Centre Hospitalier LYON SUD

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INSTITUT DE CANCÉROLOGIE
DES HOSPICES CIVILS DE LYON

Epidémiologie et nouveaux facteurs de risque du cancer bronchique

M Locatelli Sanchez
S Couraud
PJ Souquet

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CONFLITS D'INTERET

Aucun avec le sujet traité

- tabac
- cannabis
- amiante
- diesel

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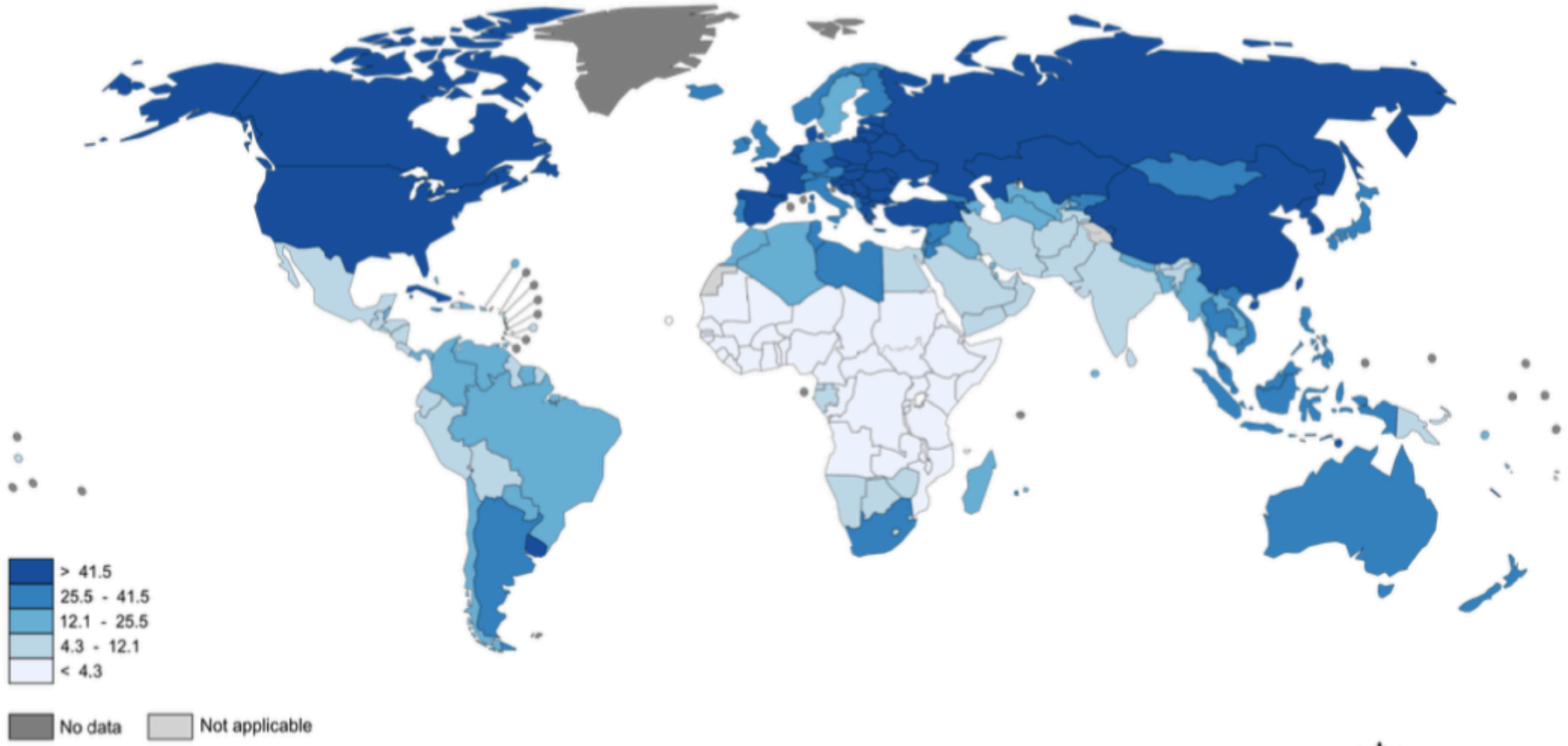
Estimated Lung Cancer Incidence Worldwide in 2012: Men



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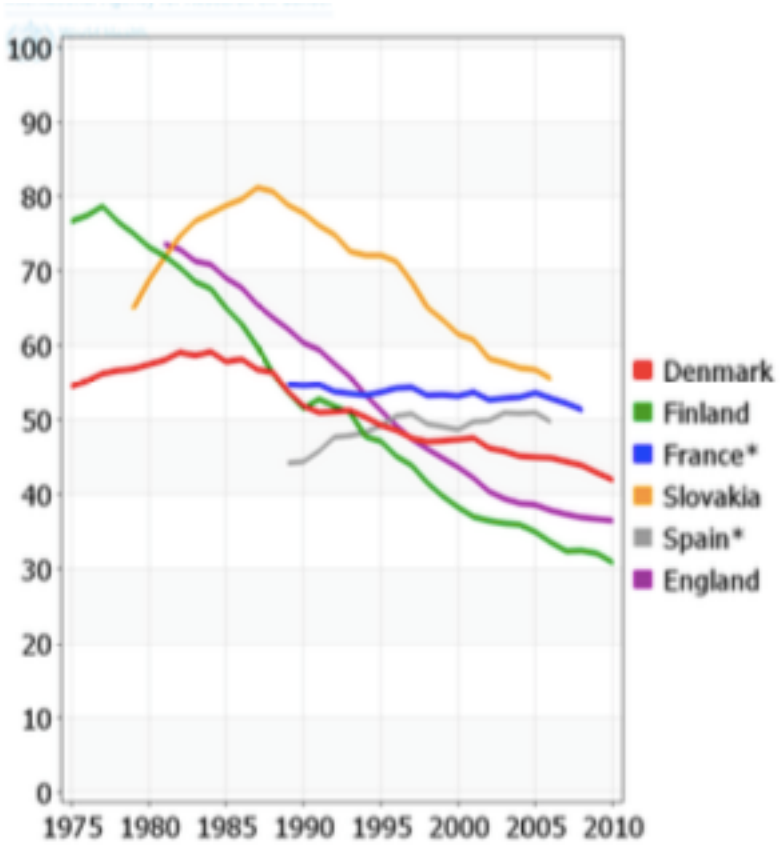
Data source: GLOBOCAN 2012
Map production: IARC
World Health Organization

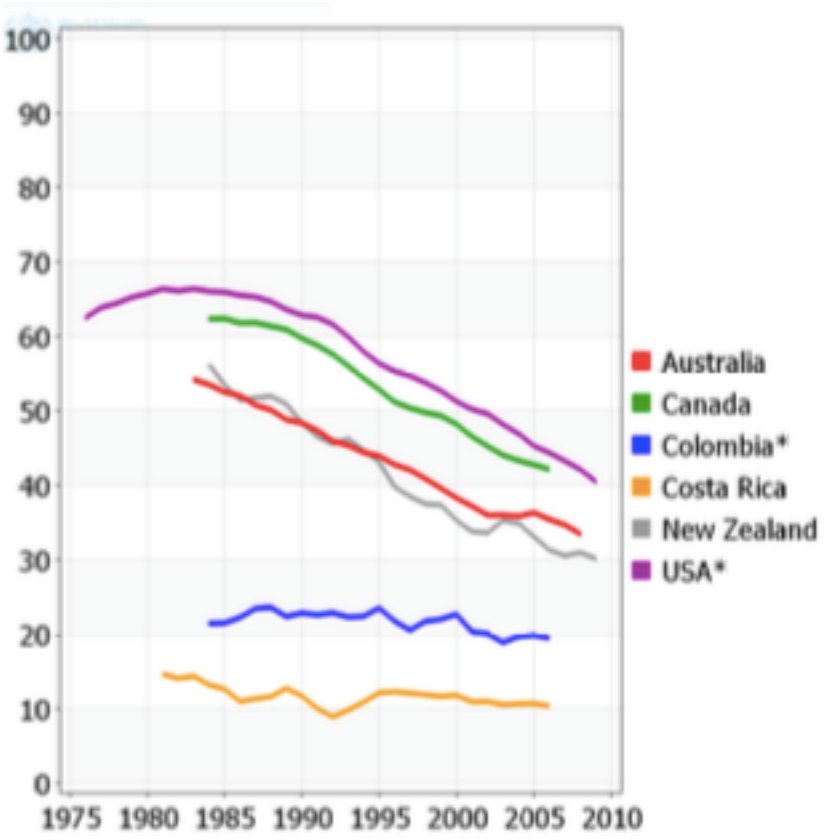
World Health Organization

Variation incidence



*Regional data

NORDCAN (www.ancr.nu)
ECO (eco.iarc.fr)
England: www.ons.gov.uk



*Regional data

CI5.iarc.fr
Australia: www.aihw.gov.au
New Zealand: www.health.govt.nz
USA: seer.cancer.gov

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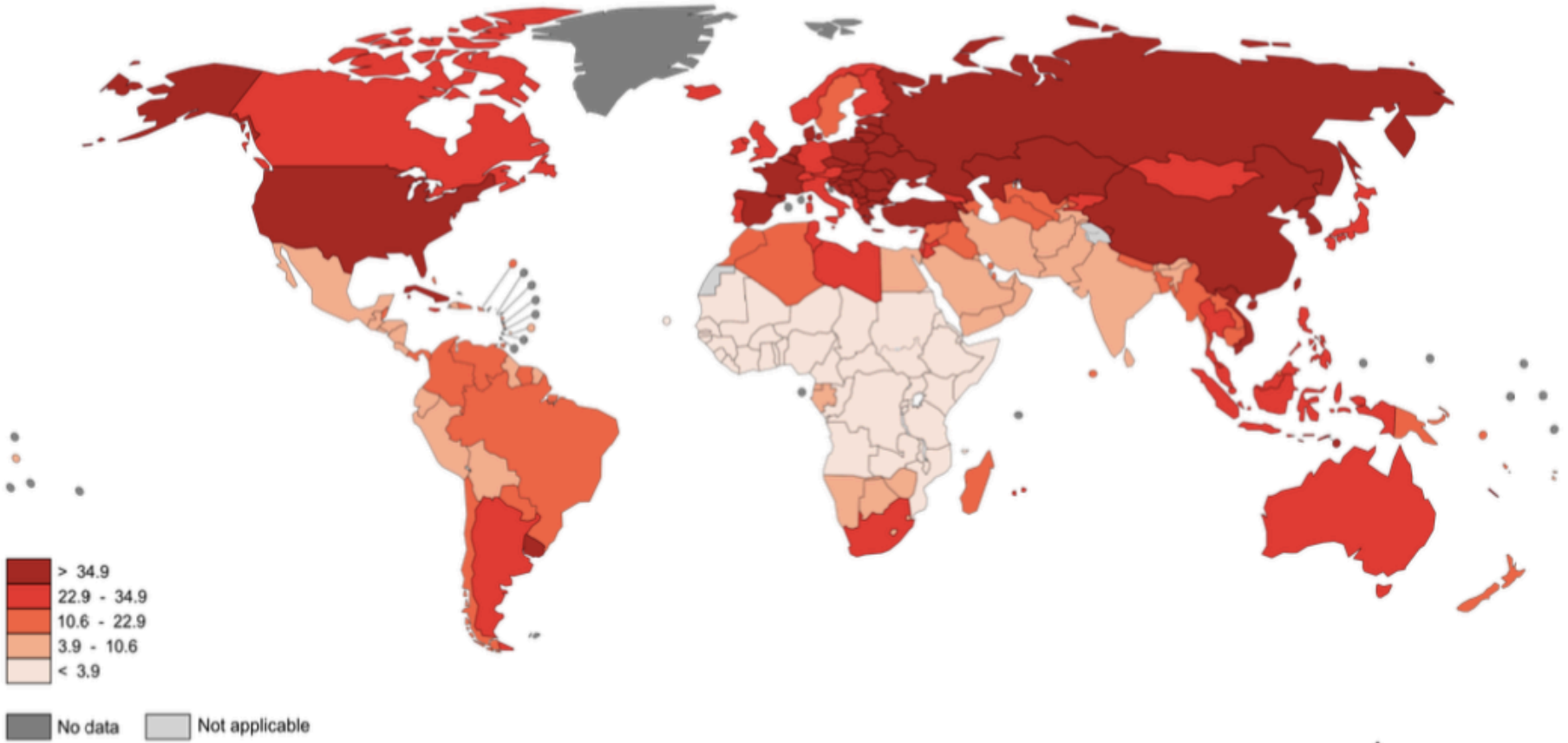
Estimated Lung Cancer Mortality Worldwide in 2012: Men



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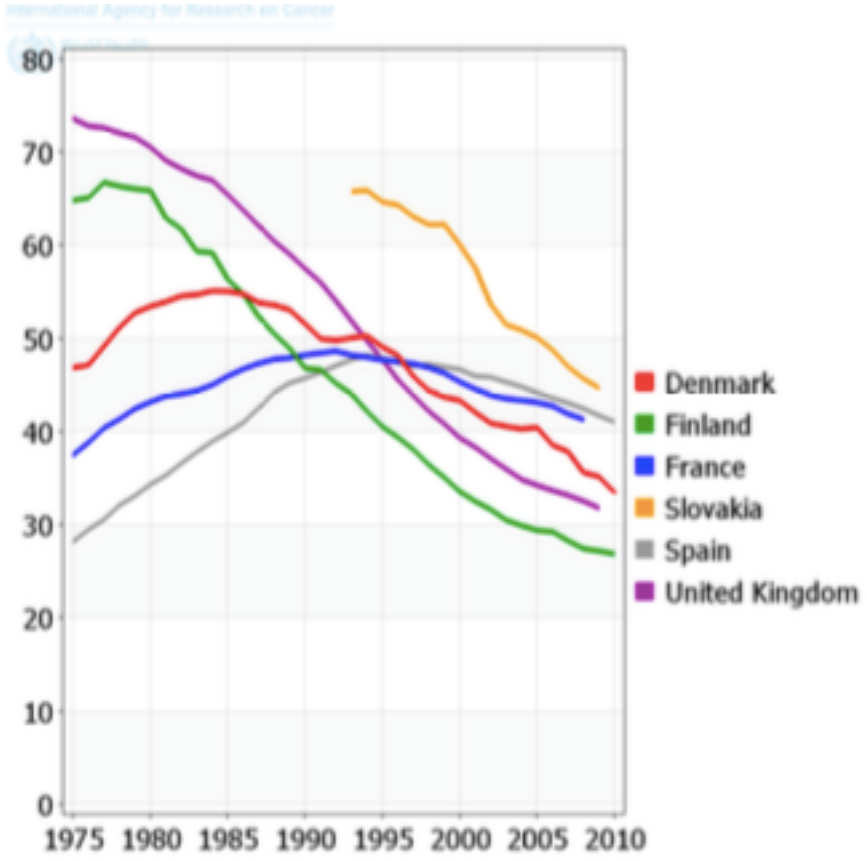
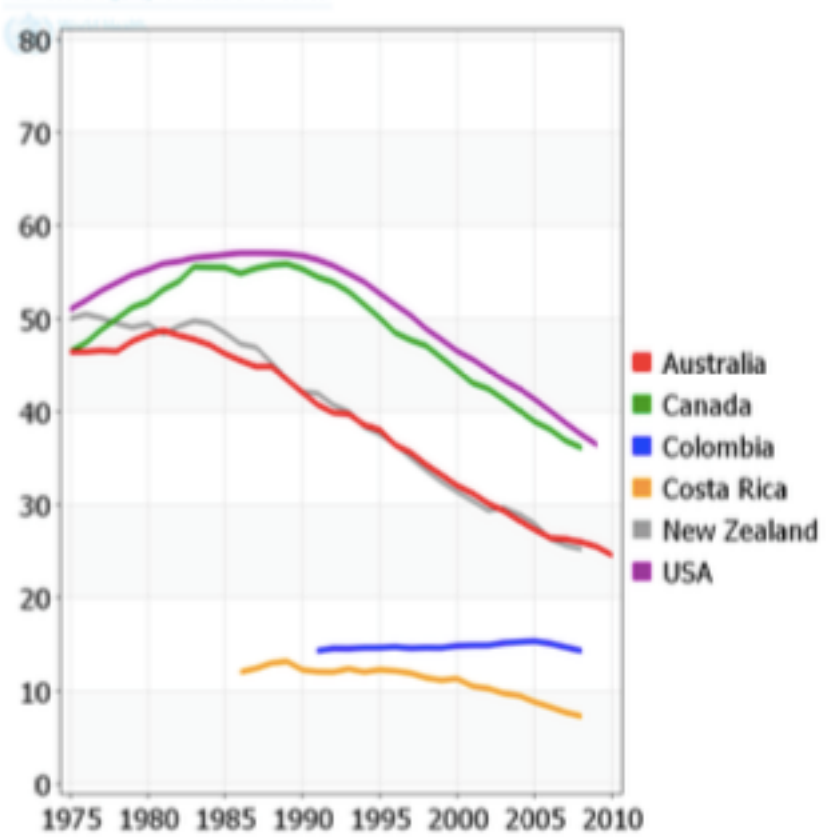
Variation mortalité



WHO (www.who.int/healthinfo/en/)



WHO (www.who.int/healthinfo/en/)

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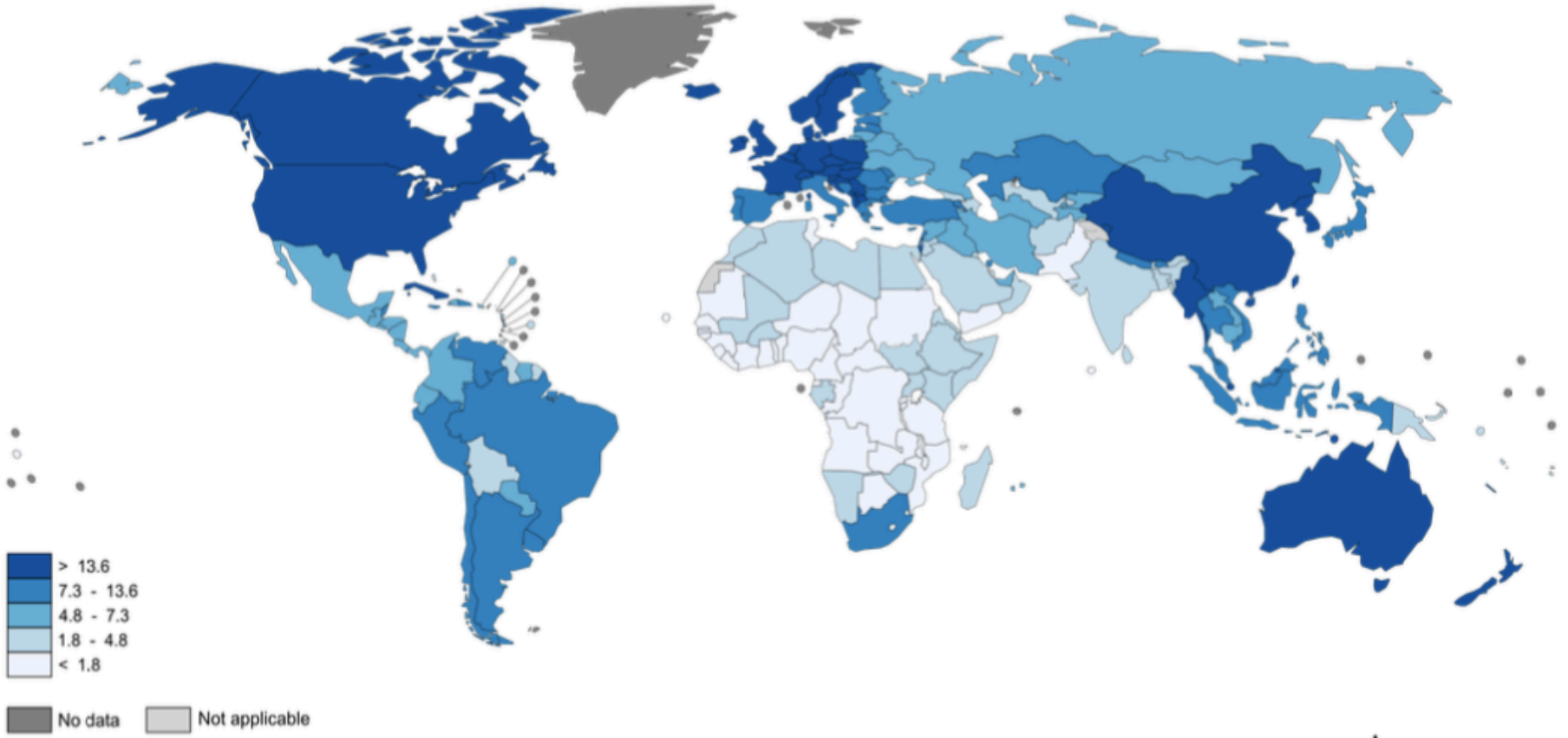
Estimated Lung Cancer Incidence Worldwide in 2012: Women



