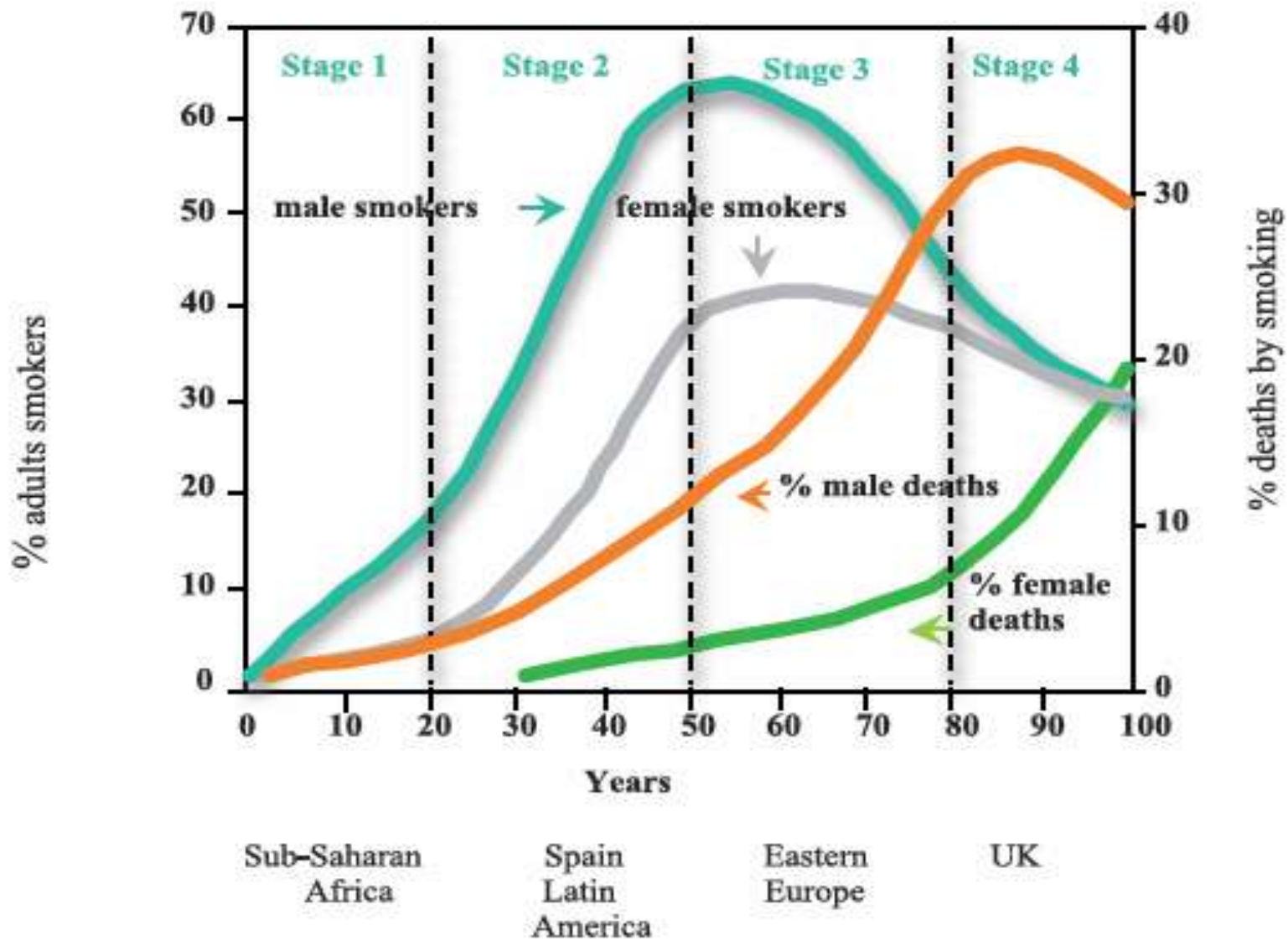
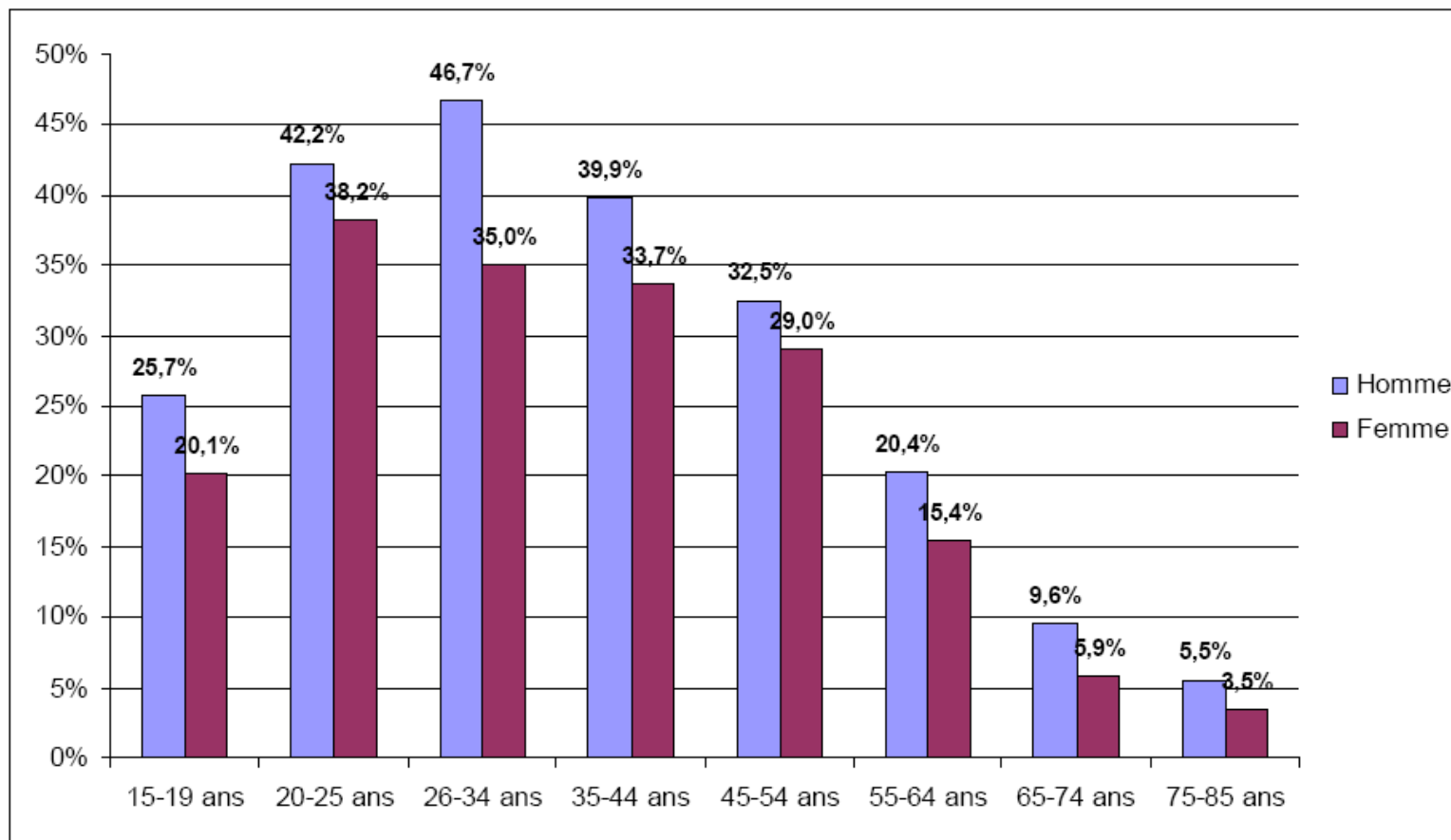


