2º Seminário Internacional Brasil sem Amianto: uma abordagem da Saúde do Trabalhador.

15 a 18 de maio de 2018
Hotel Bourbon Convention Ibirapuera

SAIBA MAIS

BRASIL SEM AMIANTO

Mesothelioma registry systems Italy and Lombardy

Dario Consonni

Epidemiology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

FONDAZIONE IRCCS CA' GRANDA
OSPEDALE MAGGIORE POLICLINICO

Sistema Sanitario Regione Lombardia

Conflicts of interest

# I served as expert for the judge in asbestos criminal trials

Outline

- **National Mesothelioma Registry (ReNaM)**
- **Lombardy Mesothelioma Registry (RML)**
  - **Geographical distribution**
  - **The asbestos-cement factory Fibronit: impact**
  - **Mesothelioma projections as of 2029**
  - **Ongoing projects**
- **Lung cancer and asbestos in the EAGLE case-control study**

Outline

- **National Mesothelioma Registry (ReNaM)**
- Lombardy Mesothelioma Registry (RML)
  - Geographical distribution
  - The asbestos-cement factory Fibronit: impact
  - Mesothelioma projections as of 2029
  - Ongoing projects
  - Lung cancer and asbestos in the EAGLE case-control study

Italy: asbestos production/import 1945-92

Amphiboles and chrysotile
3.75 million tons

Import

Production
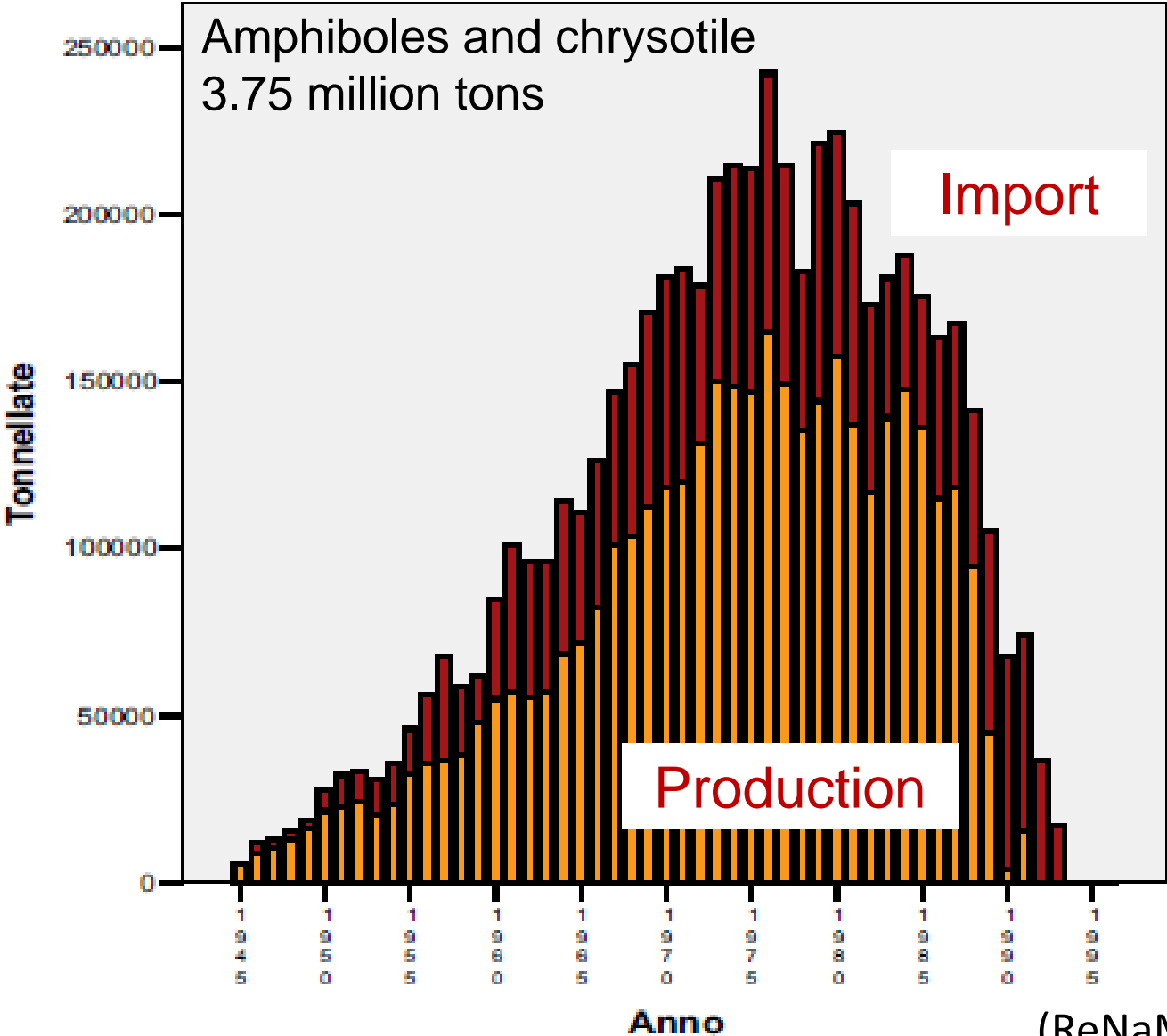
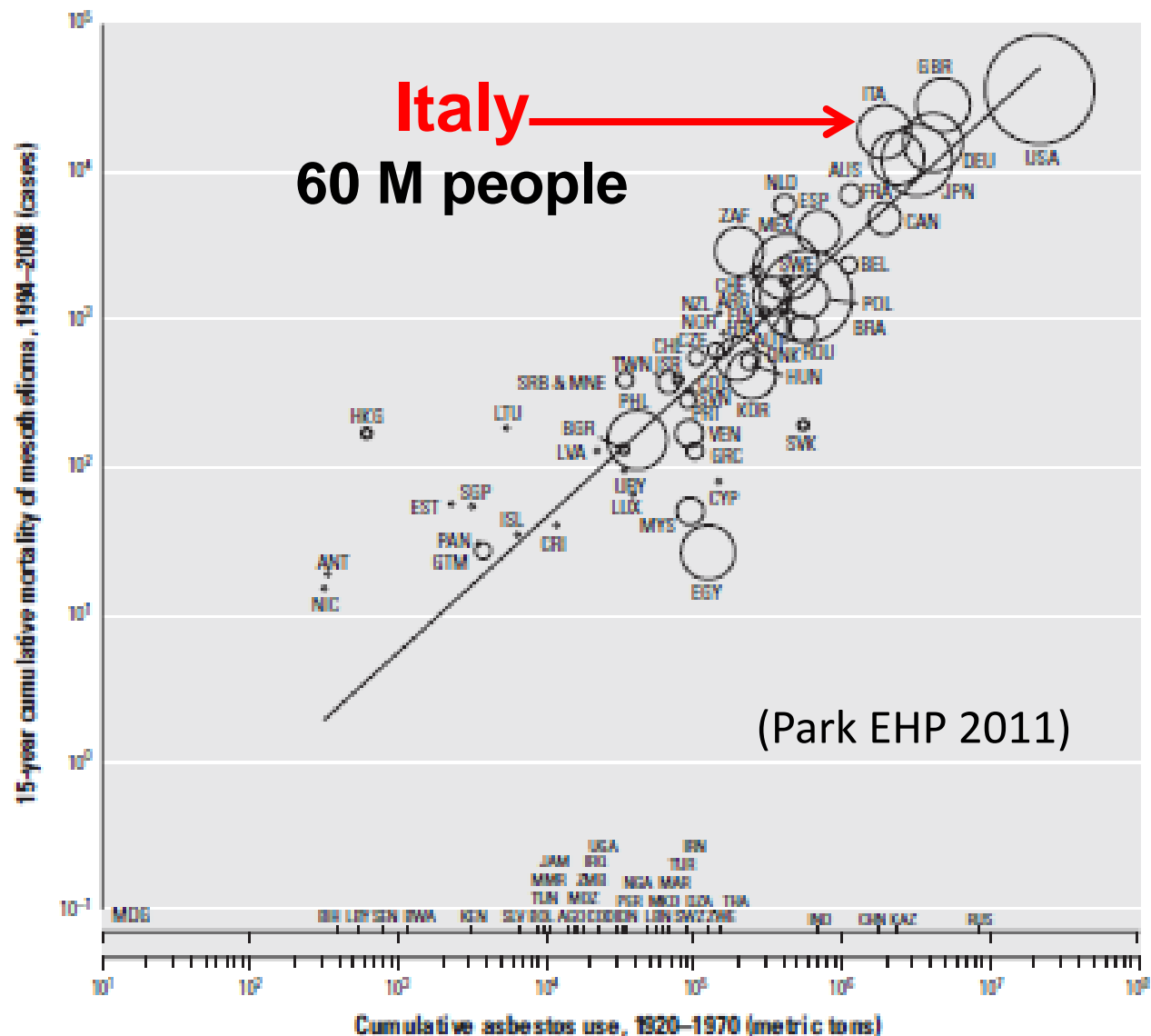Law 257/1992
asbestos ban