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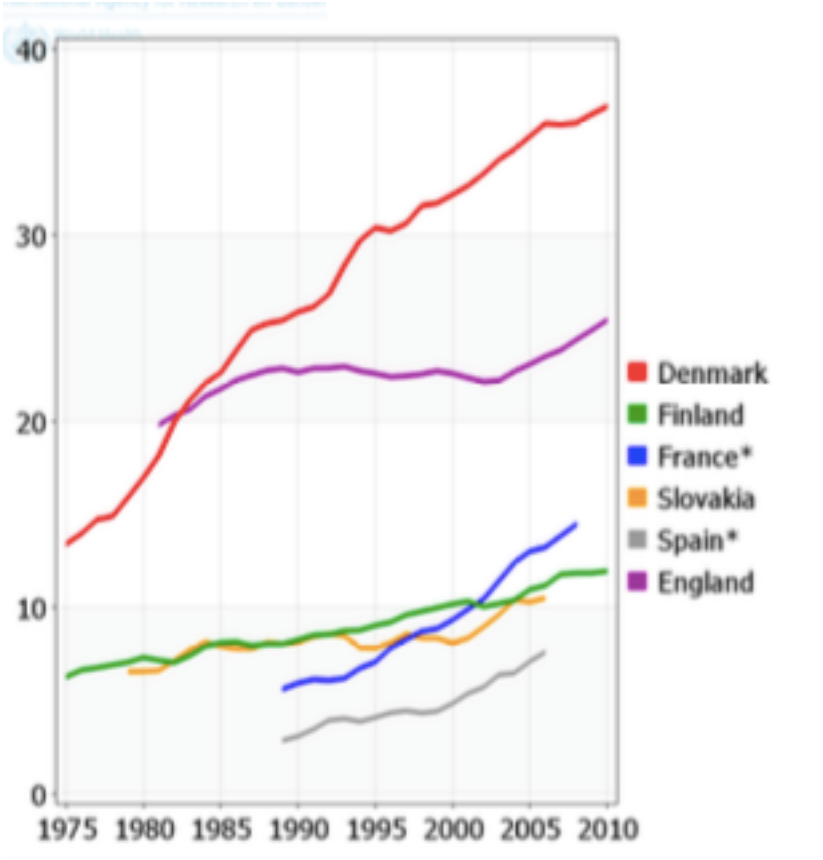
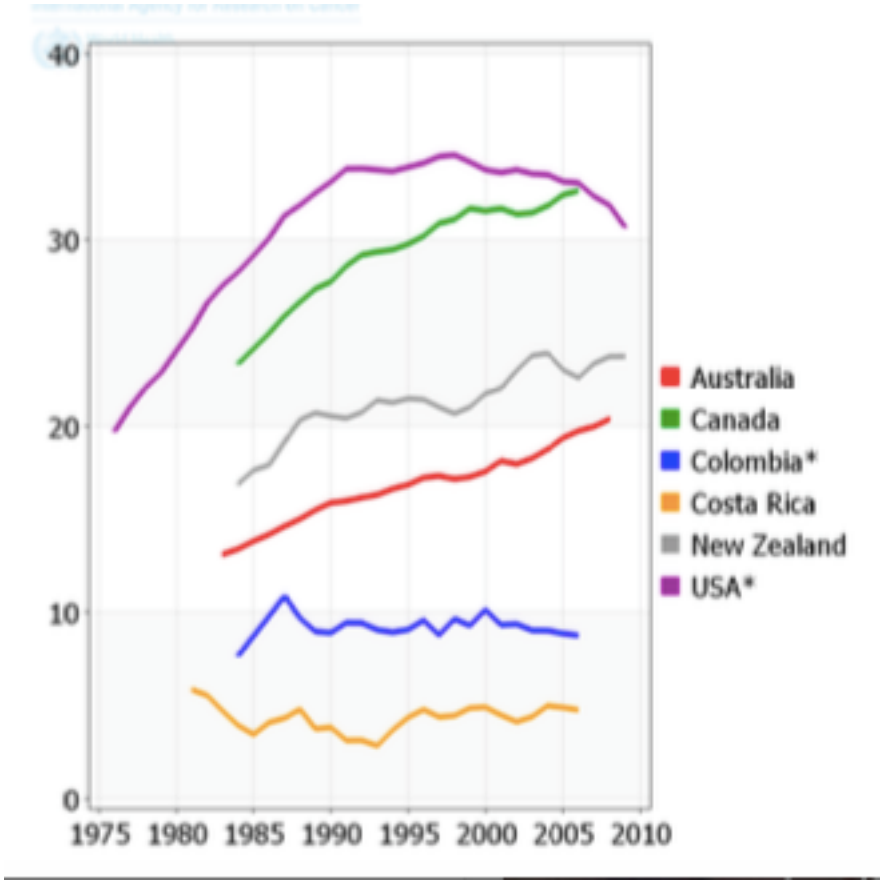
World Health Organization

Variation incidence





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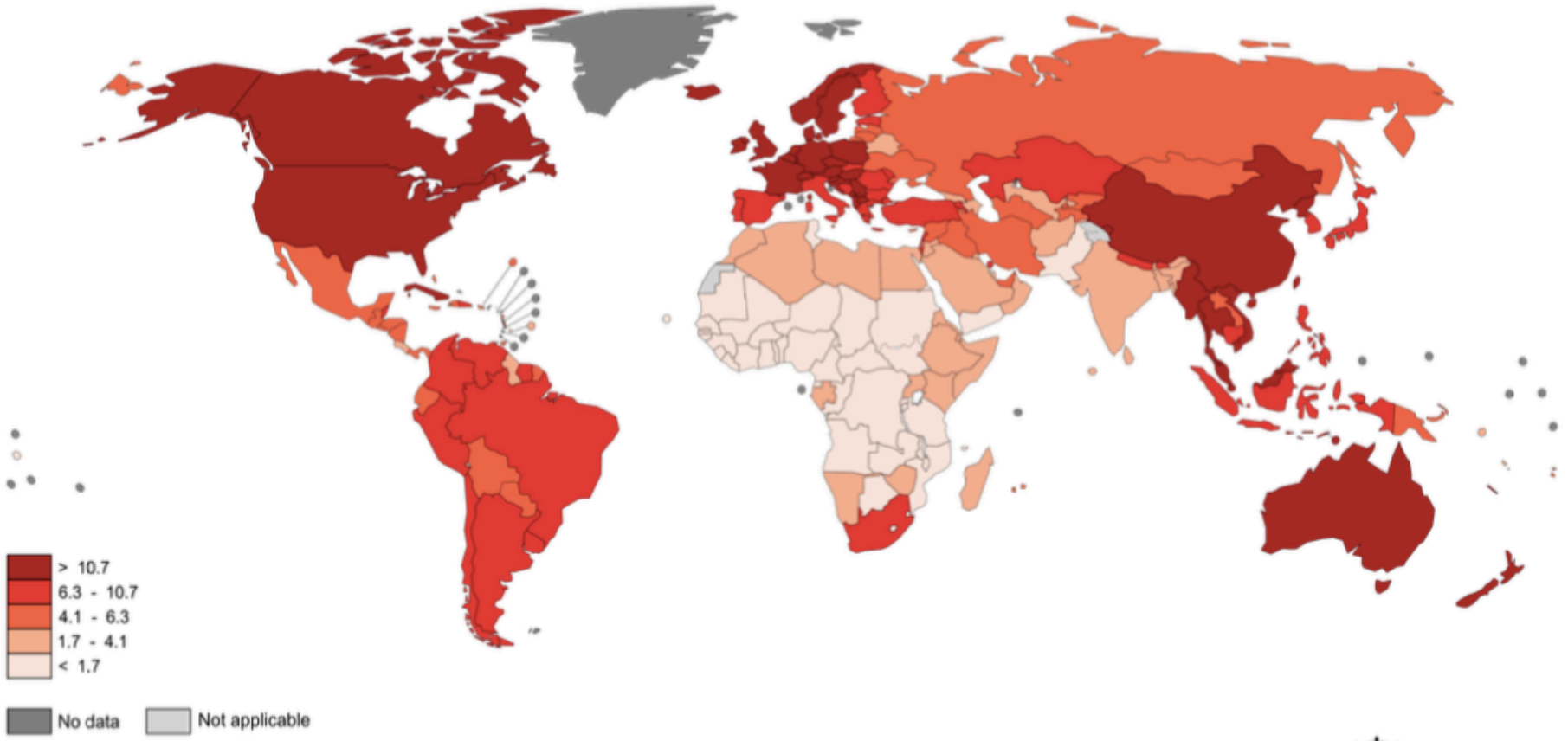

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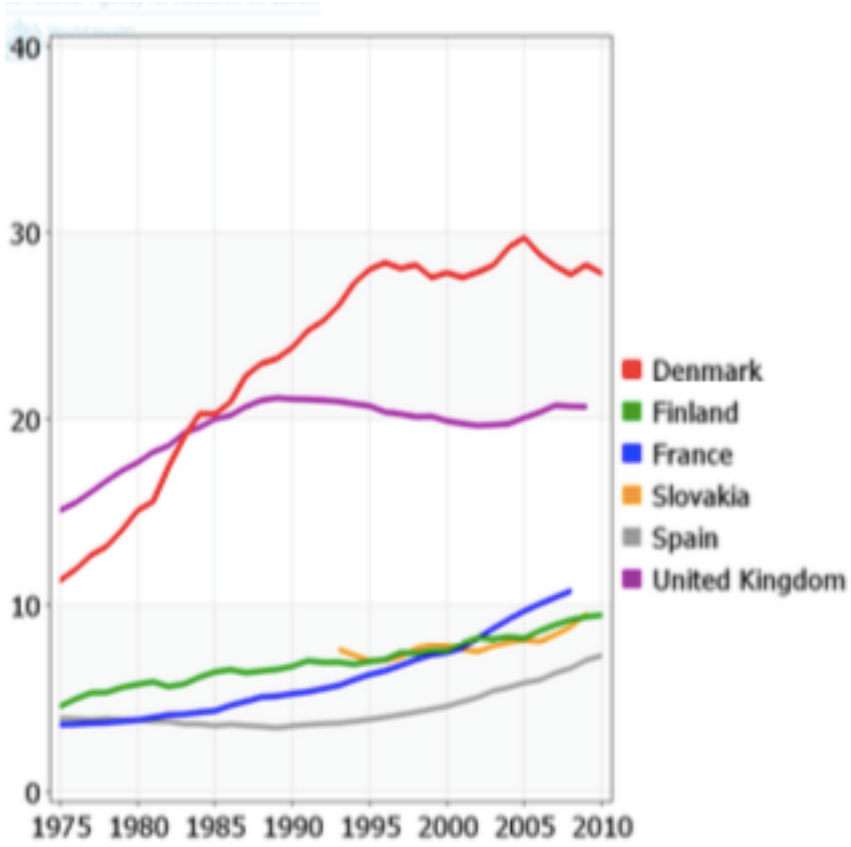
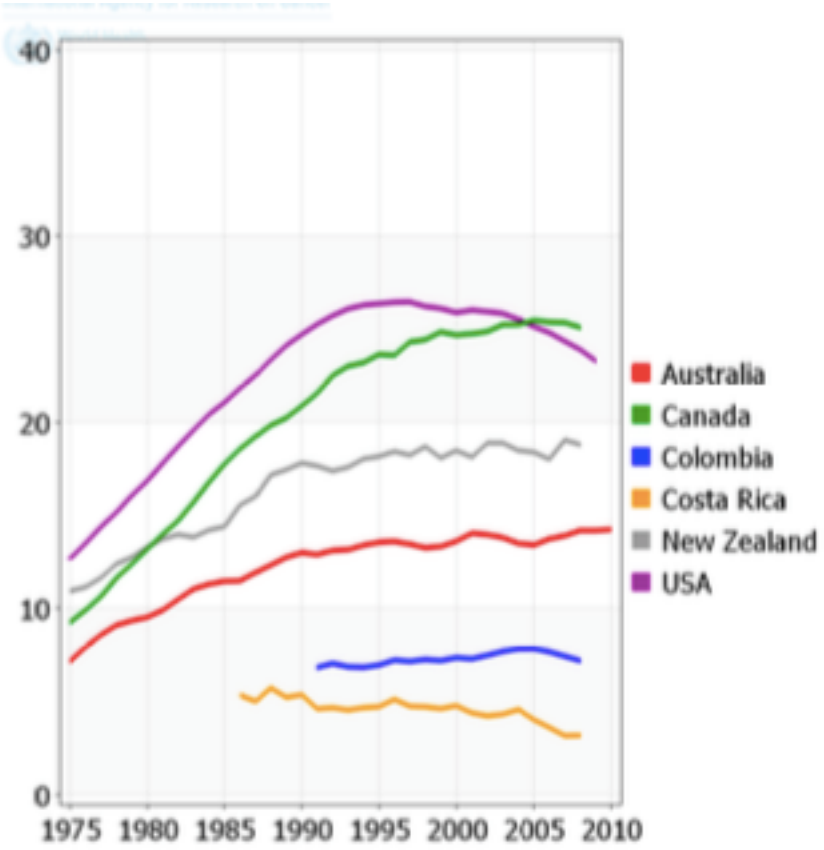


VHO (www.who.int/healthinfo/en/)



WHO (www.who.int/healthinfo/en/)

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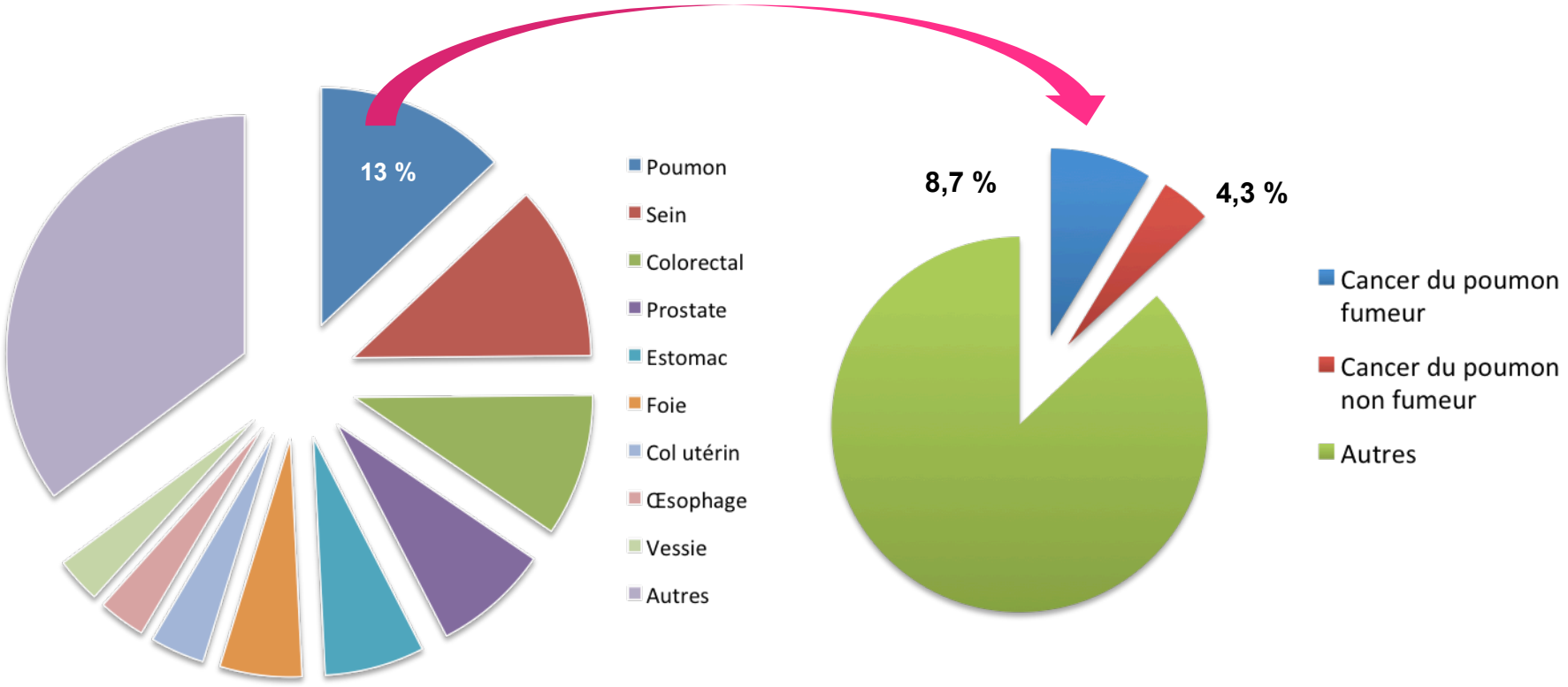
15 millions de nouveaux cas de cancers par an dans le monde
Cancer Bronchique: 13 % des cancers



WCLC 2015 - D'après Boffetta P et al., abstr. MS23.02, actualisé

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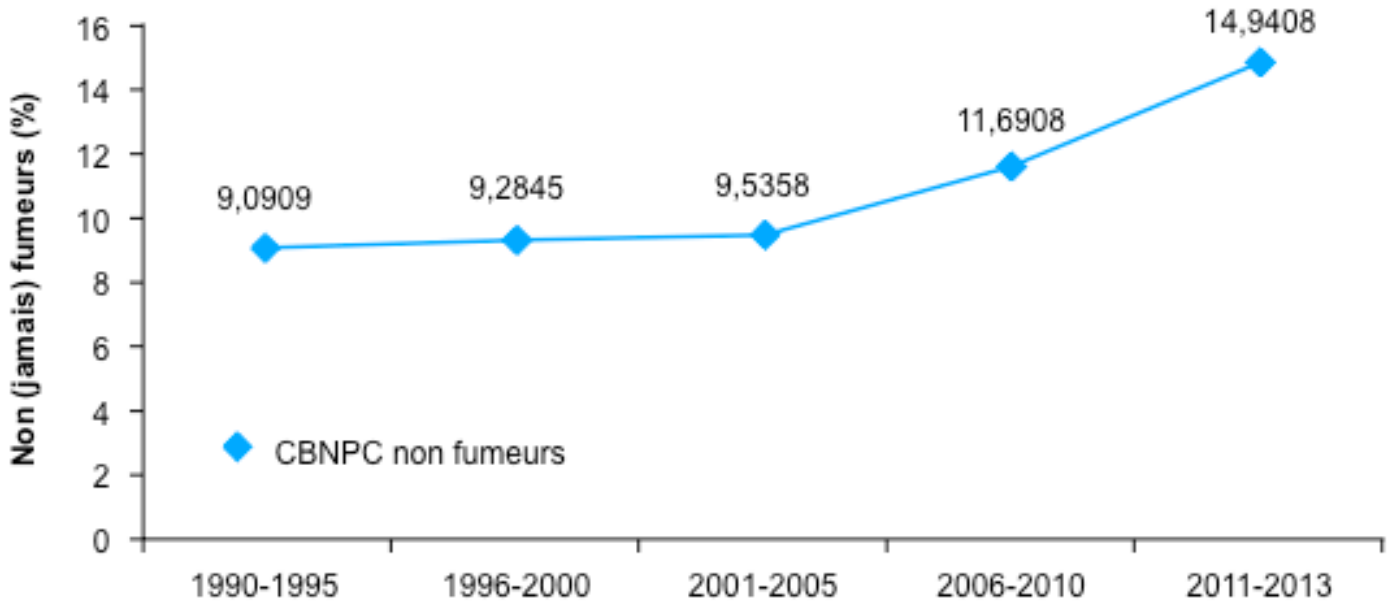
Les non-fumeurs sont-ils plus nombreux ?