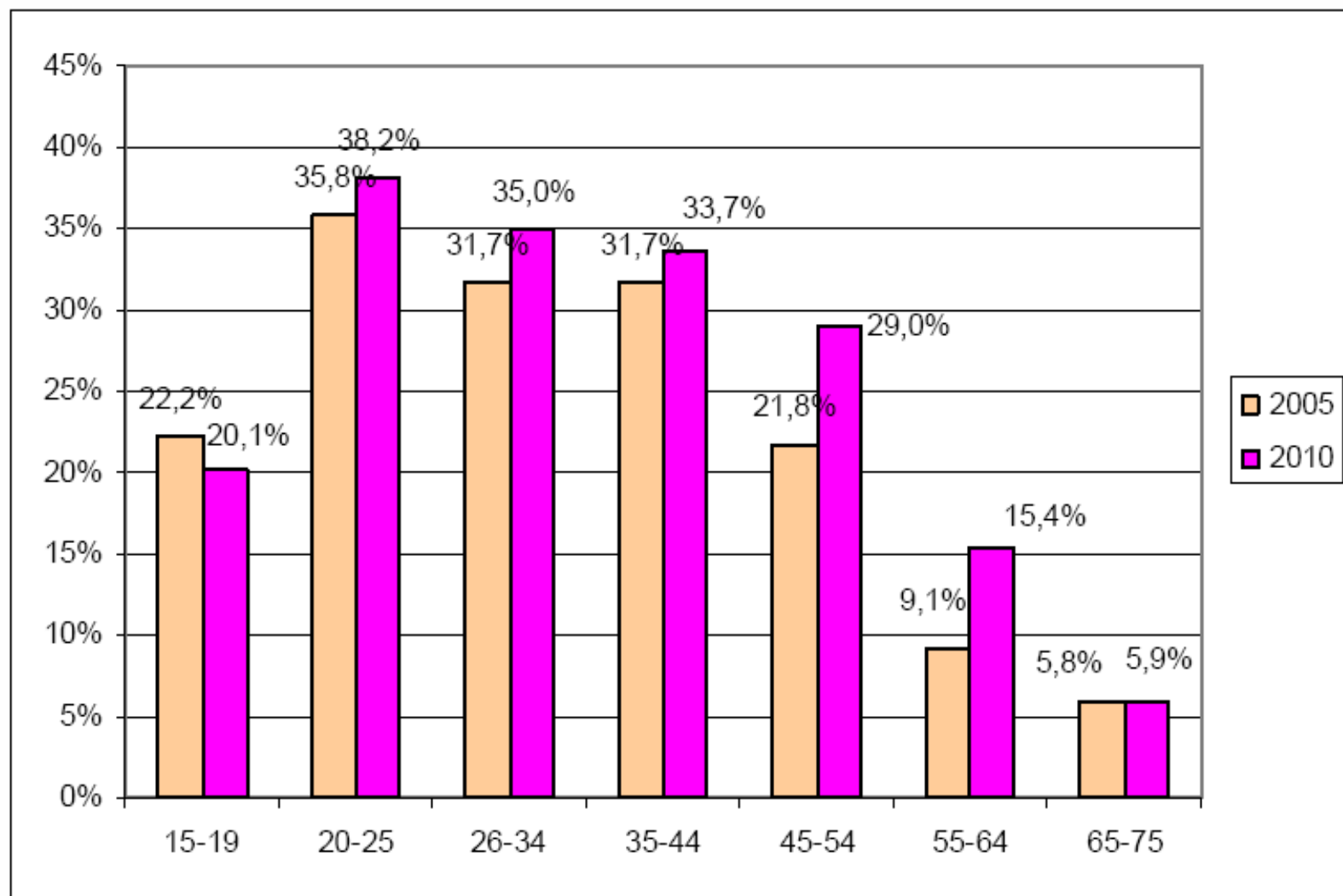
Fig. 2.2.1 Stages of the tobacco epidemic