(ReNaM 2006)

Figure 1. Relationship between 15-year cumulative mortality of mesothelioma (1994–2008) and cumulative use of asbestos (1920–1970) weighted by the size of national populations in 56 countries/entities with data for both mesothelioma and asbestos use. Asbestos use for 33 countries/entities without mesothelioma frequency data is indicated along the x-axis. The figure is based on the following regression model: $\log_{10}$(15-year cumulative mortality of mesothelioma) $= \beta_0 + \beta_1 \times \log_{10}$(cumulative use of asbestos), where $\beta_0 = -1.998$ (95% CI, –2.676 to –1.319) and $\beta_1 = 0.913$ (95% CI, 0.800 to 1.026). Adjusted $R^2 = 0.827$; $p < 0.0001$.

Italy: pleural MM mortality projections 2000-2029

Figure 2. Italian raw asbestos per capita consumption (five-year moving average - tons per 1,000,000 inhabitants), observed (1969-1999) and predicted (2000-2029) pleural mesothelioma deaths[1] (MP) among men aged 25-89 years old in Italy.
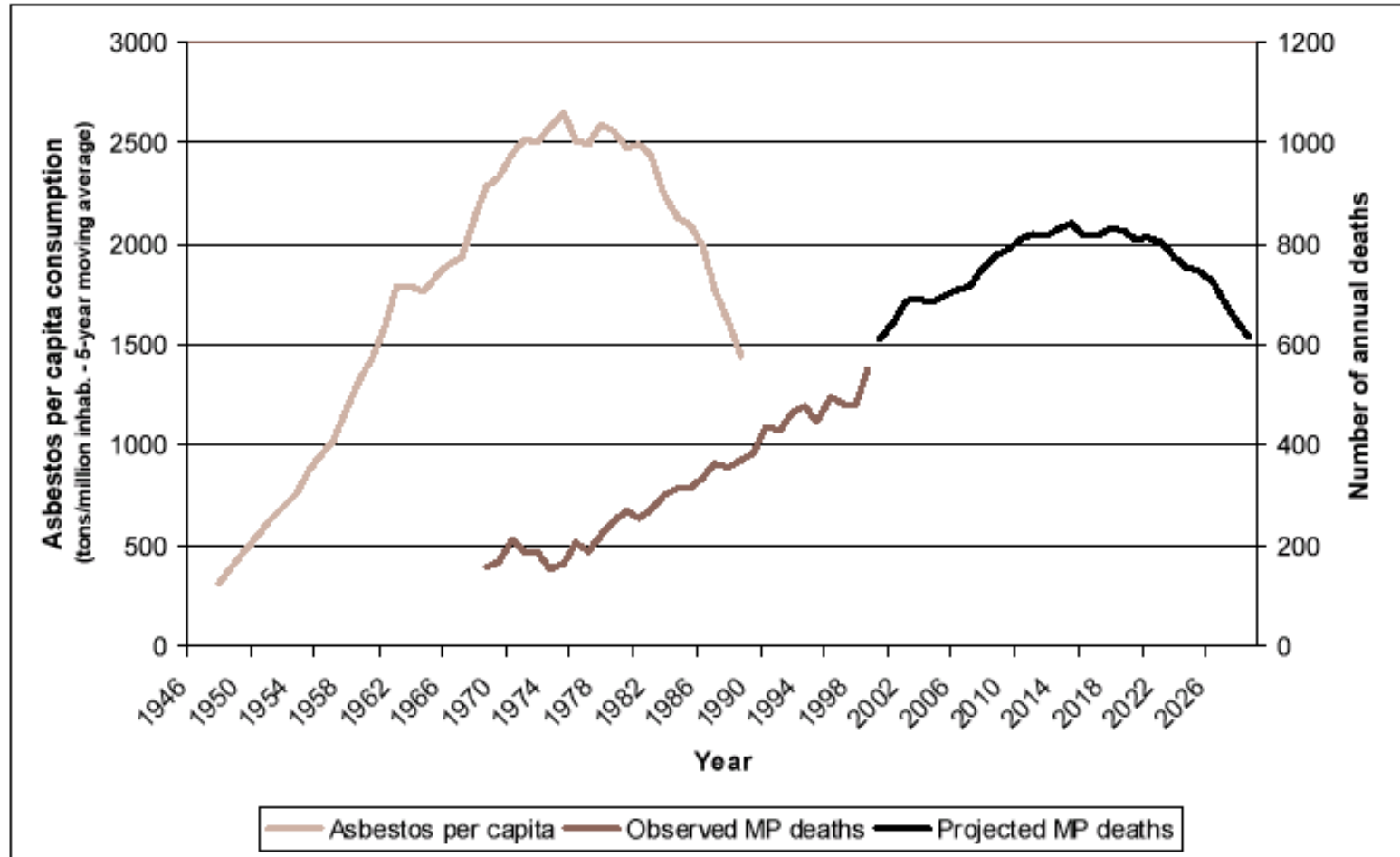
[1] Pleural mesothelioma deaths = pleural cancer deaths * 0.73.