Une analyse multivariée de 3 registres



➔ **Augmentation significative de l'incidence des non (jamais) fumeurs sur ces 3 registres**

WCLC 2015 - D'après Pelosof L et al., abstr. ORAL22.01, actualisé

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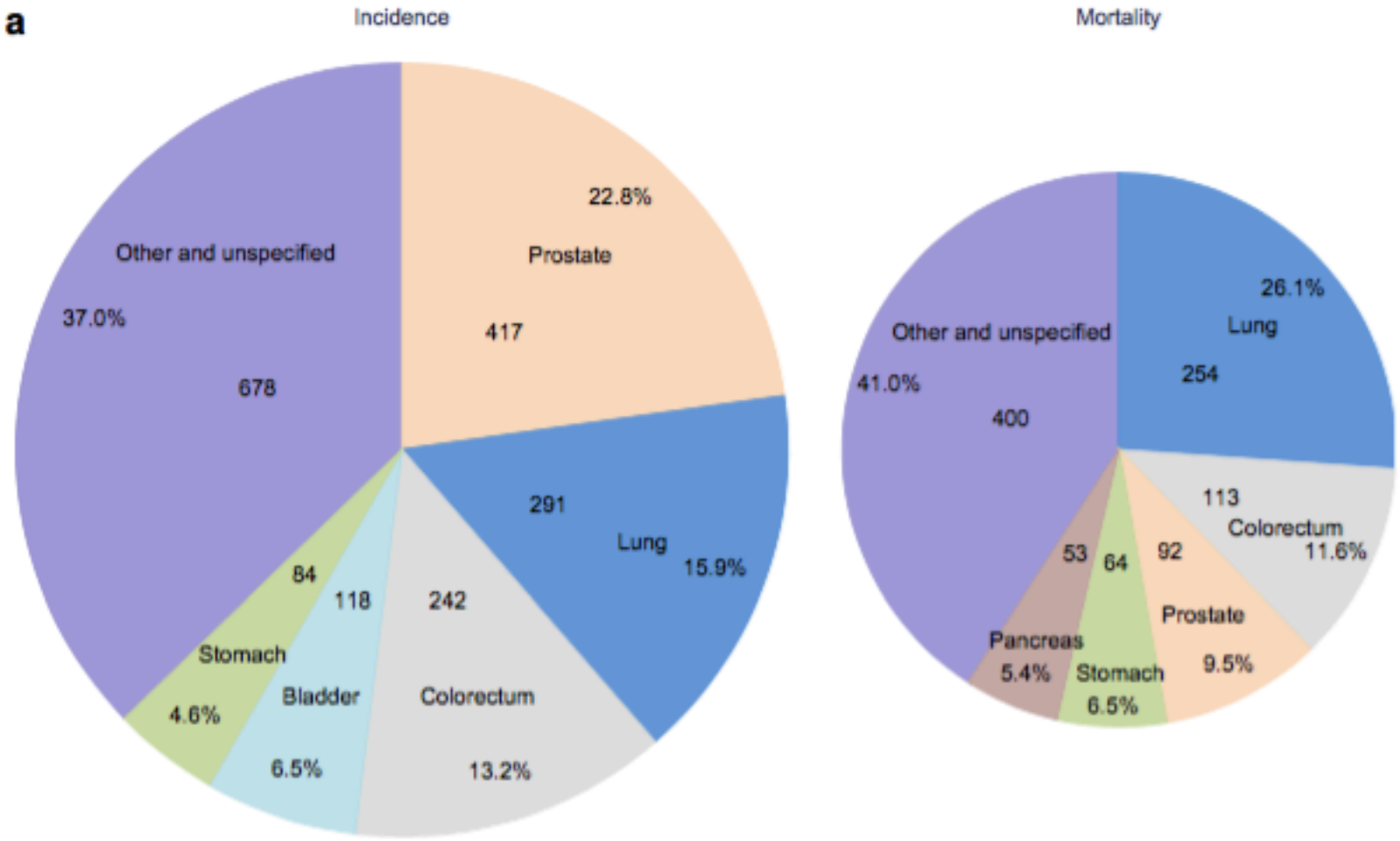
En Europe..



Ferlay J et al, EJC 2013

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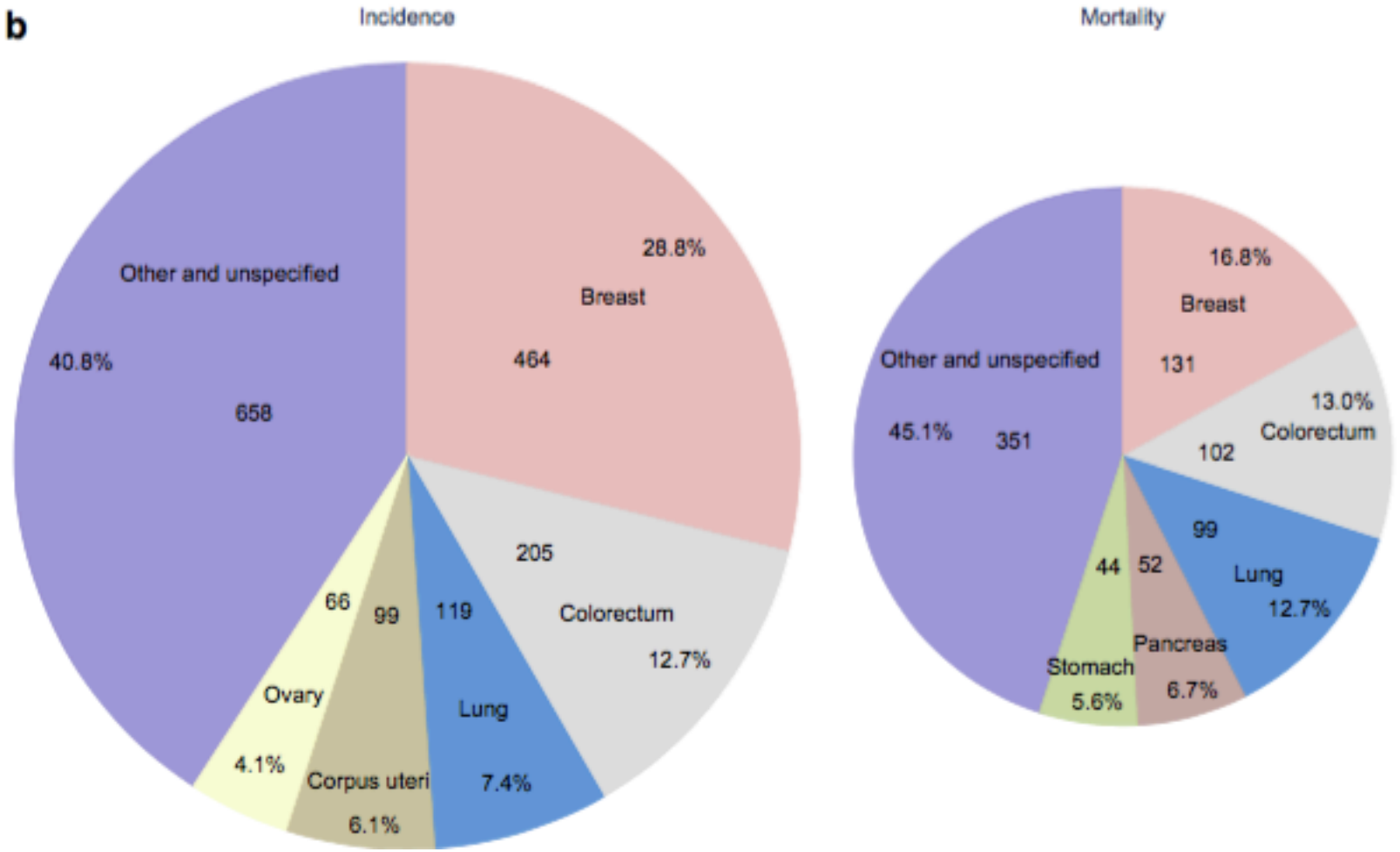
En Europe..



Ferlay J et al, EJC 2013

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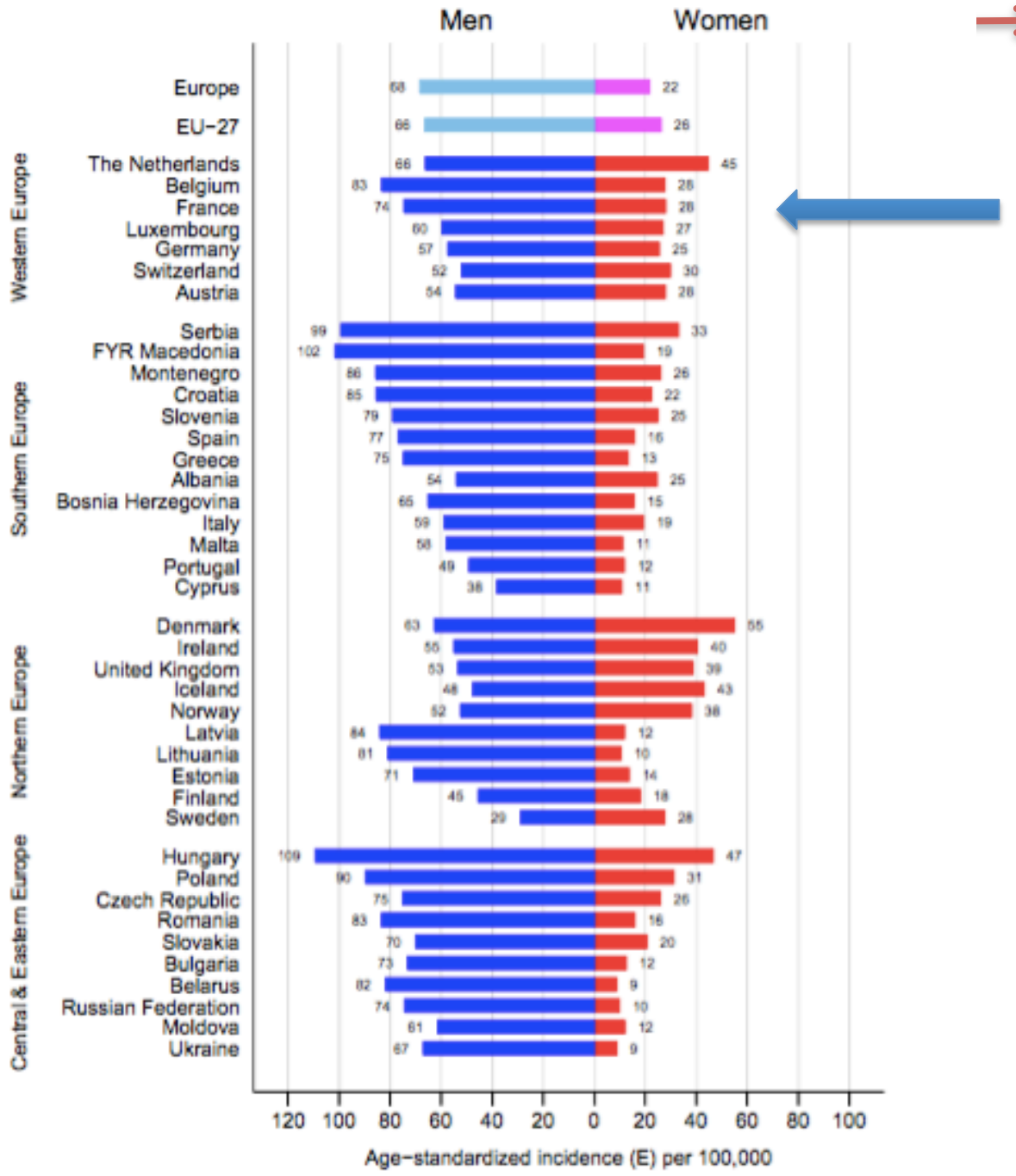

Fig. 8. Age-standardised incidence rates by sex, area and country in Europe 2012: lung cancer.

Ferlay J et al, EJC 2013

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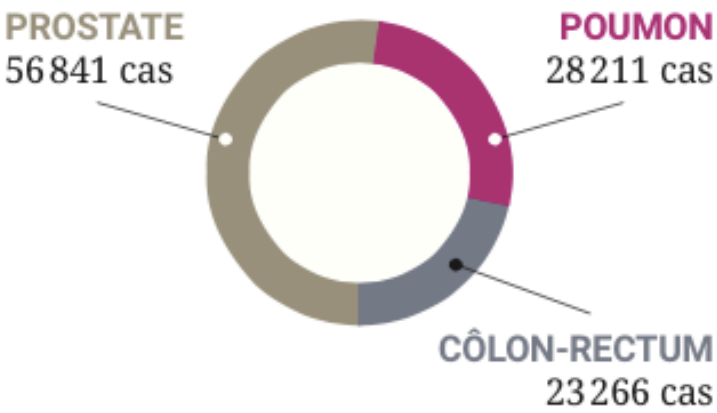
Chez les hommes

200 000 nouveaux cas de cancers
en France métropolitaine (données 2012)
+ 107 % en 32 ans

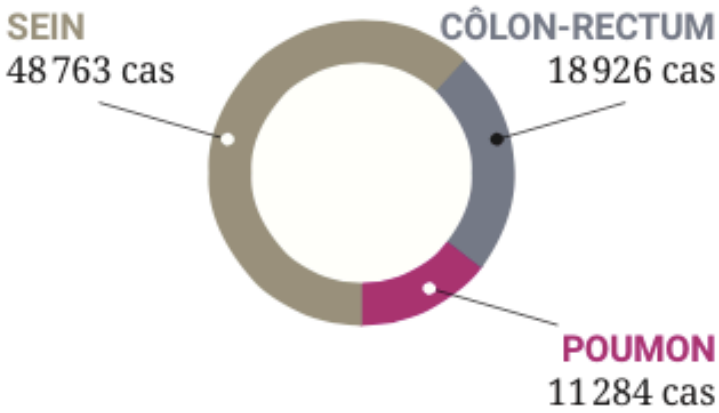
LES 3 CANCERS LES PLUS FRÉQUENTS :



Chez les femmes

155 000 nouveaux cas de cancers
en France métropolitaine (données 2012)
+ 111,4 % en 32 ans

LES 3 CANCERS LES PLUS FRÉQUENTS :



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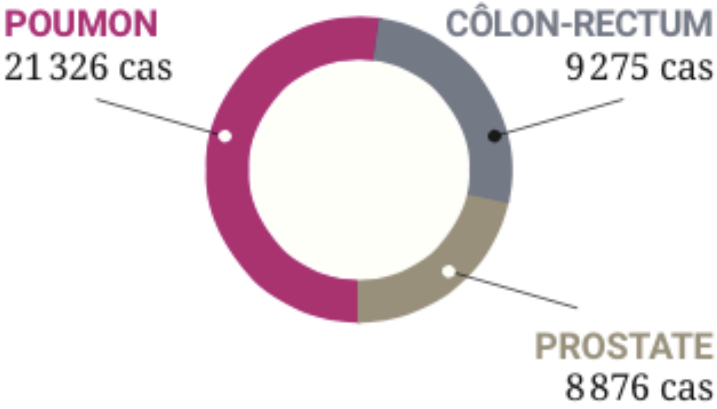
Chez les hommes

Les cancers sont la première cause à la fois de mortalité tous âges confondus et de mortalité prématurée (< 65 ans)

85 000 décès en France métropolitaine (données 2012) : +11 % en 32 ans

LES 3 CANCERS LES PLUS MEURTRIERS :

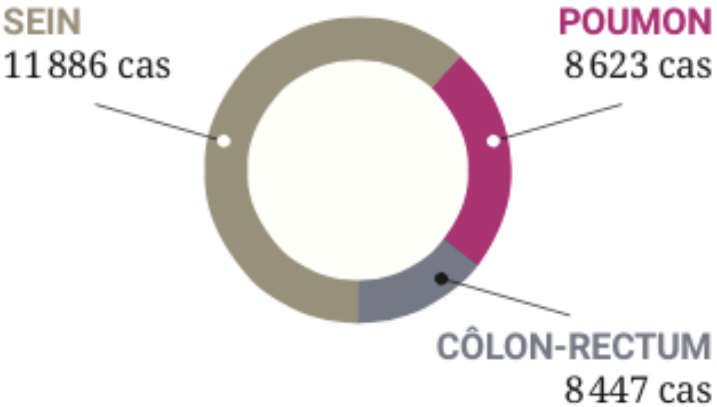


Chez les femmes

Les cancers sont la première cause de mortalité prématurée (< 65 ans) et la deuxième cause de mortalité tous âges confondus derrière les affections circulatoires.