Figure 1 : Proportions de fumeurs quotidiens de tabac en 2010, suivant l'âge et le sexe



Source : Baromètre Santé 2010, INPES

Figure 2 : Evolution de l'usage quotidien de tabac parmi les femmes (15-75 ans)



Sources : Baromètres Santé 2005 et 2010, INPES

Tableau I : Prévalence du tabagisme quotidien chez les femmes nées entre 1946 et 1965

	1946-1950	1951-1955	1956-1960	1961-1965
2005	10,5%	19,6%	23,7%	29,5%
2010	12,2%	18,4%	28,1%	29,9%

Figure 4 : Evolution du tabagisme actuel (occasionnel ou quotidien) depuis les années 1970

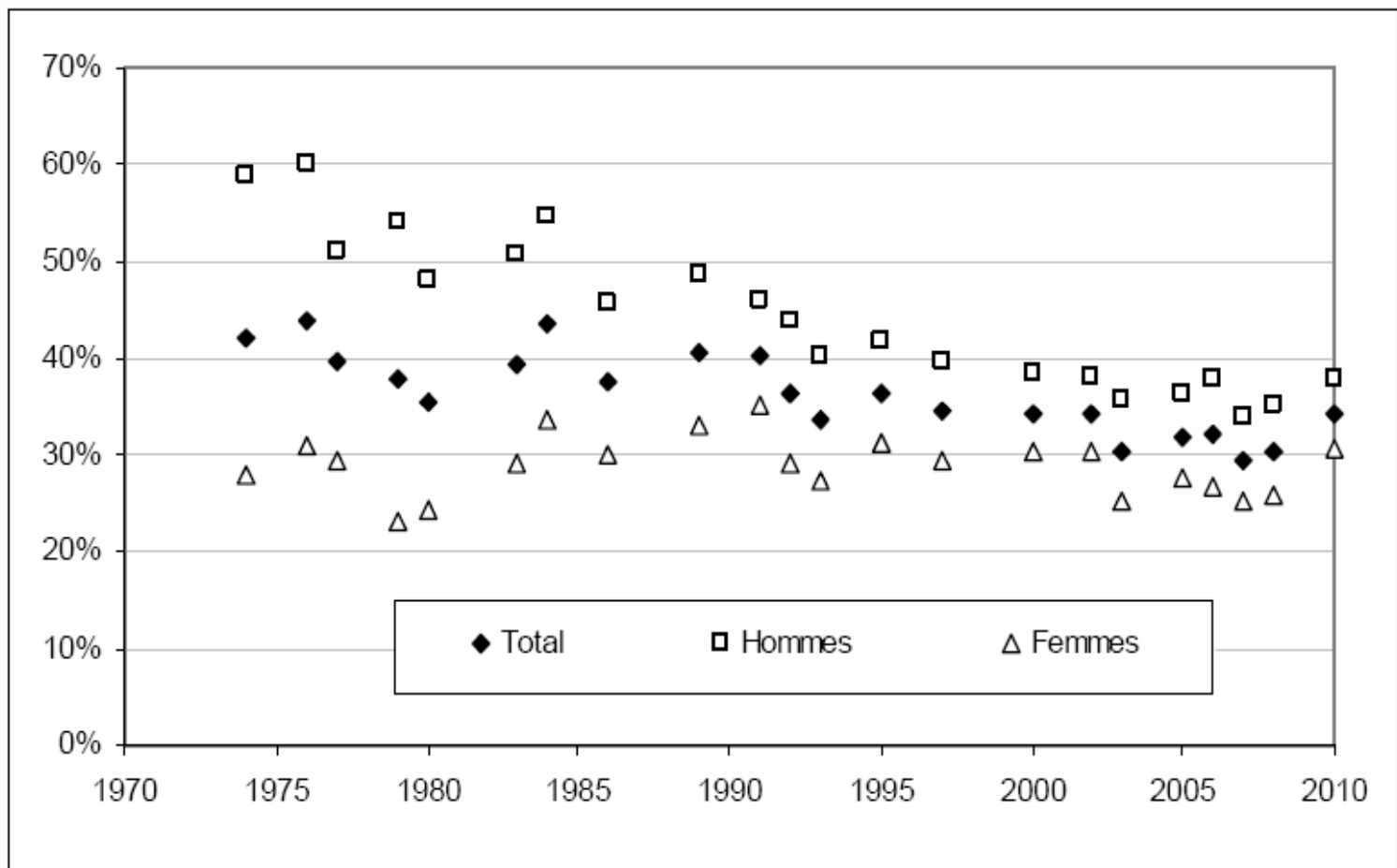


Table 1—Sex Differences in Lung Cancer

Characteristics	Sex Differences
Risk	Women may be at greater risk for lung cancer than men
Molecular variables	Different metabolism of tobacco-related carcinogens Possible association with HPV infection Women have relatively less DRC Increased frequency of K-ras
Response to therapy	Women have increased response rates to cisplatin-based chemotherapy compared with men
Outcome	Women have better outcome stage for stage than men

Table 5. Prospective studies reporting direct comparisons of lung cancer rates for women and men with comparable histories of cigarette smoking

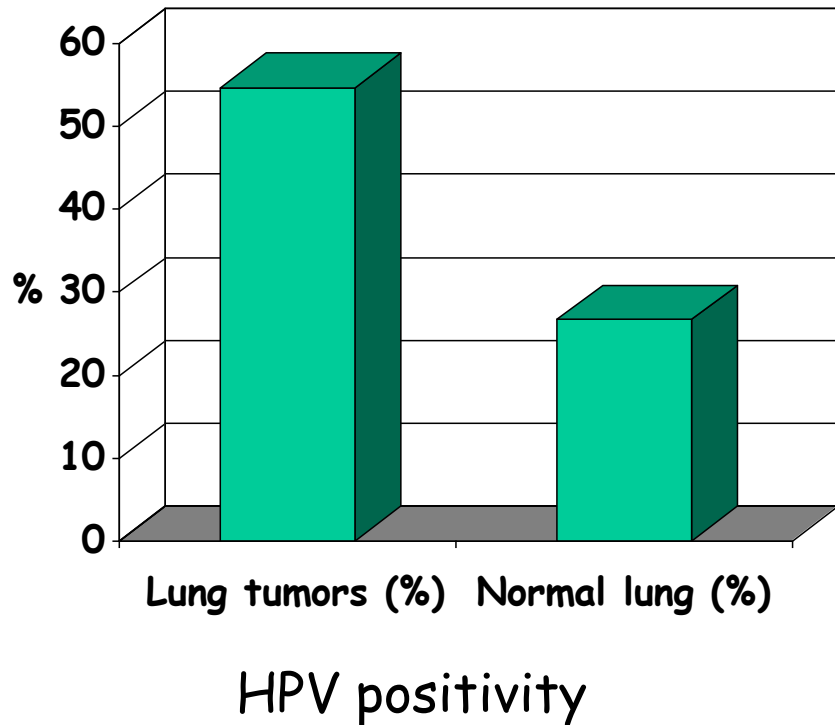
First author, year (reference)	Study description	Cases, women/men*	Hazard or rate ratio (95% CI)†
Bach, 2003 (18)	Carotene and Retinol Efficacy Trial (CARET) among heavy smokers aged 50–60 years‡ and men with high asbestos exposure aged 45–69 years in the United States; lung cancer incidence, 1985–1996; hazard ratio among ever smokers, adjusted for age, asbestos exposure, smoking duration, average number of cigarettes smoked per day while smoking, time since quitting, and study drug.	338/732	0.9 (0.9 to 1.1)§