(Marinaccio IJC 2005)

ReNaM, INAIL (Italian Compensation Authority)

Rilevazione dati di incidenza
Rilevazione dati non di incidenza
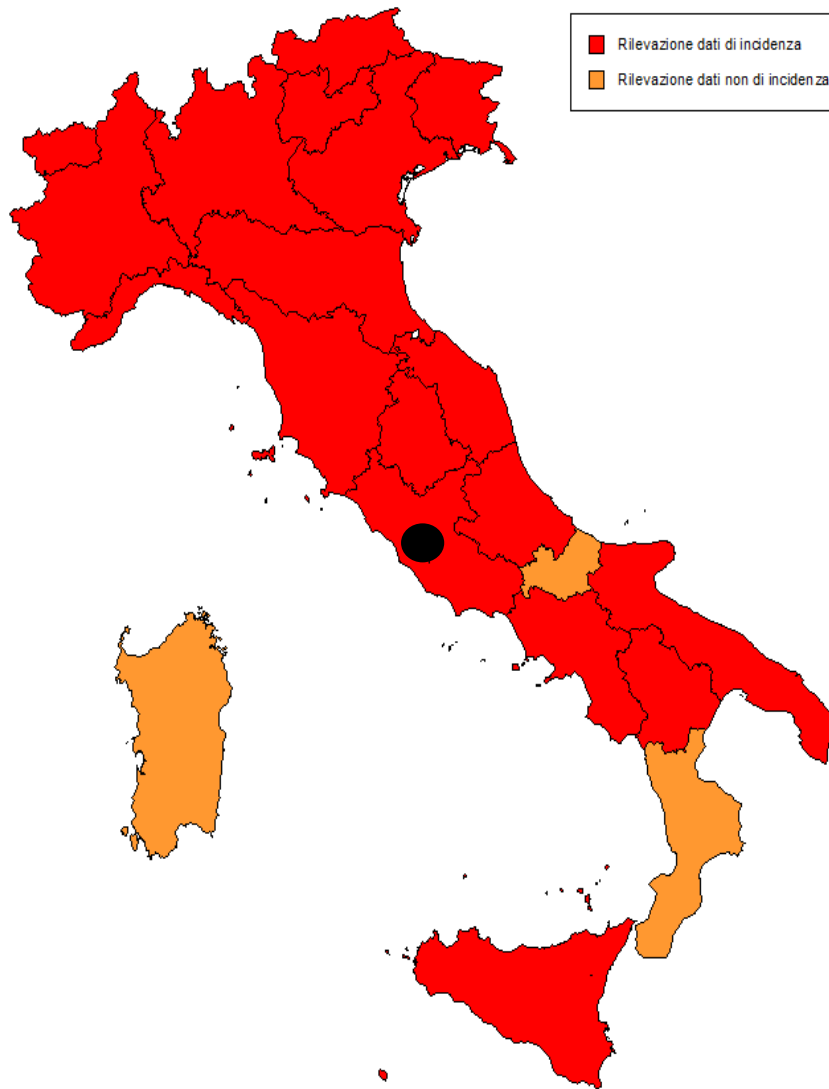
- National MM Registry (ReNaM, INAIL, Rome) **Law 308/2002**
- **Network** of Regional Operative Centers (**COR**)
- Some Regions started earlier