63 000 décès en France métropolitaine (données 2012) : +20,3 % en 32 ans

LES 3 CANCERS LES PLUS MEURTRIERS :



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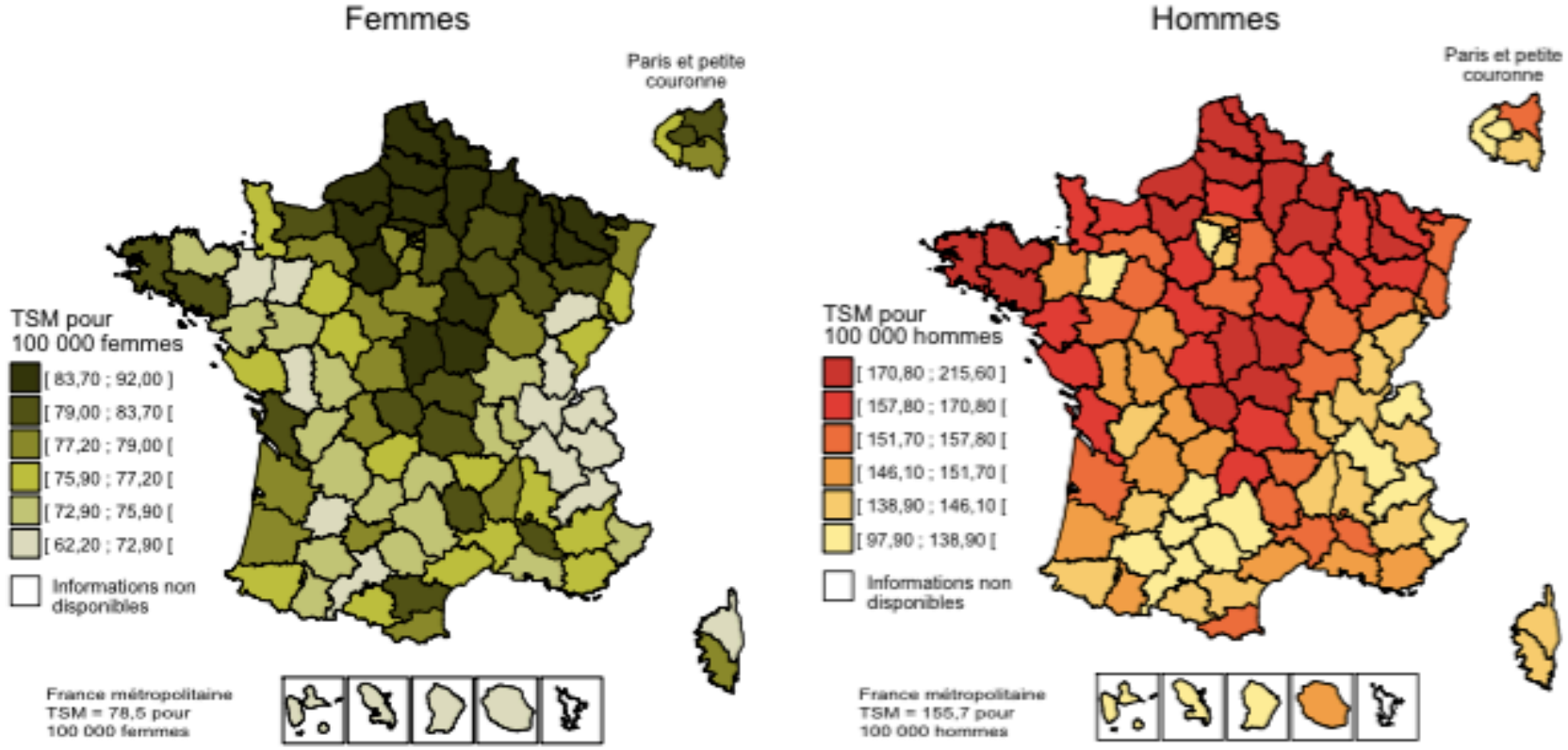
[Figure 5] Taux standardisés à la population mondiale (TSM) de mortalité par cancer à l'échelle départementale en France métropolitaine et dans les DOM (2005-2009)



Source : InVS/CépiDc/Inserm. Infographie : INCa 2013

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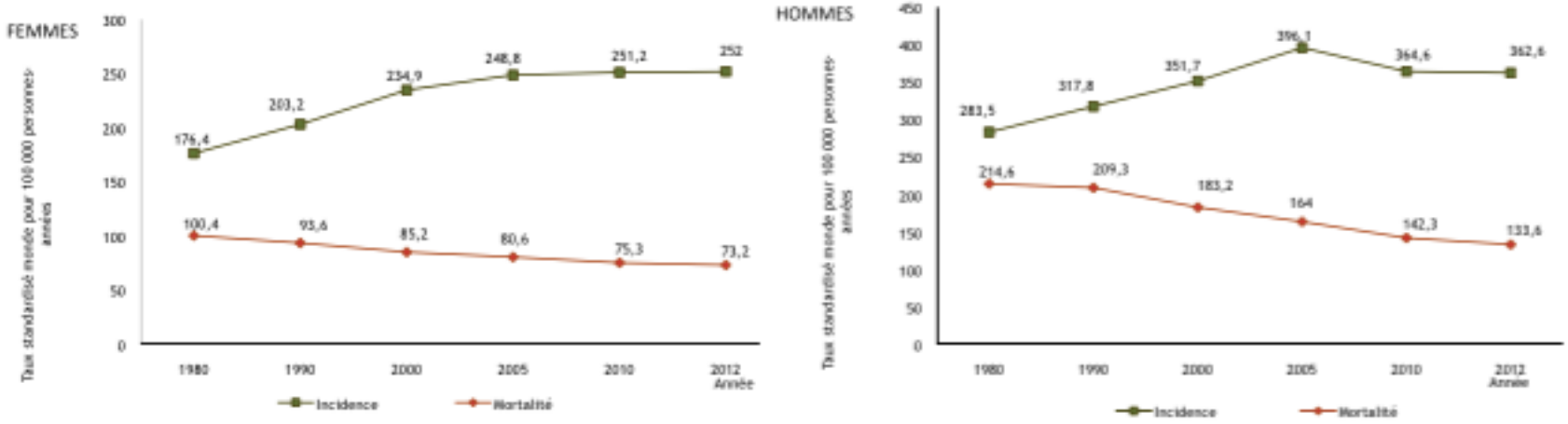
[Figure 3] Évolution (en %) de l'incidence et de la mortalité « tous cancers » (taux standardisé monde estimé) en France métropolitaine de 1980 à 2012 selon le sexe



Sources : Binder-Foucard F, 2013. Traitement : INCa 2013

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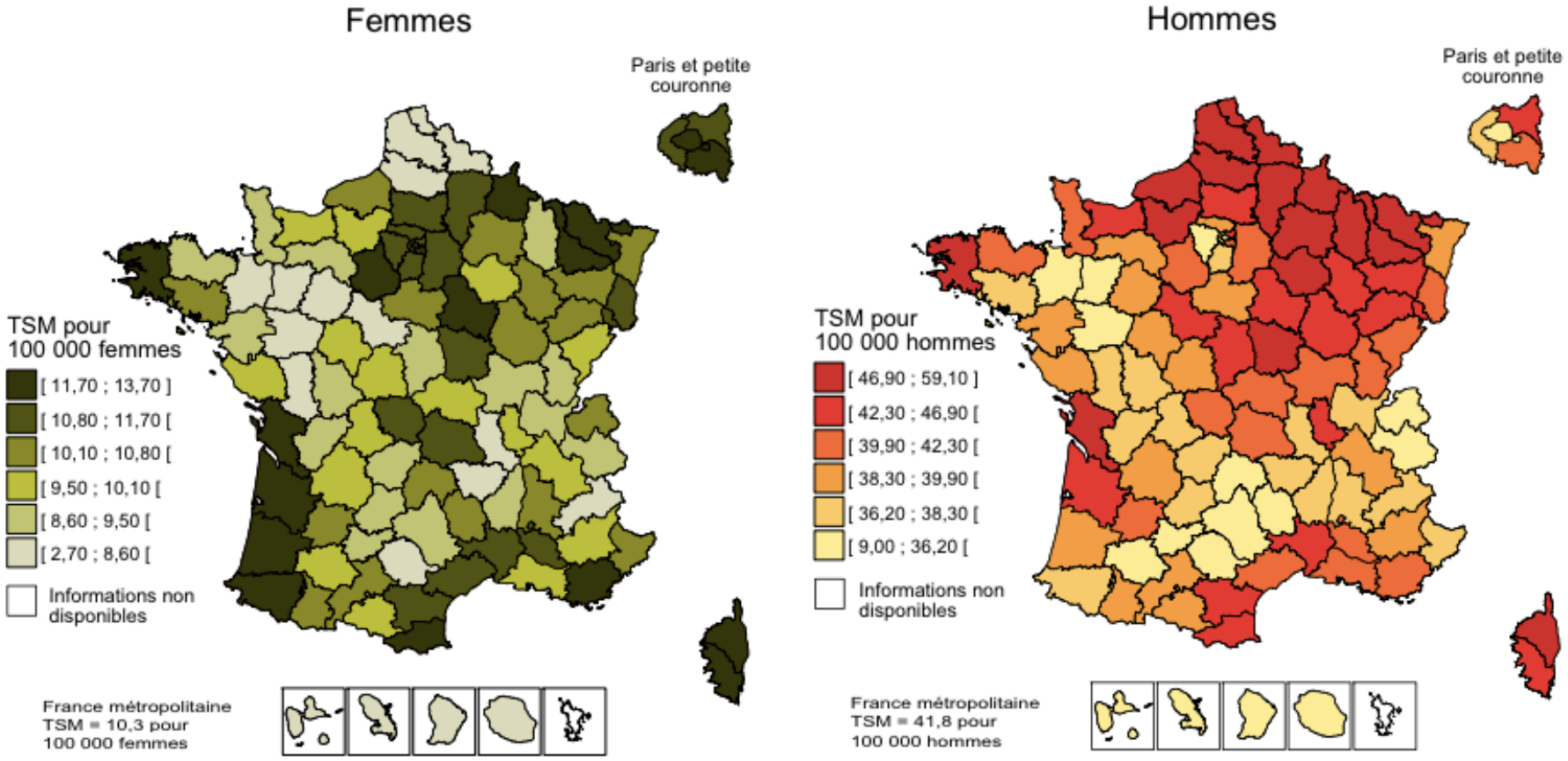
[Figure 10] Taux standardisés à la population mondiale (TSM) de mortalité par cancer du poumon à l'échelle départementale en France métropolitaine et dans les DOM (2005-2009)



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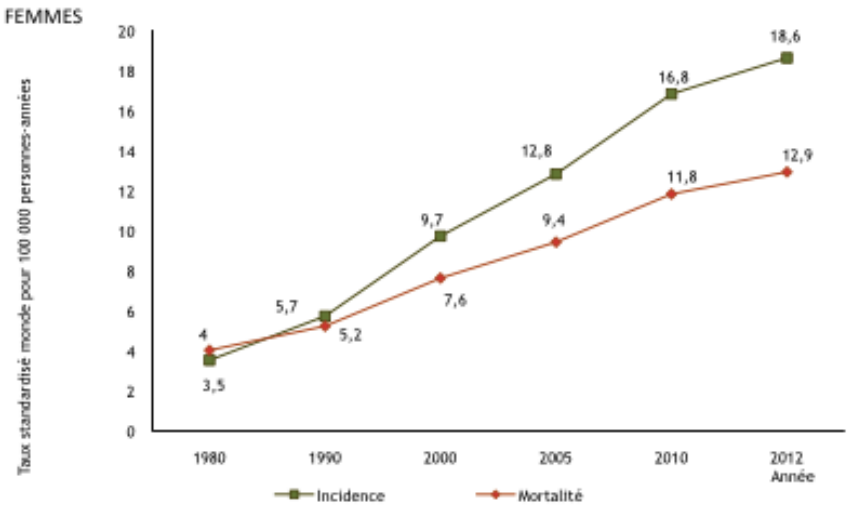
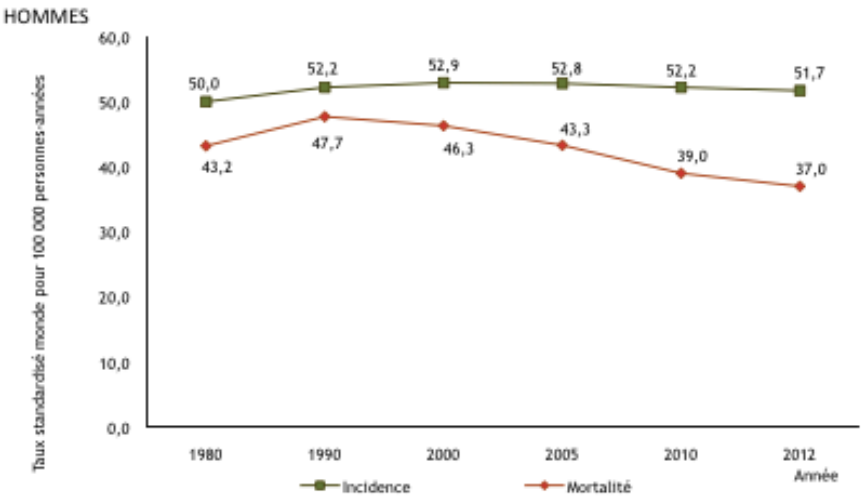
[Figure 8] Évolution de l'incidence et de la mortalité (taux standardisé monde estimé) par cancer du poumon selon le sexe de 1980 à 2012





Sources : [Binder-Foucard F, 2013.]. Traitement : INCa 2013

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France

Homme

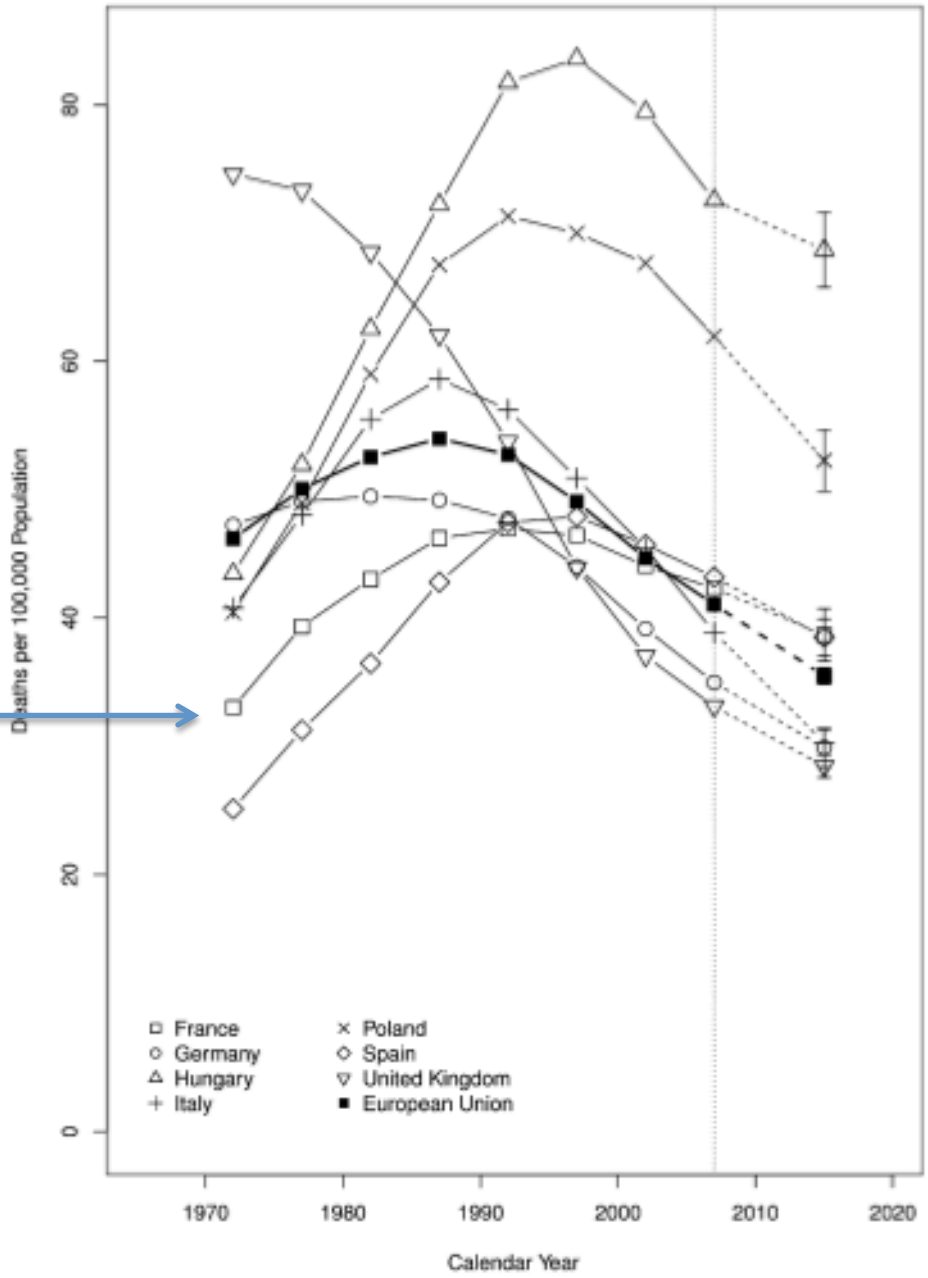

Fig. 4. Age-standardized (world standard population) death rates from lung cancer in men from selected European countries and the European Union as a whole from 1970 to 2009, and predicted rates for 2015.

Malvezzi et al, Lung Cancer 2013

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France

Femme

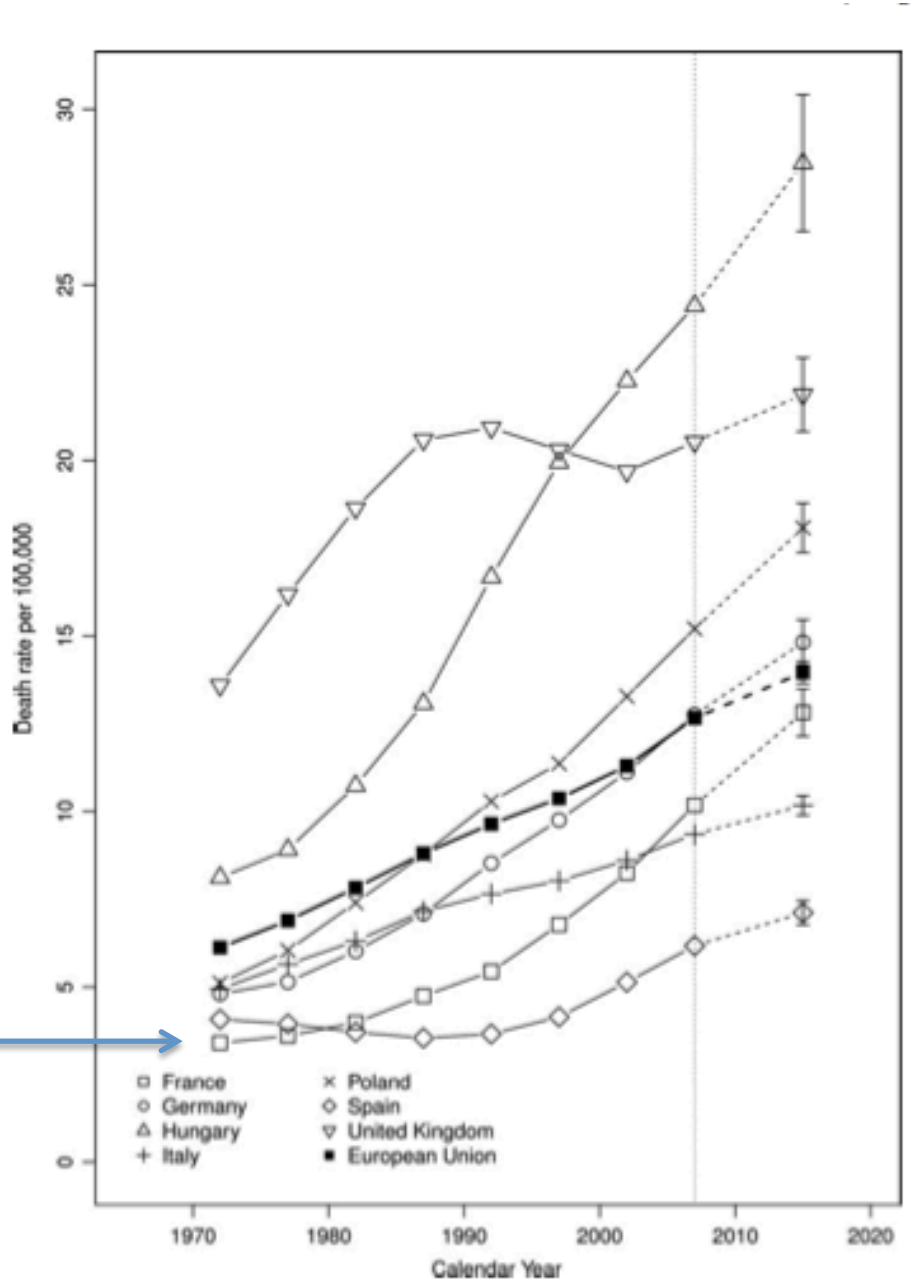

Fig. 4. Age-standardized (world population) death rates for lung cancer in women from major European countries and the European Union as a whole from 1970 and 2009, and predicted rates for 2015.