Prescott, 1998 (5)	Three Danish population-based cohort studies with subjects aged 20 years or older; lung cancer incidence, 1964–1993; rate ratio among ever smokers adjusted for age, pack-years (current), smoking duration (former), inhale (yes/no), and cohort.	203/664	0.8 (0.3 to 2.1)§
Thun, 1995 (6,7)	American Cancer Society cohort aged 30 years or older; lung cancer mortality: CPS-II, 1982–1988; rate ratio among current smokers, adjusted for age, number of cigarettes smoked per day, and smoking duration.	1077/1871	0.6 (0.6 to 0.7)
Friedman, 1997 (19)	Kaiser-Permanente cohort aged 35 years or older in the United States; lung cancer mortality, 1979–1987.		
	(i) Rate ratio among current smokers, adjusted for age and number of cigarettes smoked per day (2 levels), identical on separate adjustment for age and smoking duration.	50/51	0.8 (0.6 to 1.2)¶
	(ii) Rate ratio among former smokers, adjusted for age and duration (3 levels).	14/26	0.6 (0.3 to 1.0)¶
Nilsson, 2001 (20)	Swedish population-based cohort aged 18–69 years; lung cancer mortality, 1963–1996; rate ratio among current smokers and inhalers, adjusted for age, residence and number of cigarettes smoked per day.	84/167	<1.0#
Marang-van de Mheen, 2001 (21)	Scottish population-based cohort aged 45–64 years; lung cancer mortality, 1972–1996; estimated rate ratios among all current smokers and for those who inhaled, adjusted for age and number of cigarettes smoked per day.	217/446	<1.0**