Mesothelioma Registry: Objectives

- **Temporal trends and geographical distribution** of cases and incidence rates (could be done in any cancer registry)

- Cases by **sector**; **asbestos exposure** (patients or next-of-kin interviewed with a Standardized Questionnaire)

- **Medico-legal assistence** to patients and families (compensation for **occupational** and – since a few years – also **non-occupational** cases)

- E**pidemiological studies** on the asbestos-mesothelioma association

Epidemiology of malignant mesothelioma in Italy: surveillance systems, territorial clusters and occupations involved

Alessandro Marinaccio, Alessandra Binazzi, Michela Bonafede, Davide Di Marzio, Alberto Scarselli; Regional Operating Centres

Table 1 Italian National Mesothelioma Register (ReNaM) archives. Collected malignant mesothelioma cases by gender, age at diagnosis, period of incidence, anatomical site, diagnostic certainty level and morphology. ReNaM archives updated at December 2016, diagnosis period 1993–2015*, Italy

Variables	Men		Women		All	
	N	%	N	%	N	%
Age class						
≤44	326	1.7	166	2.1	492	1.8
45–64	5,343	27.2	1,856	24.0	7,199	26.3
65–74	7,360	37.5	2,477	32.1	9,837	36.0
≥75	6,604	33.6	3,224	41.7	9,828	35.9
Anatomical site						
Pleura	18,473	94.1	6,977	90.3	25,450	93.0
Peritoneum	1,042	5.3	727	9.4	1,769	6.5
Pericardium	39	0.2	19	0.2	58	0.2
Tunica vaginalis testis	79	0.4			79	0.3

19, 633 M   7,723 F   27,356 All
About 1,500 cases/year; M/F ratio = 2.5

Variables	Men		Women		All	
	N	%	N	%	N	%
Diagnostic evaluation						
Definite MM	16,075	81.9	5,928	76.8	22,003	80.4
Probable or possible MM	3,558	18.1	1,795	23.2	5,353	19.6
Morphology						
Epithelioid	1,0845	55.2	4,422	57.3	15,267	55.8
Biphasic	2,188	11.1	692	9.0	2,880	10.5
Fibrous	1,684	8.6	421	5.5	2,105	7.7
MM NOS*	2,469	12.6	986	12.8	3,455	12.6
Not available	2,447	12.4	1,202	15.5	3,649	13.3
Overall	19,633	100.0	7,723	100.0	27,356	100.0

Table 2 Italian National Mesothelioma Register (ReNaM) archives. Collected malignant mesothelioma cases by modality of asbestos exposure and gender. ReNaM archives updated at December 2016, diagnosis period 1993–2015*, Italy