Bosetti C et al, Lung Cancer 2012

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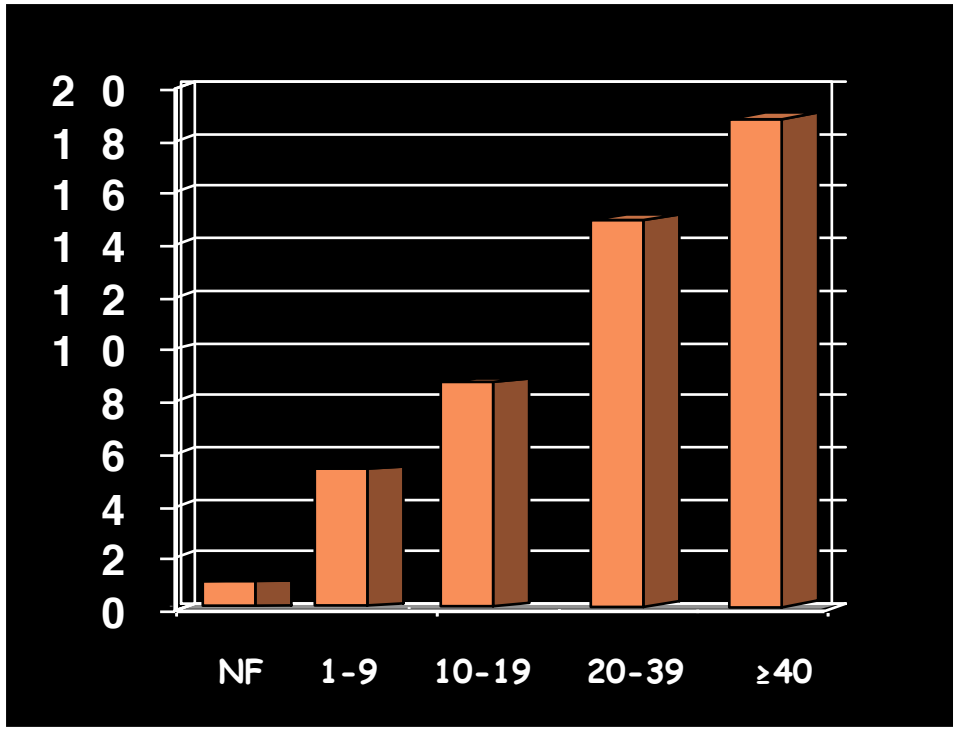
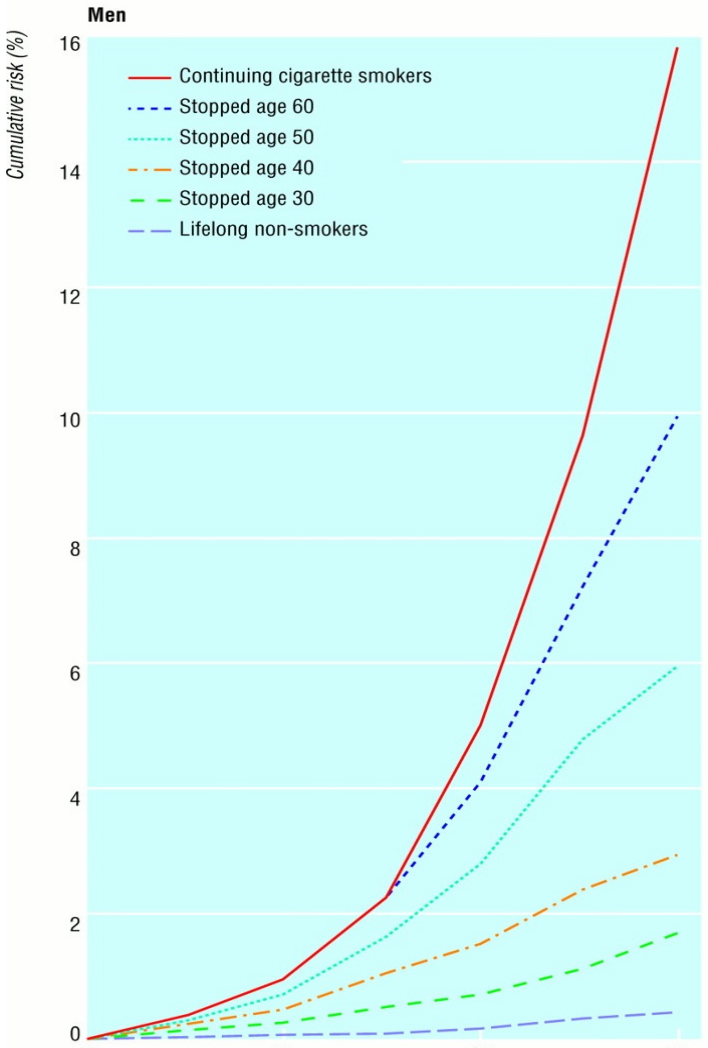
LES ETIOLOGIES

Le tabac reste la principale cause





Et son arrêt la meilleure prévention

Peto et al, BMJ 2000;321:323-329

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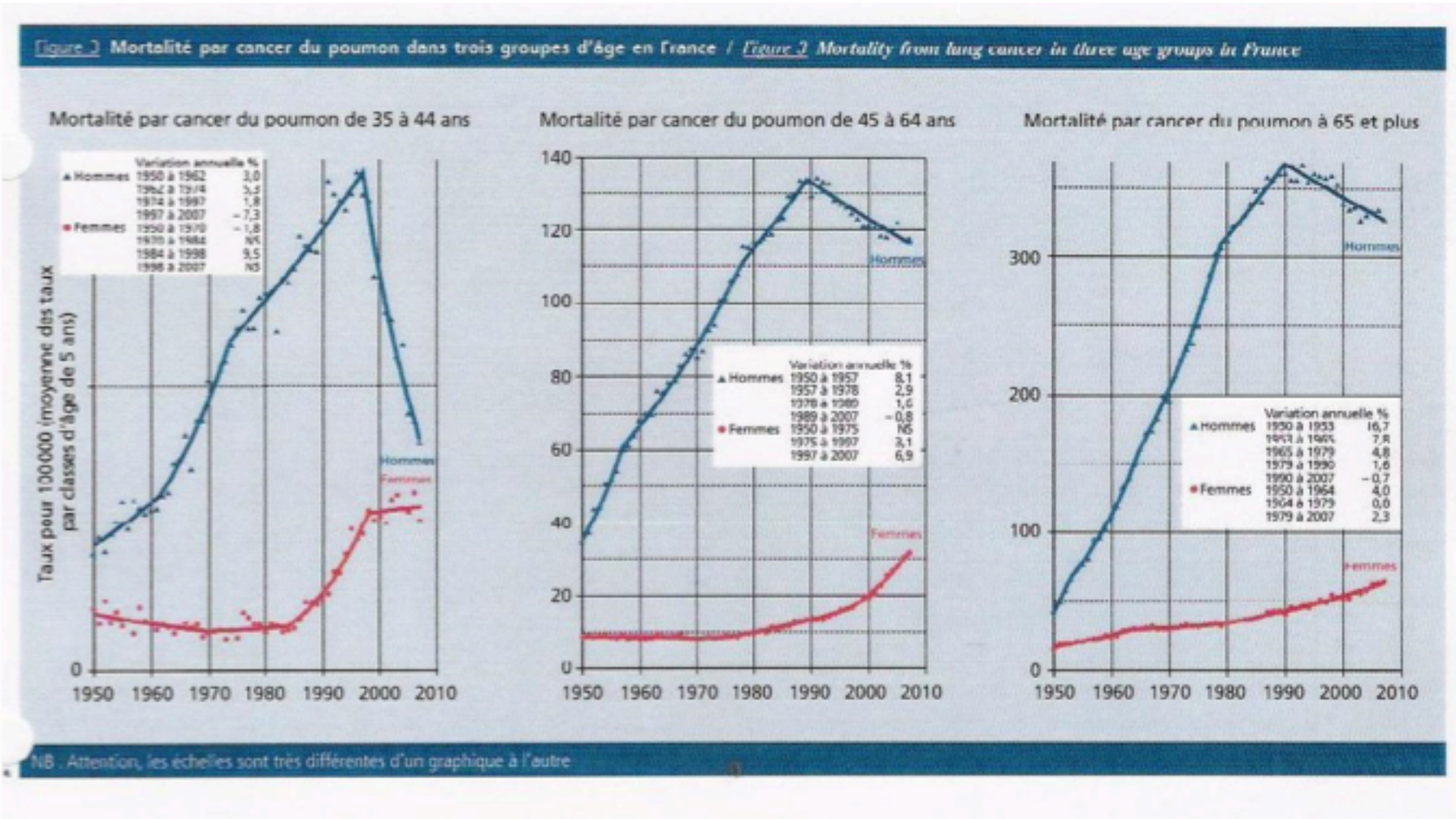

BEH, Mai 2010

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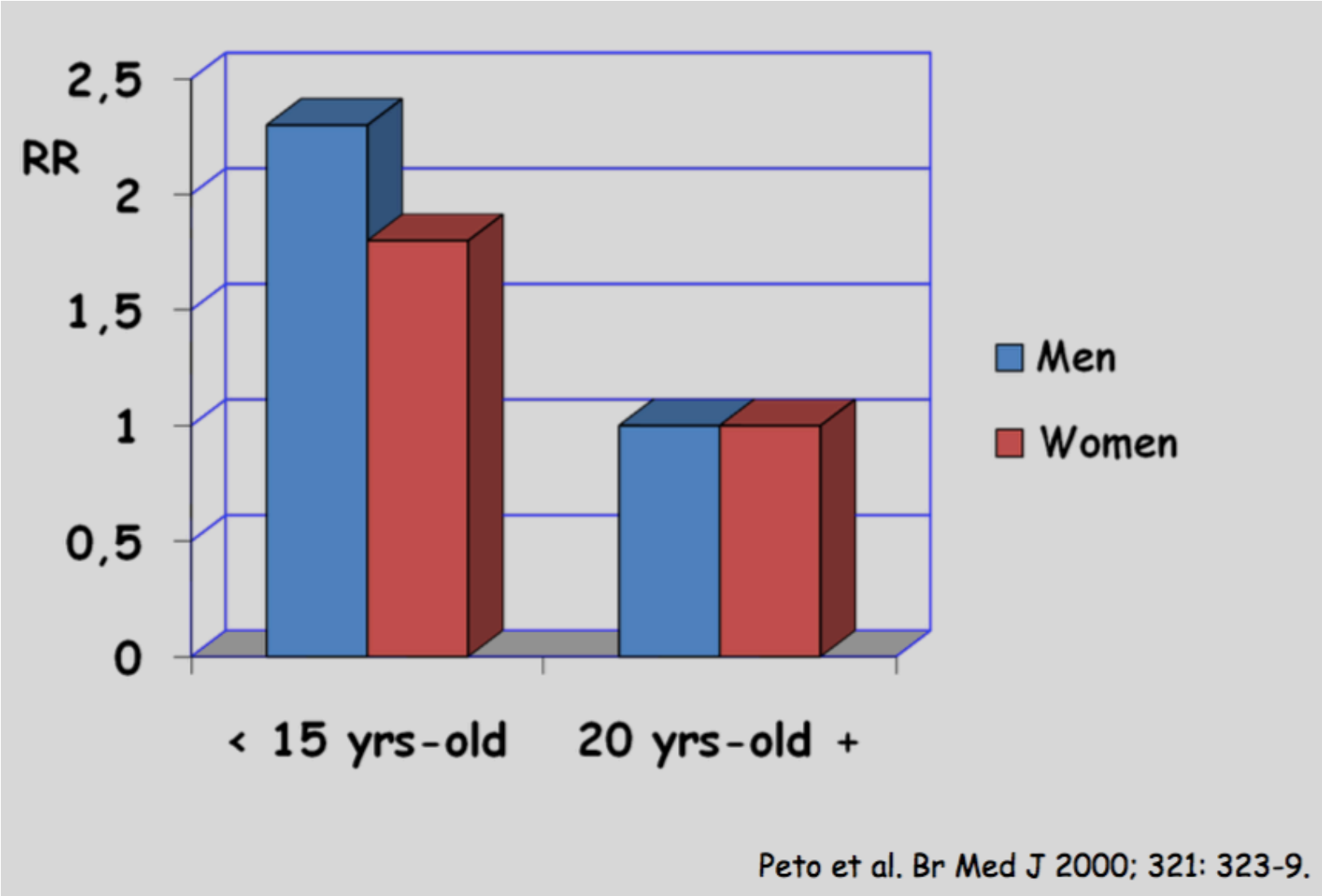
Effet de l'age de l'initiation du tabagisme



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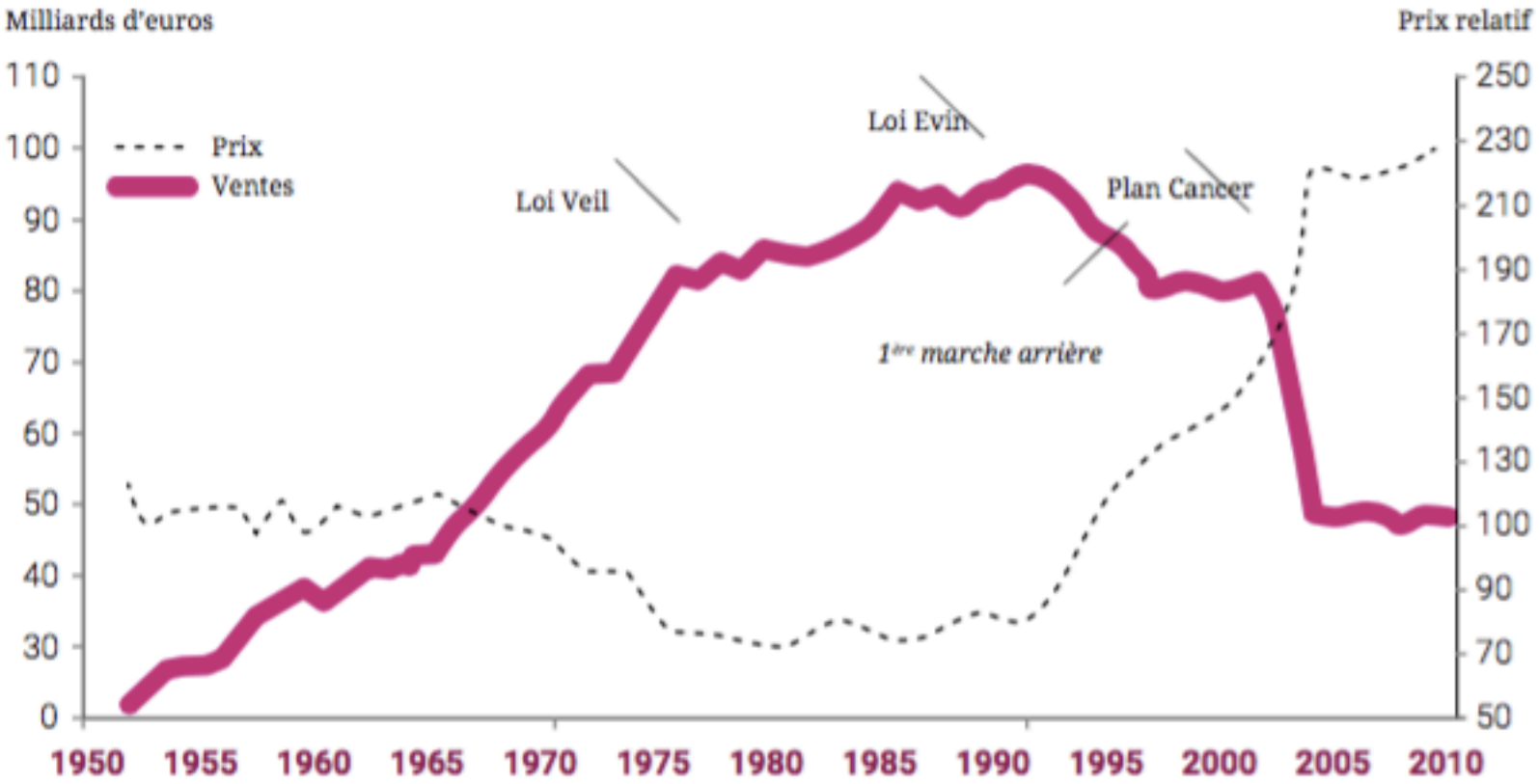
Évolution des ventes de cigarettes en milliards de cigarettes et prix relatif des cigarettes (référence 100 en 1970). Source : Elsevier