Lung cancer rates in men and women with comparable histories of smoking

Table 4. Hazard ratios for lung cancer for women in the Nurses' Health Study cohort compared with men in the Health Professionals Follow-up Study cohort, 1986–2000*

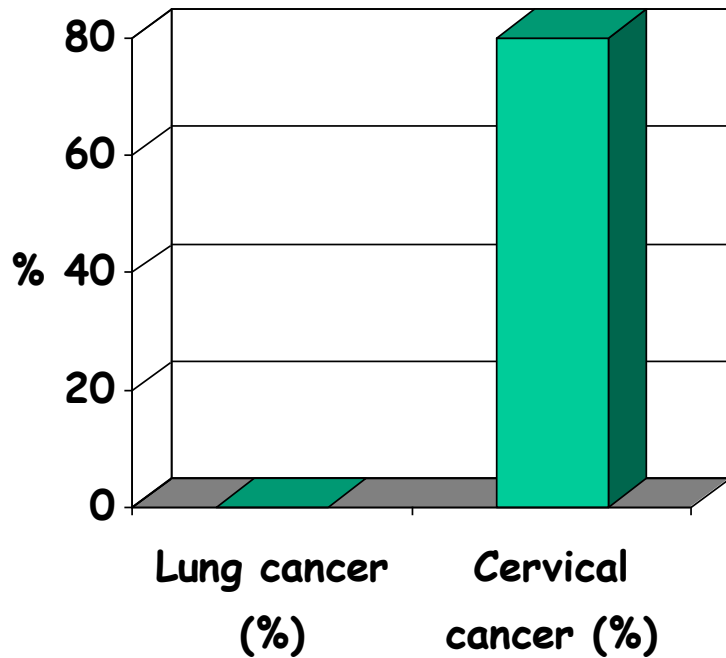
Analysis model	Current smokers	Former smokers	Ever smokers
Model 1 (no smoking factors)			
Cases, women/men	540/120	415/191	955/311
Hazard ratio (95% CI)	0.99 (0.79 to 1.24)	1.47 (1.19 to 1.80)	1.22 (1.05 to 1.42)
Model 2 (with number of cigarettes smoked per day, age at start, time since quitting)†			
Cases, women/men‡	509/110	398/176	907/286
Hazard ratio (95% CI)	1.11 (0.87 to 1.42)	1.18 (0.93 to 1.49)	1.11 (0.95 to 1.31)
Model 3 (with pack-years, time since quitting)†			
Cases, women/men‡	510/120	408/186	918/306
Hazard ratio (95% CI)	0.99 (0.78 to 1.24)	1.29 (1.03 to 1.62)	1.08 (0.92 to 1.27)

The Association of Human Papillomavirus 16/18 Infection with Lung Cancer among Nonsmoking Taiwanese Women



- Lung cancer is the leading cause of cancer death in Taiwanese women since 1982. High lung cancer mortality ratio of male:female in Taiwan (2:1) was observed, although less than 10% of female lung cancer patients are smokers
- In this study, 141 lung cancer patients and 60 noncancer control subjects were enrolled to examine whether HPV 16/18 DNA existed in lung tumor and normal tissues by nested PCR and in situ hybridization (ISH), respectively
- 77 (54.6%) of 141 lung tumors had HPV 16/18 DNA compared with 16 (26.7%; $p = 0.0005$) of 60 noncancer control subjects
- ISH data showed that HPV 16/18 DNA was uniformly located in lung tumor cells, but not in the adjacent nontumor cells

Human papillomavirus infection is not associated with bronchial carcinoma.