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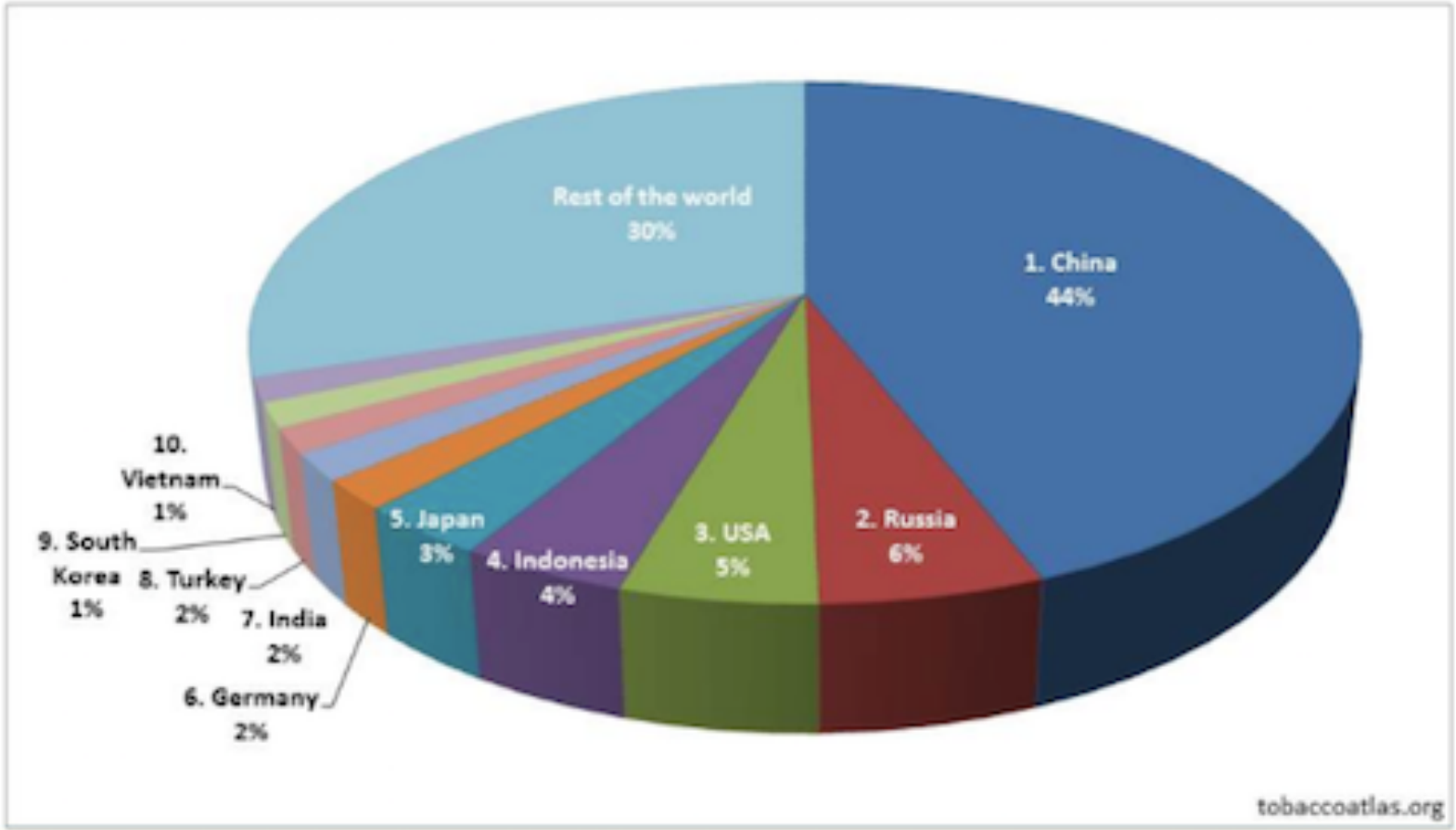
Top 10 Cigarette Consumers, 2014



Relation BPCO et cancer bronchique

	CBNPC, BPCO = 0 Vs controles n=1646	CBNPC BPCO Vs controles n= 1464
Ex fumeurs	2,05 *	10,76 *
Fumeurs actifs	4,17 *	45,02 *
Paquets- années		
<20	1,34 *	2,90 *
20 – 40	2,56 *	13,90 *
40 – 60	4,27 *	32,92 *
> 60	5,81 *	53,78 *

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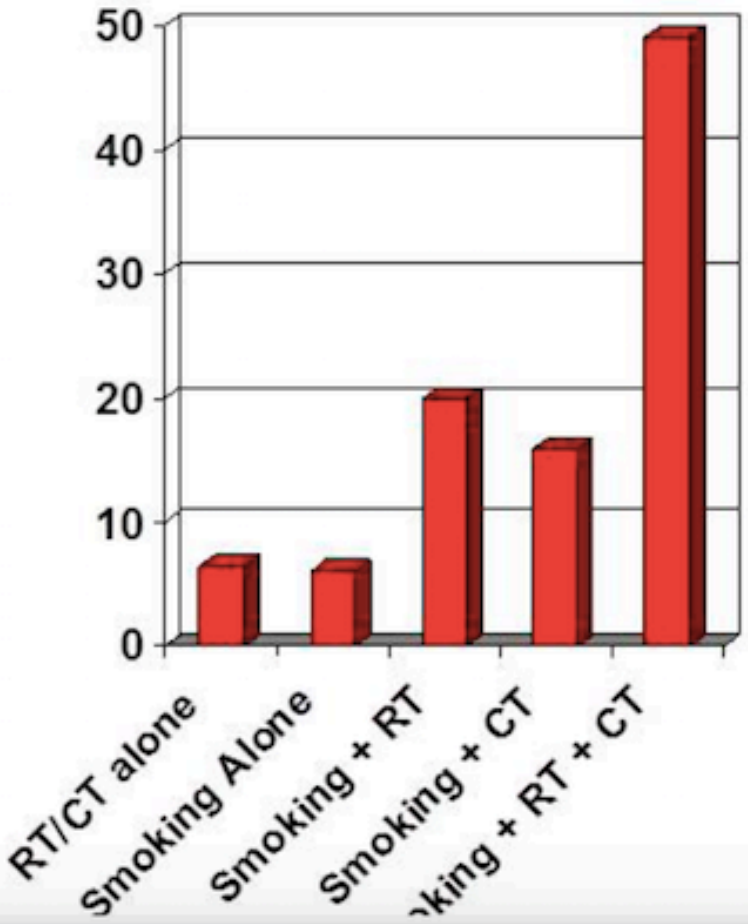
Risk of lung cancer in 19,046 HD patients

- In former smokers (prior to diagnosis)
  - HR for lung cancer 4-9
- In current smokers (at diagnosis)
  - HR 6 with smoking
  - HR 20 with smoking + radiotherapy (RT)
  - HR 16 with smoking + alkylating agent (AA)



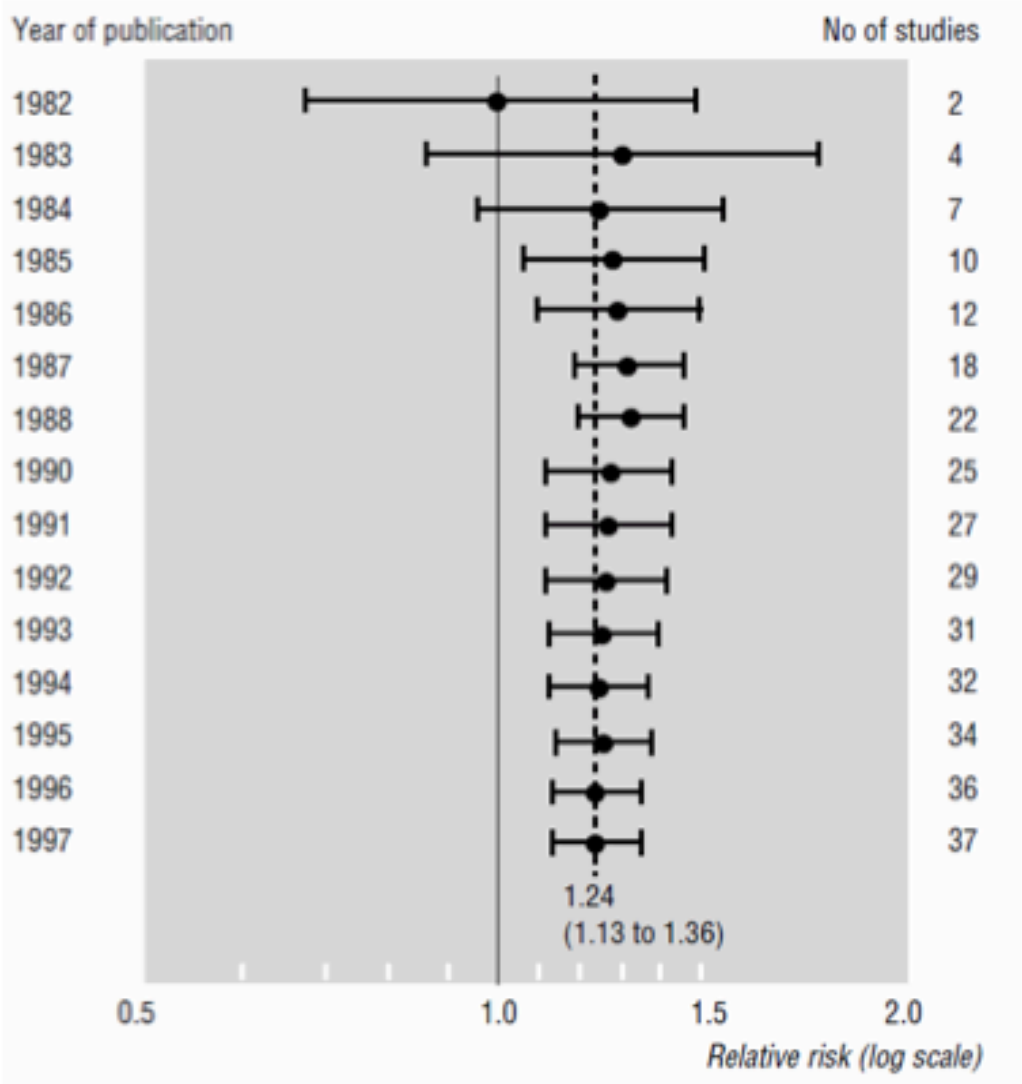
Tabagisme et cancer de prostate

Causes de décès	% dècès	HR pour les fumeurs
Mal. Cardio Vasc	50,3 %	3,05
C Bronchique	9,9 %	4,09
Autres cancers	15,6 %	
C Prostate	8,7 %	

G Warren et al, WCLC, 2015 Plen 1.03

Tabagisme passif: un rôle bien connu…

The accumulated evidence on lung cancer and environmental tobacco smoke



Hackshaw AK, et al. *BMJ* 1997;315:980–88

Courtesy S Couraud

Cannabis, marijuana, haschich

Marijuana
(Herbe, pot, beuh)

Feuille séchées et broyées de cannabis

THC 1 à 25%

Haschisch
(Hasch)

Résine du chanvre (couvre les fleurs et les feuilles du sommet de la plante): la résine est raclée, pressée en blocs.

THC 10 à 30%
si non coupée

Huile

Le cannabis est trempé dans un solvant, ensuite évaporé pour obtenir un concentré de THC

THC 60 à 80%

Inhalée
(Joint)

Ingéré
(Space-cake)

D'après S Couraud

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- Actuellement au vue des données de la littérature, il n'y a pas d'argument pour affirmer que la marijuana est cancérigène pour le poumon. Si elle entraine plus de bronchite aigue et de symptômes respiratoires, elle ne semble pas associée à la BPCO
- Néanmoins multiples biais (suivi peu prolongé, tabagisme associé, report pas forcement exhaustif de la consommation
- Augmentation de la charge du THC avec les années dans les « cigarettes »

Forest plot

Study name	Cases No. (exp.)	Controls No. (exp.)	OR	IC_{95}	P-value
New Zealand study	78 (18)	324 (25)	2,17	1,04-4,52	0,039
MSH-PMH study	431 (39)	308 (41)	0,57	0,30-1,07	0,079
Moffit Cancer study	497 (7)	897 (18	1,06	0,42-2,69	0,906
MSKCC study	94 (2)	87 (2)	1,00	0,12-8,52	0,997
ReSoluCENT study	449 (12)	332 (7)	0,90	0,32-2,56	0,843
UCLA study	610 (147)	1 037 (228)	0,86	0,64-1,16	0,324
Pooled (all studies)	2 159 (225)	2 985 (321)	0,95	0,66-1,38	0,807

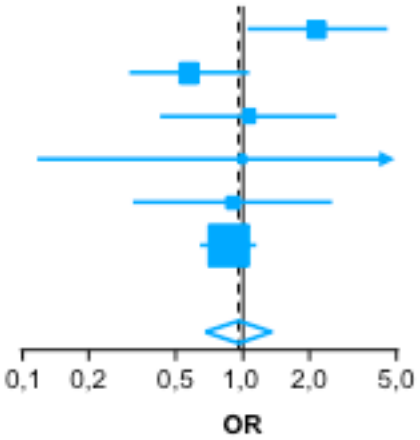

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TABLE 2

Cannabis use, tobacco use and age of onset of cannabis use as continuous variables

Characteristic	RR of lung cancer	95% CI
Pack-year of cigarette smoking*	1.07	(1.05 to1.09)
Joint-year of cannabis smoking**	1.08	(1.02 to1.15)
Joint-years to 5 yrs prior to diagnosis§	1.10	(1.02 to1.18)

*Adjusted for age, sex, ethnicity, family history of lung cancer and joint-years of cannabis use

**Adjusted for age, sex, ethnicity, family history of lung cancer and pack-years

§Adjusted for age, sex, ethnicity, family history of lung cancer, pack-years and age of onset of cannabis use

Aldington S, Eur Respir J, 2008

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Etude de cohorte suédoise, 50.000 jeunes de 18 à 20 ans, consommation de cannabis (déclarée..) entre 1969 et 1970 et suivi jusqu'en 2009 pour le dg de Cancer bronchique

Table 4 Crude and adjusted hazard ratios (HRs) and 95 % CIs for lung cancer ($n = 179$) among 44,257 conscripts, in relation to lifetime frequency of cannabis-use categories

Cannabis smoking	Crude HR (95 % CI)	Tobacco-adjusted[a] HR (95 % CI)	Fully adjusted[b] HR (95 % CI)
Never (reference)	1.0	1.0	1.0
Once	2.07 (1.06–4.06)	1.48 (0.75–2.91)	1.52 (0.77–3.01)
2–4 times	0.95 (0.39–2.33)	0.65 (0.26–1.58)	0.66 (0.27–1.62)
5–10 times	1.02 (0.32–3.20)	0.66 (0.21–2.09)	0.68 (0.21–2.16)
11–50 times	2.69 (1.26–5.74)	1.68 (0.78–3.62)	1.68 (0.77–3.66)
More than 50 times	3.72 (1.96–7.06)	2.24 (1.17–4.29)	2.12 (1.08–4.14)

[a] Adjusted for tobacco smoking, using the following categories of tobacco use: do not smoke (reference category), daily smoking of 1–10 cigarettes per day, and daily smoking of more than 10 cigarettes per day

[b] Adjusted for tobacco smoking [do not smoke (reference category), daily smoking of 1–10 cigarettes per day, and daily smoking of more than 10 cigarettes per day]; level of alcohol consumption [abstainers (0 g 100 % alcohol/consumption per week; reference category), light (1–100 g/ consumption per week), moderate (101–250 g/consumption per week), and high (more than 250 g/consumption per week)]; respiratory conditions [any of the following diagnosed at conscription, chronic bronchitis, emphysema, pneumonia, and asthma: no (reference category)/yes]; and conscripts' SES in 1970 [high/intermediate nonmanual (reference category), low nonmanual, manual skilled and unskilled, others (farmers, self-employed, and unclassified)]

RC Callaghan et al Causes Control 2013

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TABLE 4. Adjusted Odds Ratios and 95% CI for Cannabis Smoking and Lung Cancer, and Interaction with Tobacco Smoking Status in Case Control Studies in Morocco, Tunisia and Algeria

		Morocco (114 Cases, 227 Controls)		Tunisia (149 cases, 188 controls)		Algeria (167 Cases, 340 Controls)		Overall (430 Cases, 755 Controls)	
Cannabis exposure[a]									
Never		1	(Reference)	1	(Reference)	1	(Reference)	1	(Reference)
Ever		2.2	1.1, 4.5	4.1	1.8, 9.0	2.0	0.7, 5.3	2.4	1.5, 3.7
Combined exposure[b]									
Tobacco	Cannabis								
Never	Never	1	(Reference)	1	(Reference)	1.	(Reference)	1	(Reference)
Former	Never	2.9	0.9, 9.9	1.4	0.5, 4.2	10.6	3.7, 30.9	4.1	2.3, 7.5
Former	Ever	15.5	3.7, 65.1	2.1	0.5, 8.1	65.3	11.6, 367.5	11.9	5.3, 26.8
Current	Never	15.5	4.7, 51.5	3.2	1.3, 8.2	24.5	8.2, 73.6	11.3	6.2, 20.5
Current	Ever	16.3	4.0, 67.1	26.3	4.6, 149.7	12.2	2.0. 73.9	18.4	8.2. 41.6

OR, odds ratio; CI, confidence interval.

[a]OR were derived from a logistic regression adjusting for age, occupational exposure, country (in pooled analysis) and tobacco in categories of duration of exposure (never, former, <25 yr, 25–35 yr, >35 yr).

[b]OR were adjusted for age, occupational exposure, country (in pooled analysis) and lifetime pack-years tobacco smoking.

A Sasco et al, J Thorac Oncol 2008

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Eur Respir J 2008; 31: 227–228
DOI: 10.1183/09031936.00157607

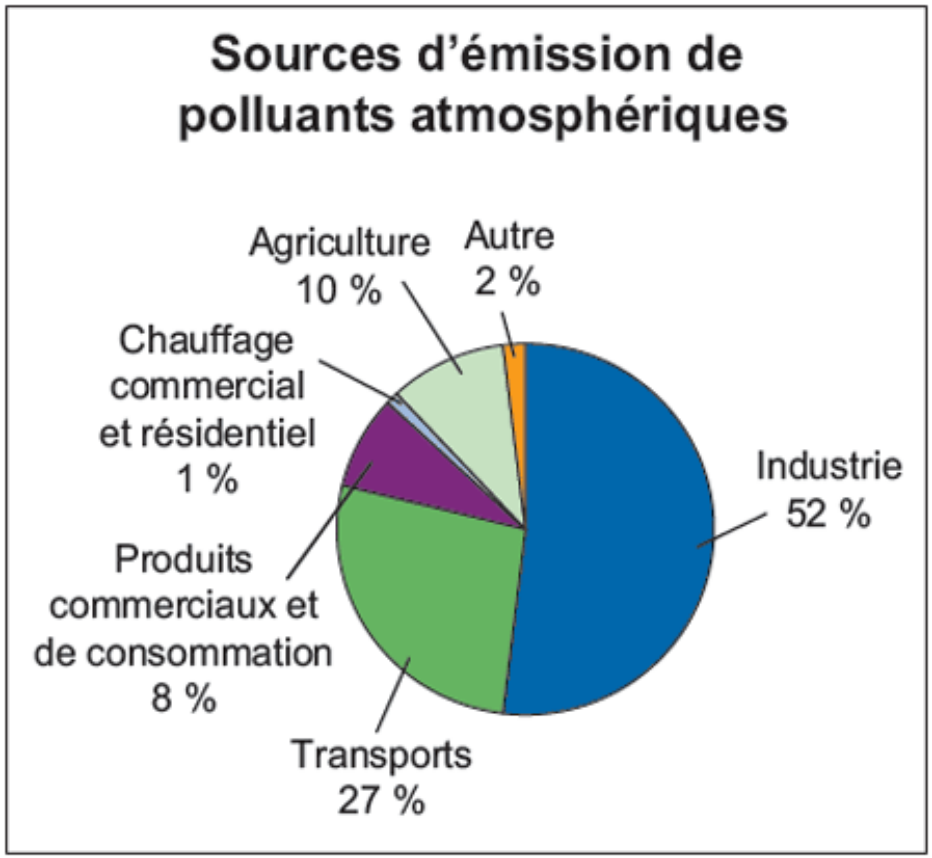
EDITORIAL

Cannabis: the next villain on the lung cancer battlefield?

C. Brambilla*,# and M. Colonna*,¶

D'où vient la pollution atmosphérique ?

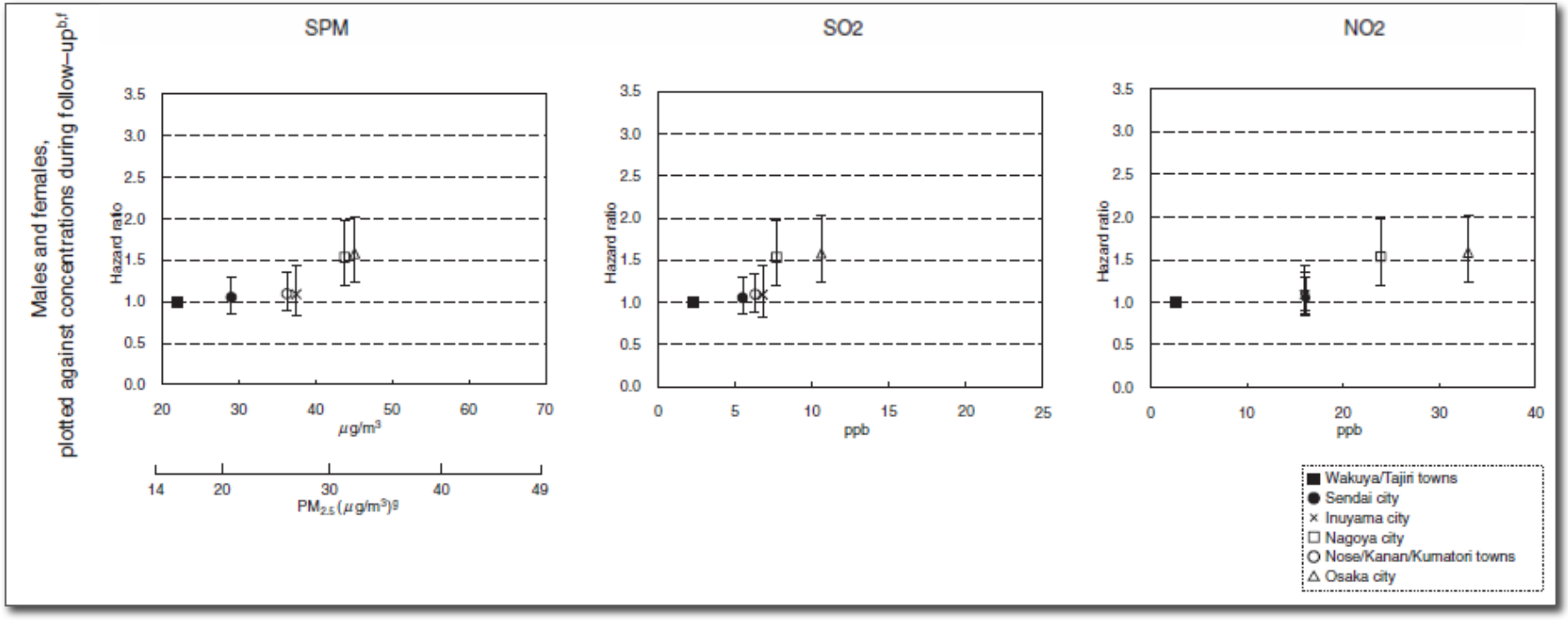
- Pollution naturelle
  - Feu de forêt
  - Eruption volcanique
  - Erosion éolienne
  - Foudre, algues, pollen
- Pollution humaine
  - Industries
  - Transport
  - Agriculture
  - Combustion biomasse
  - Résidentiel / tertiaire



Courtesy S Couraud

Pollution atmosphérique

- Responsable de **5 à 7% des CB**.
- Katanoda et al: Japon, 67000 personnes:
  - Risque de cancer bronchique augmenté de manière dose-dépendante à la pollution



Courtesy S Couraud

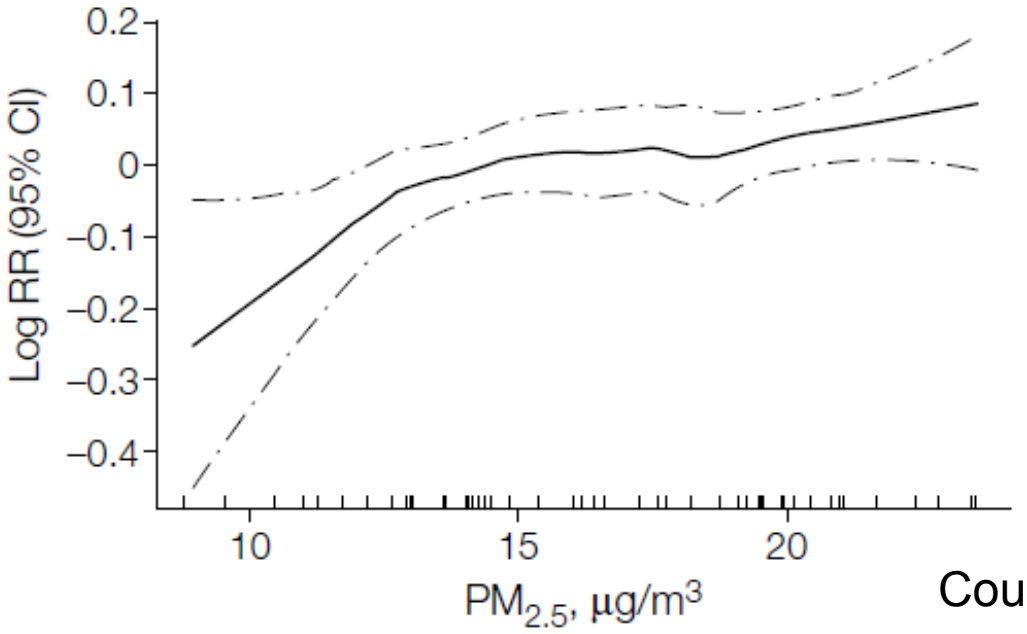
Tredaniel J. et al. *Rev Mal respir*. 2009; 26(4): 437-45
Katanoda K et al. *J Epidemiol*. 2011; 21(2): 132-43

PM2.5 et mortalité par cancer broncho-pulmonaire

Table 2. Adjusted Mortality Relative Risk (RR) Associated With a 10-µg/m³ Change in Fine Particles Measuring Less Than 2.5 µm in Diameter

	Adjusted RR (95% CI)*		
Cause of Mortality	1979-1983	1999-2000	Average
All-cause	1.04 (1.01-1.08)	1.06 (1.02-1.10)	1.06 (1.02-1.11)
Cardiopulmonary	1.06 (1.02-1.10)	1.08 (1.02-1.14)	1.09 (1.03-1.16)
Lung cancer	1.08 (1.01-1.16)	1.13 (1.04-1.22)	1.14 (1.04-1.23)
All other cause	1.01 (0.97-1.05)	1.01 (0.97-1.06)	1.01 (0.95-1.06)

*Estimated and adjusted based on the baseline random-effects Cox proportional hazards model, controlling for age, sex, race, smoking, education, marital status, body mass, alcohol consumption, occupational exposure, and diet. CI indicates confidence interval.



Courtesy S Couraud

Pope CA III, *JAMA*. 2002;287(9):1132-1141.

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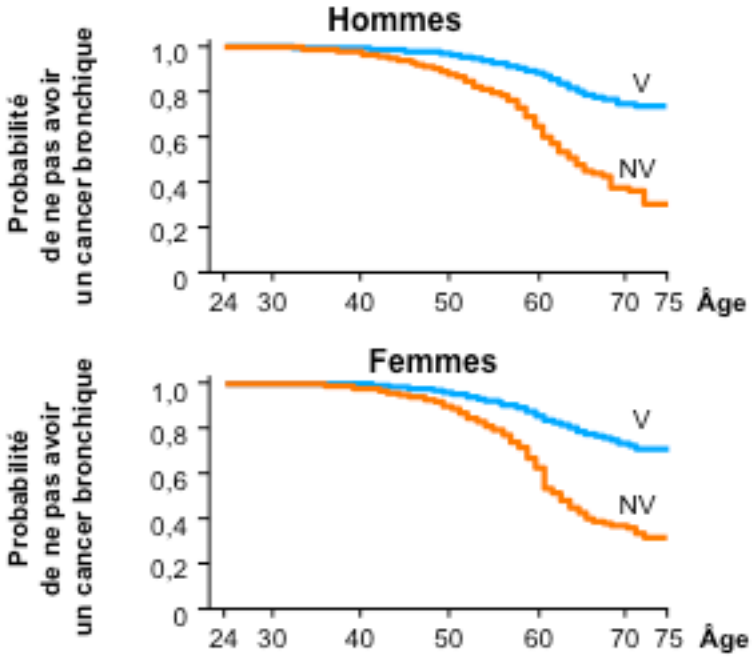
Pollution domestique

- Changement de logement avec une meilleure ventilation (V) [81 % des cas]
- 21 232 résidents, Chine,1976-1992
- RR pour la ventilation
  - Hommes : 0,59 (IC_{95} : 0,49-0,71)
  - Femmes : 0,51 (IC_{95} : 0,44-0,65)



Radon

Analyse des études cas-contrôles

	Cas	Contrôles	RR (IC_{95})
États-Unis/Canada	3 662	4 966	1,10 (0,99-1,26)
Chine	1 050	1 995	1,13 (1,01-1,36)
Europe	7 148	14 208	1,08 (1,03-1,16)

Effet synergique tabac/radon

	0 Bq/m³	100 Bq/m³	400 Bq/m³
Non-fumeur	1,0	1,2	1,6
Fumeur	25,8	29,9	42,3

L'OMS recommande un taux maximal de 100 Bq/m³ (148 pour les États-Unis). Le respect des normes permettrait de réduire de plus de 20 % le nombre de cancers liés au radon aux États-Unis et de 35 % en Suède.
En France dans les zones à risque, dépistage des taux élevés de radon dans les lieux publics mais pas dans les habitations individuelles

WCLC 2015 - D'après Boffetta P et al., abstr. MS23.02 et Melloni B et al., abstr. MS23.01, actualisés

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Radon et cancers bronchiques

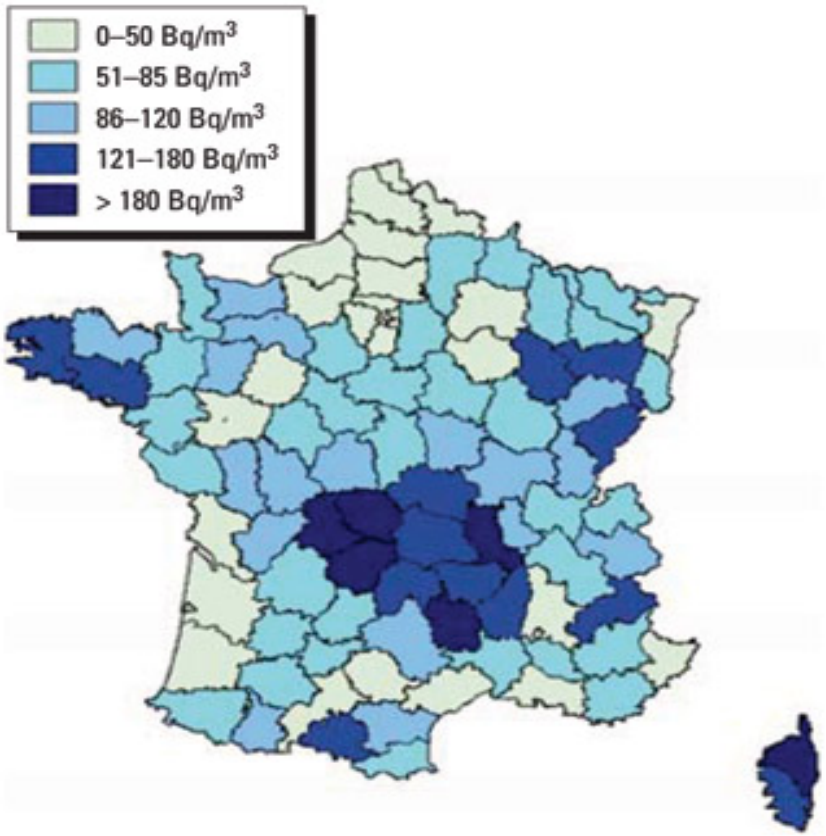
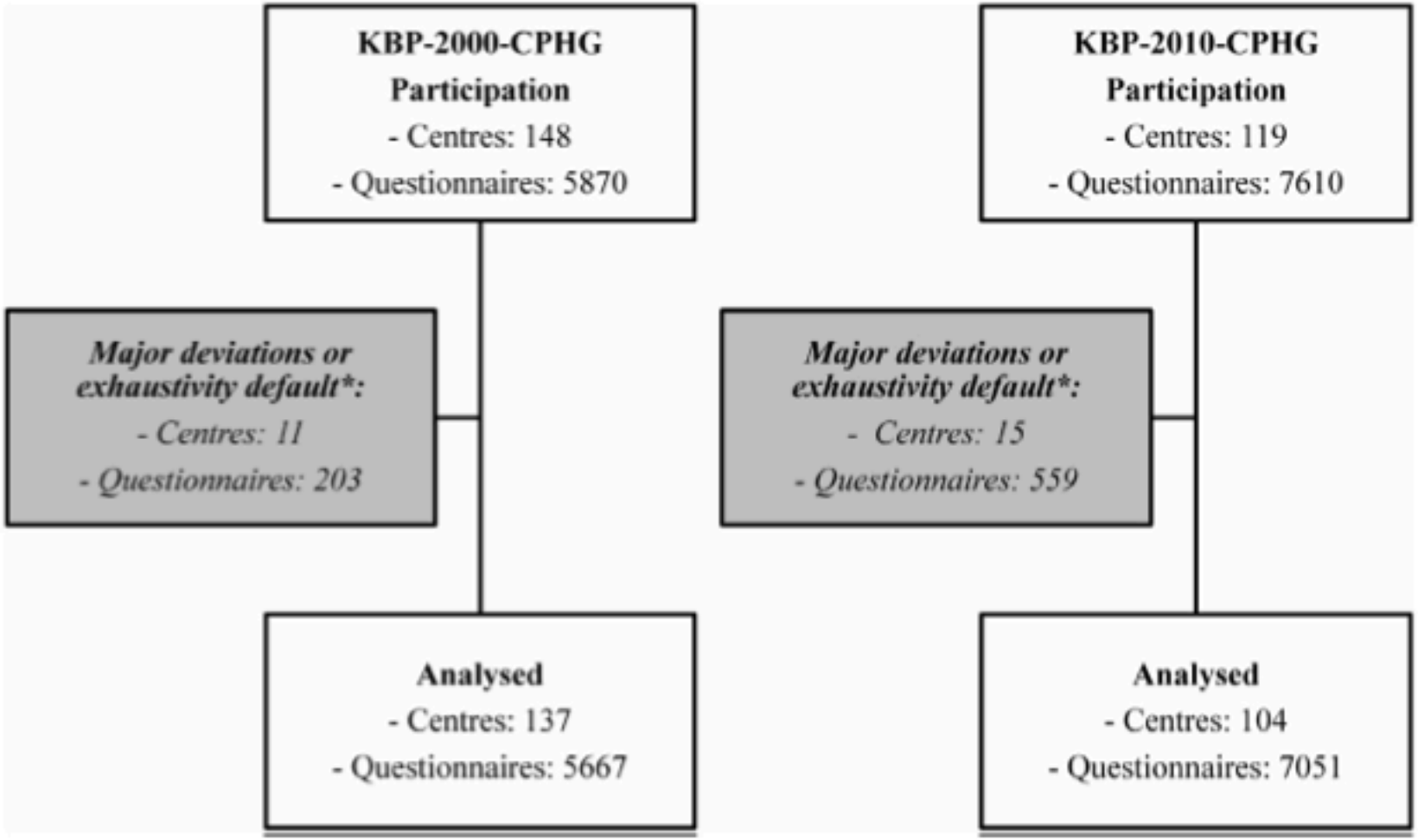


Figure 1. Average indoor radon concentration by department in France (Gambard et al. 2000).

This study is the first assessment of the nationwide risk associated with residential radon exposure in France. Such an assessment is a topic of concern to the European Community and the World Health Organization. This lung cancer risk assessment is the first to consider simultaneously different exposure-response relations and thus to compare the risks estimated by each. When we take into account uncertainties related to the exposure/response relation and geographic variations in radon exposure, we find that the total number of lung cancer deaths in 1999 attributable to indoor radon exposure in France ranges from 1,234 (90% UI, 593,156) to 3,108 (90% UI, 2,996-3,221). Of the 25,134 lung cancer deaths in France during 1999, **indoor radon probably caused 5-12%**.



Locher C, Lung Cancer 2013

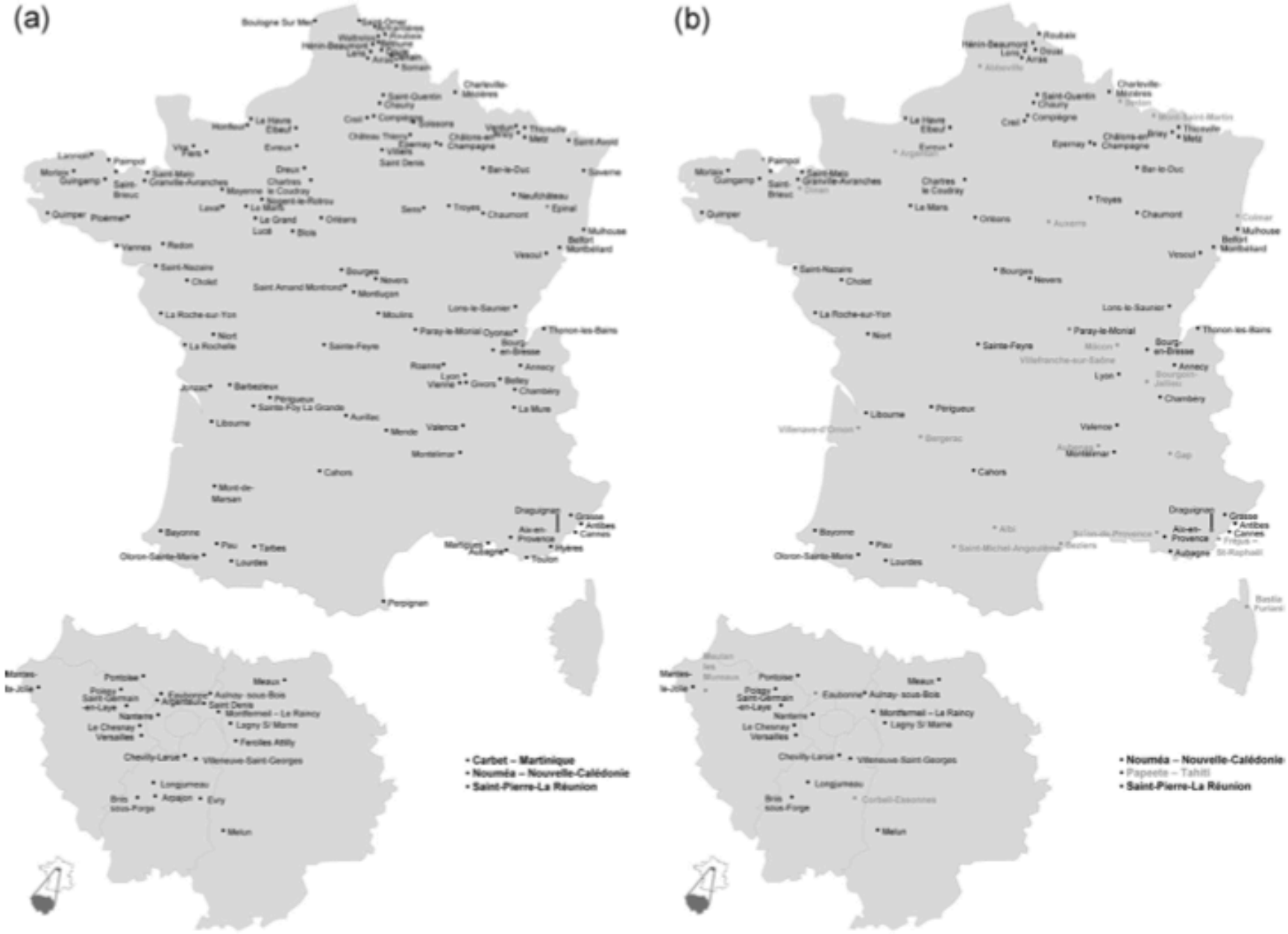

(a)
(b)
• Carbet – Martinique
• Nouméa – Nouvelle-Calédonie
• Saint-Pierre-La Réunion
• Nouméa – Nouvelle-Calédonie
• Papeete – Tahiti
• Saint-Pierre-La Réunion

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Table 1
Comparison of main patient characteristics between the KBP-2000-CPHG and KBP-2010-CPHG studies.