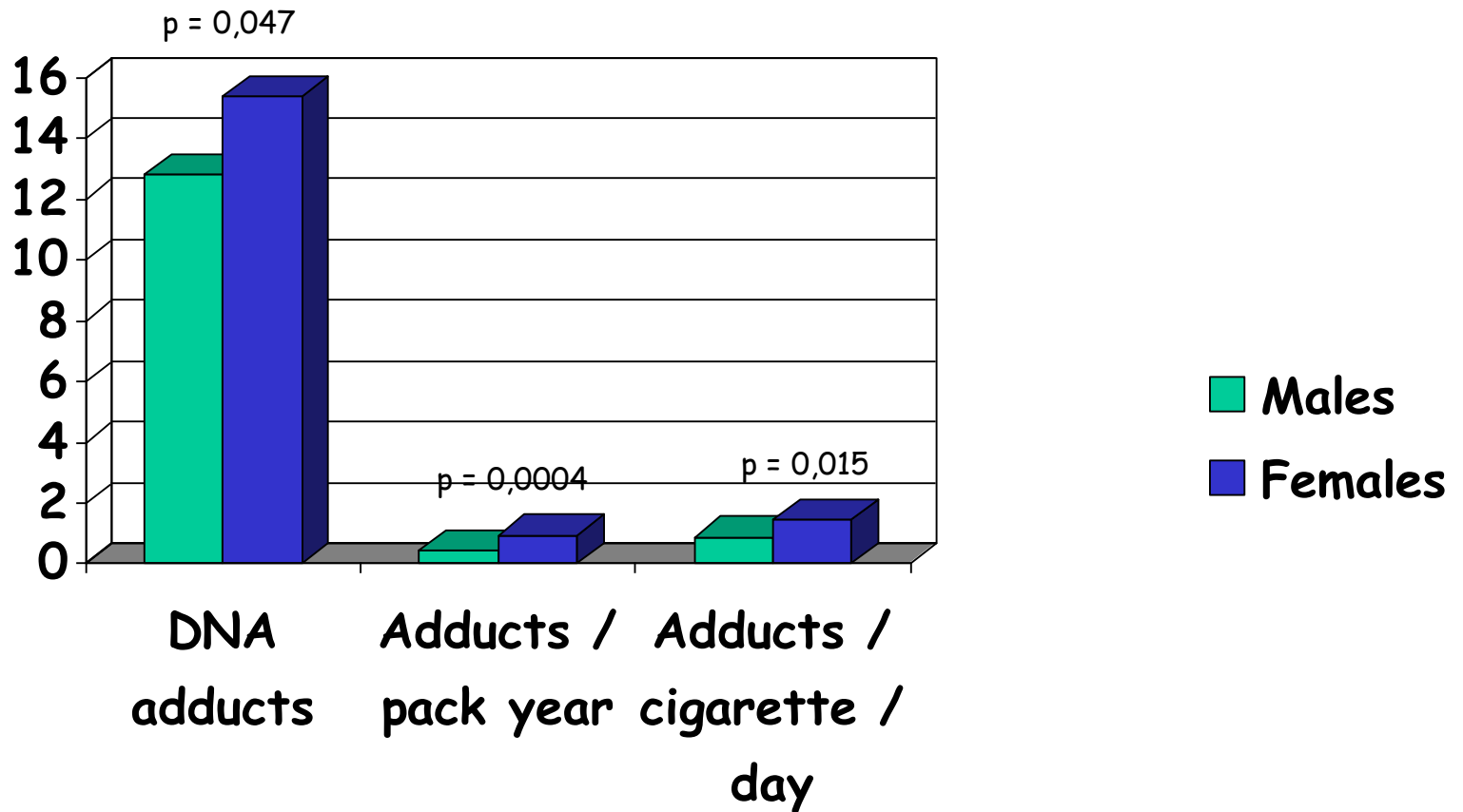
HPV positivity by
in situ hybridization and PCR

- An analysis of paraffin-embedded tissue from 32 squamous bronchial carcinomas and 15 cervical cancers utilizing both in situ hybridization and PCR techniques was negative for HPV in the lung cancer cases, while 12 of the 15 cervical cases were positive
- CC: it is possible that an association of HPV in lung cancer reflects the coexistence of increased and earlier smoking behavior with more frequent sexual contacts.