	2000 *N* = 5667	2010 *N* = 7051	*p*-value
Sex: *N* (%)	*n* = 5667	*n* = 7051	<0.0001
- Male	4763 (84.0)	5340 (75.7)	
- Female	904 (16.0)	1711 (24.3)	
Age	n = 5664	*n* = 7051	
- Mean ± SD (years)	64.3 ± 11.5	65.5 ± 11.3	
- *N* (%)			<0.0001
≤50 years	783 (13.8)	615 (8.7)	
51–60 years	1270 (22.4)	1899 (26.9)	
61–70 years	1743 (30.8)	2066 (29.3)	
71–80 years	1530 (27.0)	1732 (24.6)	
>80 years	338 (6.0)	739 (10.5)	

Locher C, Lung Cancer 2013

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Table 1
Comparison of main patient characteristics between the KBP-2000-CPHG and KBP-2010-CPHG studies.

	2000 *N* = 5667	2010 *N* = 7051	*p*-value
Smoking			
- Smoking status: *N* (%)	*n* = 5586	*n* = 7008	<0.0001
- Never-smoker	402 (7.2)	762 (10.9)	
Former smoker	2253 (40.3)	2795 (39.9)	
Smoker	2931 (52.5)	3451 (49.2)	
Current and former-smokers			
Number of packet-years	*n* = 5112	*n* = 5945	0.0006
Mean ± SD	44.4 ± 21.4	43.0 ± 21.4	
Duration of smoking	*n* = 4926	*n* = 5268	0.43
Mean ± SD (years)	37.3 ± 11.5	37.5 ± 11.6	
Former-smokers			
Smoking cessation/lung cancer time	*n* = 2177	*n* = 2647	<0.0001
Mean ± SD (years)	11.3 ± 9.8	14.8 ± 11.6	
Performance status at diagnosis: *N* (%)	*n* = 5656	*n* = 6976	<0.0001
0 – Fully active	1518 (26.8)	1902 (27.3)	
1 – Restricted in heavy physical work	2131 (37.7)	2904 (41.6)	
2 – Up and about more than half the day	1004 (17.8)	1284 (18.4)	
3 – In bed or sitting in a chair more than half the day	817 (14.4)	693 (9.9)	
4 – In bed or in a chair all the time	186 (3.3)	193 (2.8)	

Locher C, Lung Cancer 2013

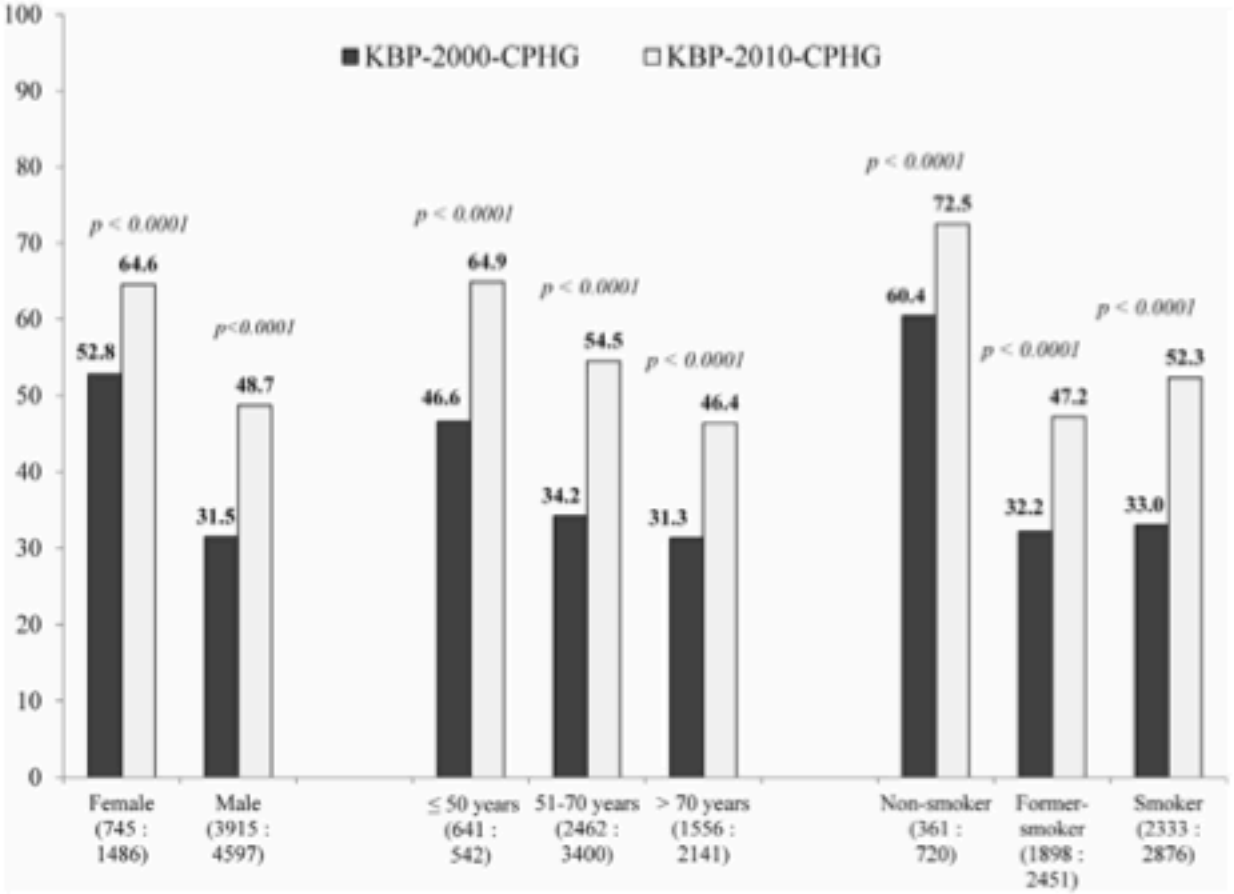

Fig. 3. Adenocarcinoma rate according to patient characteristics (i.e., sex, age, and smoking status) – NSCLC patients. NSCLC: non-small-cell lung cancer.

Locher C, Lung Cancer 2013

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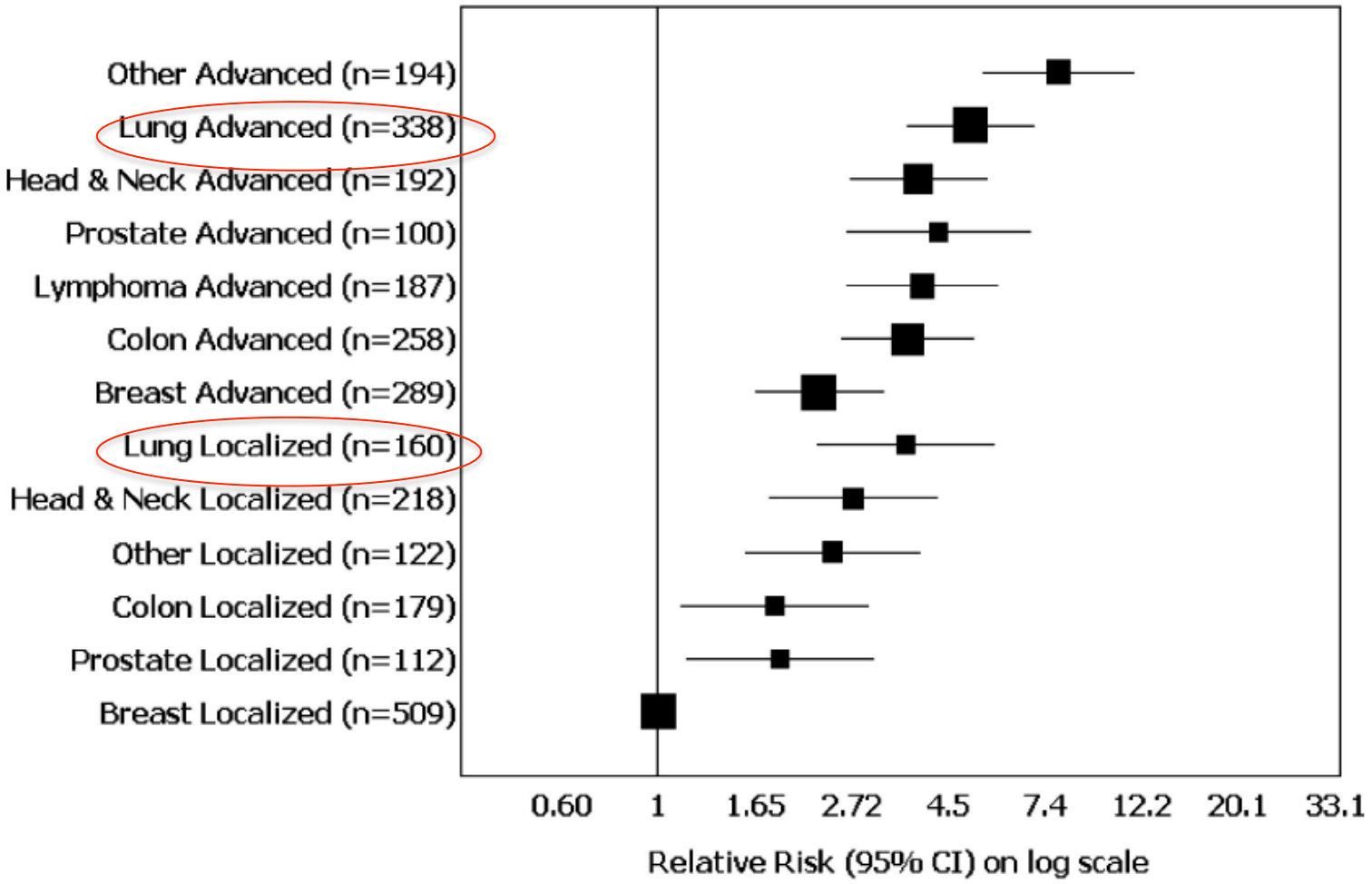
Relative Risk of Poor Performance Status* (Patient-rated)

(n=2858 patients)



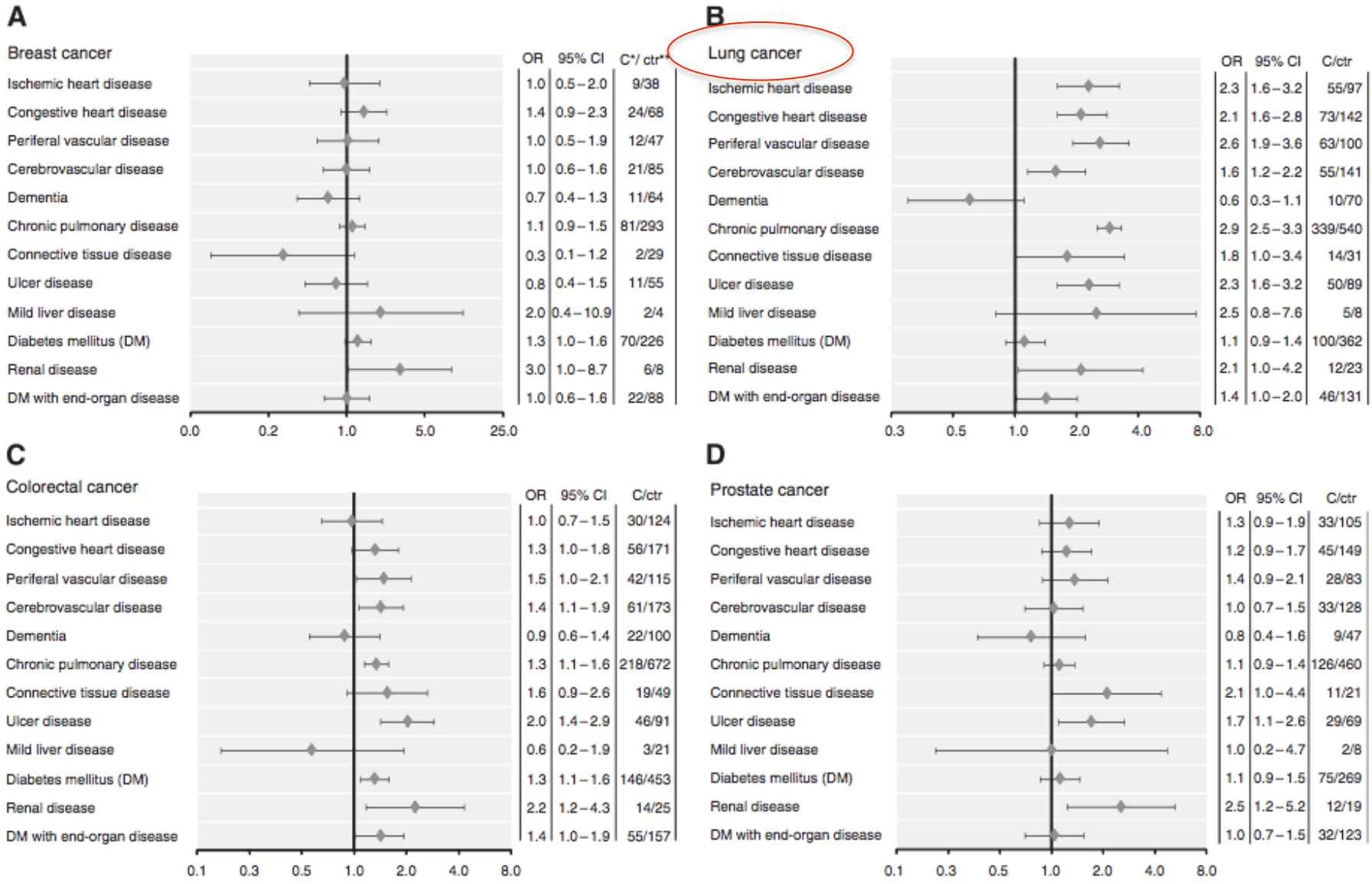


Figure 2 Forest plot of ORs associating Charlson comorbidity items with a diagnosis of cancer according to cancer site.

TL Jorgensen et al, Br J Cancer, 2012

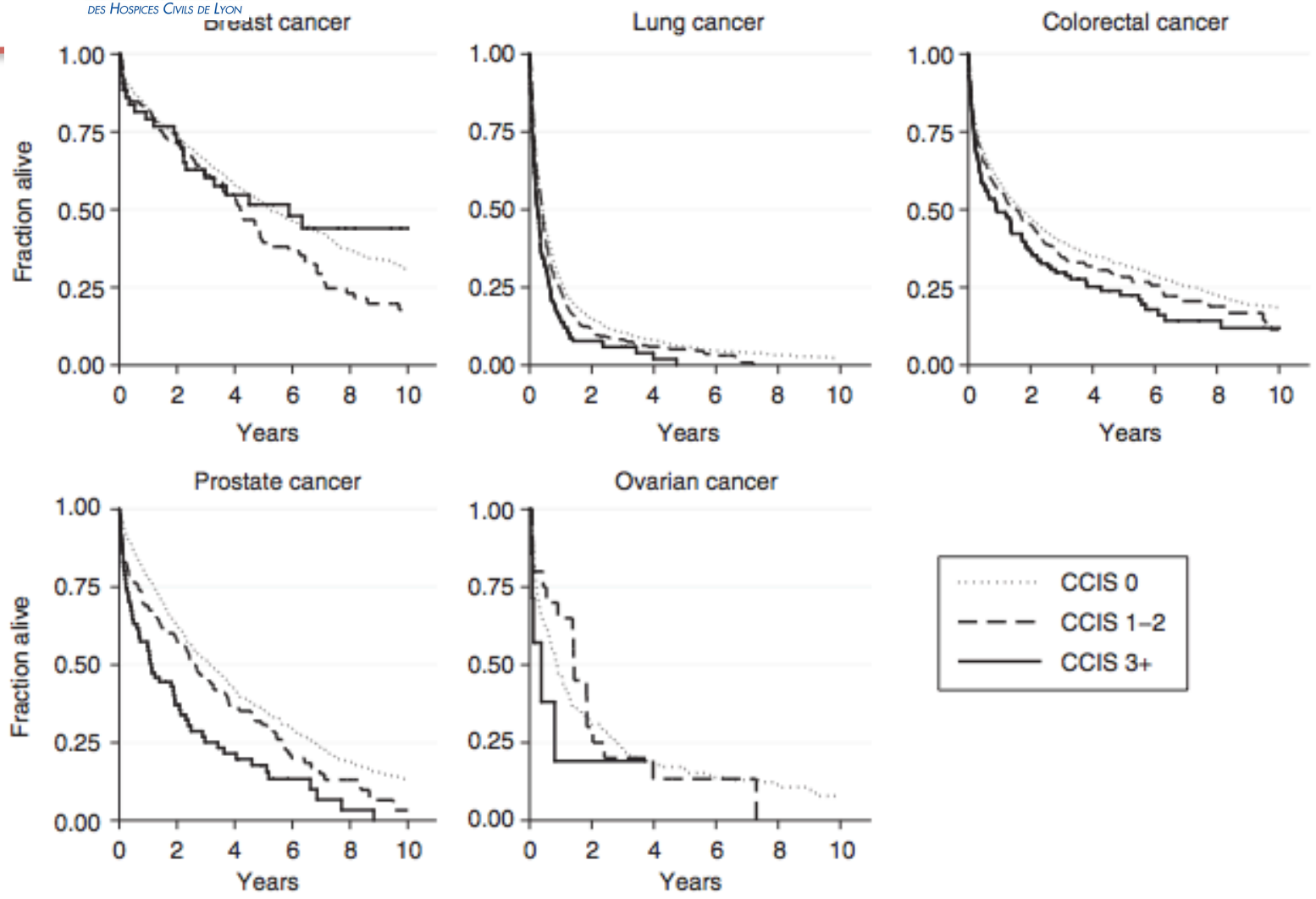


Figure 3 Overall survival according to CCIS and cancer site.

TL Jorgensen et al, Br J Cancer, 2012

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