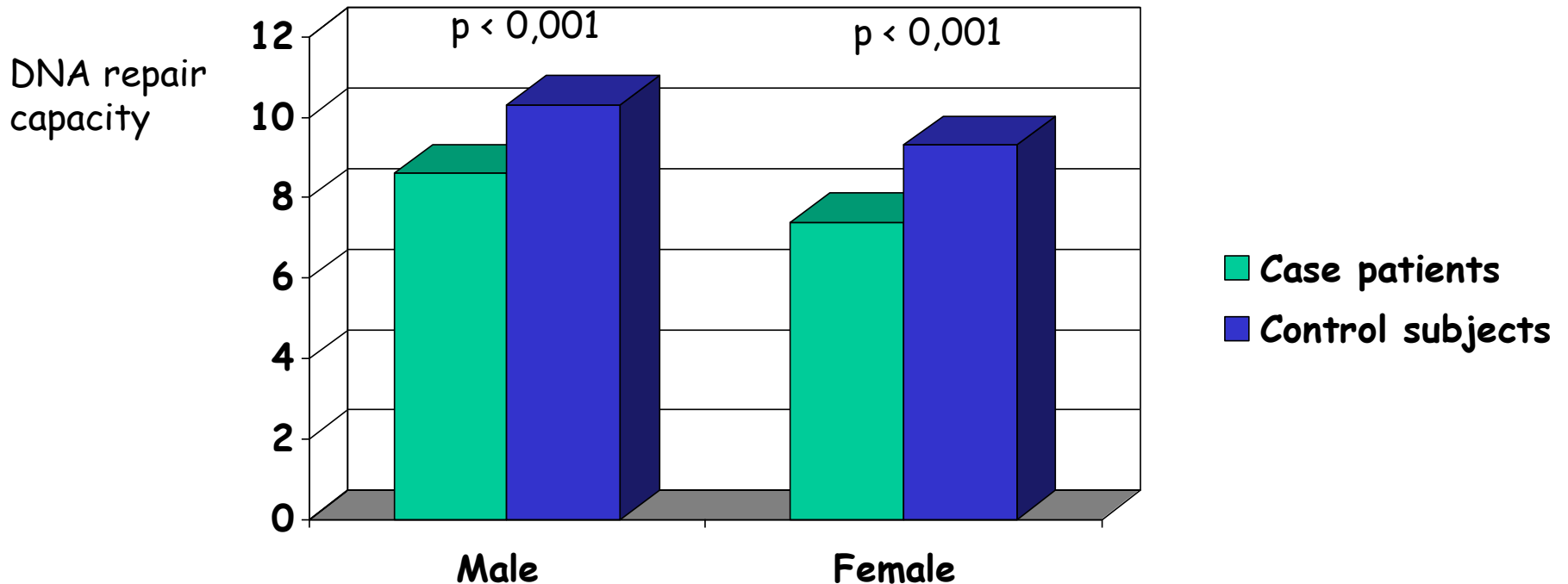
Sex-specific expression of gastrin-releasing peptide receptor: relationship to smoking history and risk of lung cancer

- GRPR is a receptor for the hormone GRP, which mediates cell proliferation in the lung
- Female never-smokers express this gene in their airway epithelial cells at a significantly higher frequency compared with males, perhaps related to the fact that the GRPR gene is located on the X chromosome (and women escape X-inactivation of the gene).

Sex differences in lung CYP1A1 expression and DNA adduct levels among lung cancer patients.



Repair of tobacco carcinogen-induced DNA adducts and lung cancer risk: a molecular epidemiologic study



Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial

- Lung cancer incidence was not affected :
 - 54 vs 50; HR, 1.04; 95% CI, 0.71-1.53

Hormone Replacement Therapy and Lung Cancer Risk.

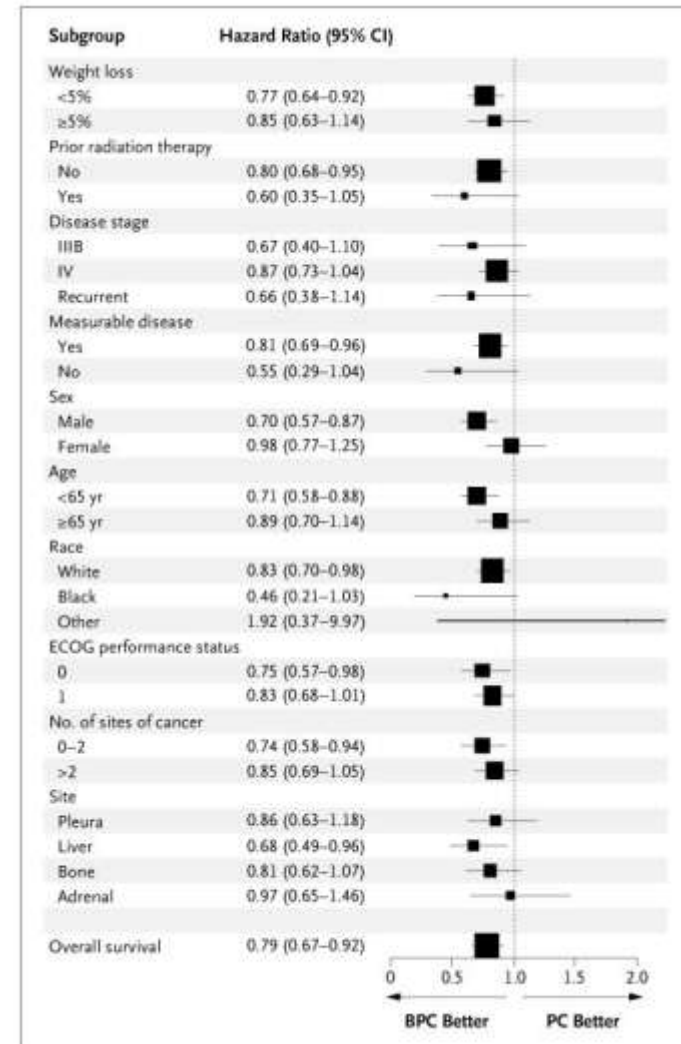
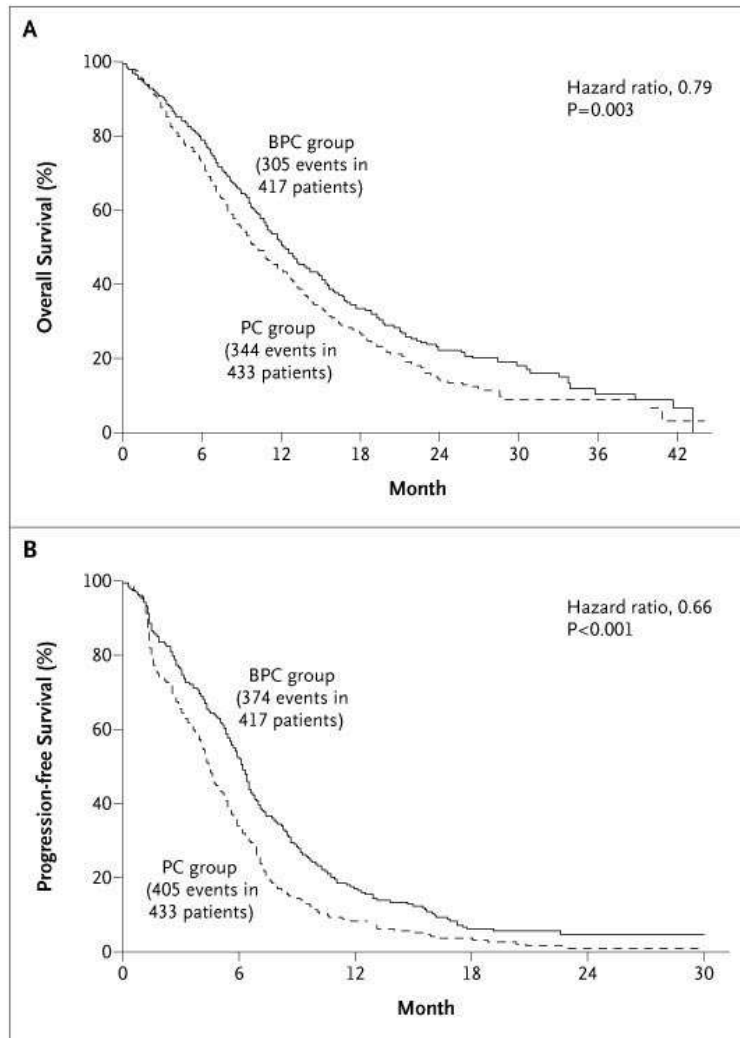
A Case-Control Analysis

- self-reported HRT use was compared among 499 women with lung cancer and 519 healthy age-matched controls
- HRT use was associated with an overall reduced risk of 34% [OR = 0.66; 95%CI: 0.51-0.89] of lung cancer, after adjusting for age, ethnicity, smoking status, education, body mass index, and menopausal status.

Table 1A 5-year survival rates in men and women by stage in NSCLC and SCLC [13]

	NSCLC		SCLC	
	Men (%)	Women (%)	Men (%)	Women (%)
All stages	14.9	19.6	5.6	7.2
Local disease	46.6	56.0	20.7	21.6
Regional disease	15.9	18.5	9.9	11.7
Metastatic disease	2.0	2.3	1.8	2.2

Paclitaxel-Carboplatin Alone or with Bevacizumab for Non-Small-Cell Lung Cancer



CONCLUSION

- The importance of stratification by sex in future trials is evident

European code against cancer

Many aspects of general health can be improved and many cancer deaths prevented, if we adopt healthier lifestyles:

1. Do not smoke; if you smoke, stop doing so. If you fail to stop, do not smoke in the presence of non-smokers.
2. Avoid Obesity.
3. Undertake some brisk, physical activity every day.
4. Eat a variety of vegetables and fruits every day: eat at least five portions daily. Limit your intake of foods containing fats from animal sources.
5. If you drink alcohol, whether beer, wine or spirits, moderate your consumption to two drinks per day if you are a man or one drink per day if you are a woman.
6. Care must be taken to avoid excessive sun exposure. It is specifically important to protect children and adolescents. For individuals who have a tendency to burn in the sun active protective measures must be taken throughout life
7. Comply strictly with regulations aimed at preventing occupational or environmental exposure to known cancer-causing substances. Follow advice of National Radiation Protection Offices.

There are Public Health programmes which could prevent cancers developing or increase the probability that a cancer may be cured:

8. Women from 25 years of age should participate in cervical screening. This should be within programmes with quality control procedures in compliance with "EU Guidelines for Quality Assurance in Cervical Screening".
9. Women from 50 years of age should participate in breast screening. This should be within programmes with quality control procedures in compliance with "EU Guidelines for Quality Assurance in Mammography Screening".
10. Men and women from 50 years of age should participate in colorectal screening. This should be within programmes with built-in quality control procedures.
11. Participate in vaccination programmes against Hepatitis B Virus infection.

Total Number of Cancer Deaths Avoided From 1991 to 2006 in Males and from 1992 to 2006 in Females.