Modality of exposure	Incidence period (1993–2015)		
	Male (%)	Female (%)	Total (%)
Occupational, definite	9,300 (59.3)	987 (17.3)	10,287 (48.1)
Occupational, probable	1,358 (8.7)	191 (3.3)	1,549 (7.2)
Occupational, possible	2,246 (14.3)	736 (12.9)	2,982 (13.9)
Familial	152 (1.0)	895 (15.7)	1,047 (4.9)
Environmental	409 (2.6)	530 (9.3)	939 (4.4)
Other non-occupational	128 (0.8)	194 (3.4)	322 (1.5)
Unlikely	268 (1.7)	308 (5.4)	576 (2.7)
Unknown	1,824 (11.6)	1,861 (32.6)	3,685 (17.2)
Total defined	15,685 (100.0)	5,702 (100.0)	21,387 (100.0)
Total	19,633 (100.0)	7,723 (100.0)	27,356 (100.0)
Total defined	15,685 (79.9)	5,702 (73.8)	21,387 (78.2)
Total undefined	3,948 (20.1)	2,021 (26.2)	5,969 (21.8)

*, case list for year 2015 is not complete and collection of data is to be considered on going.

Rates by municipality 1993-2015

Men

Women
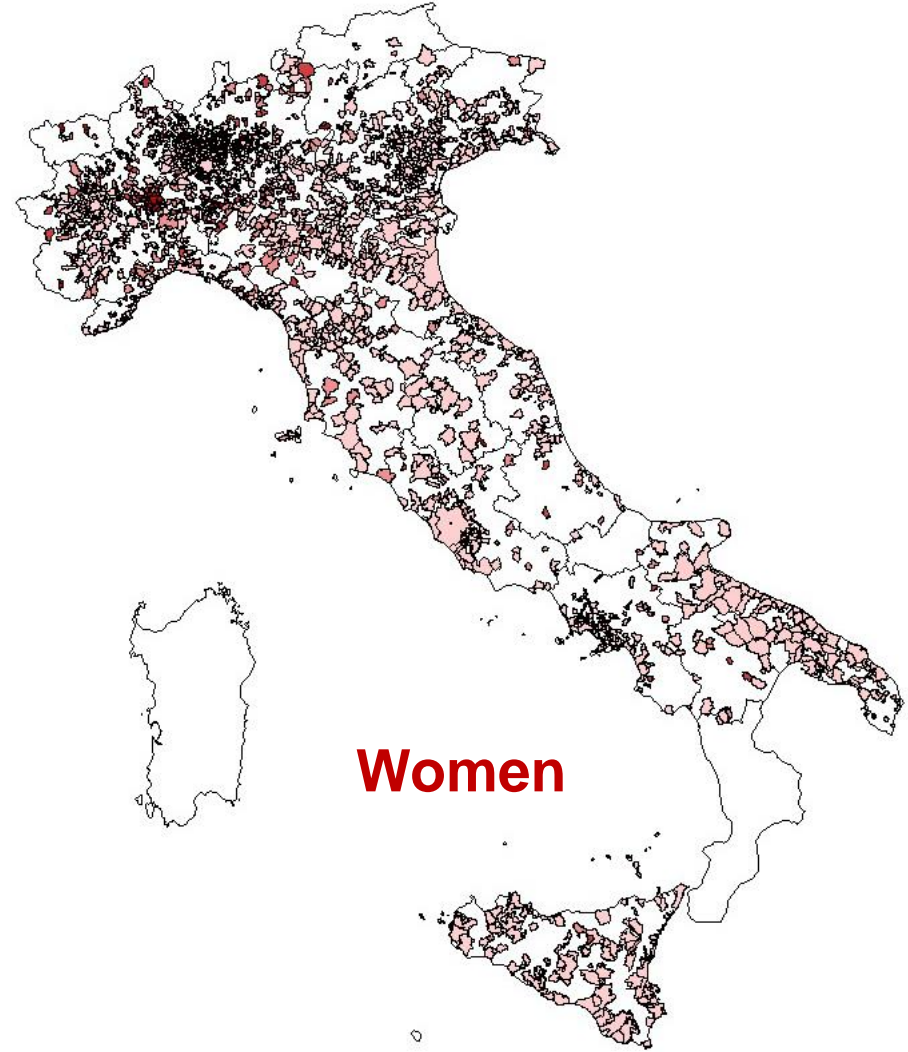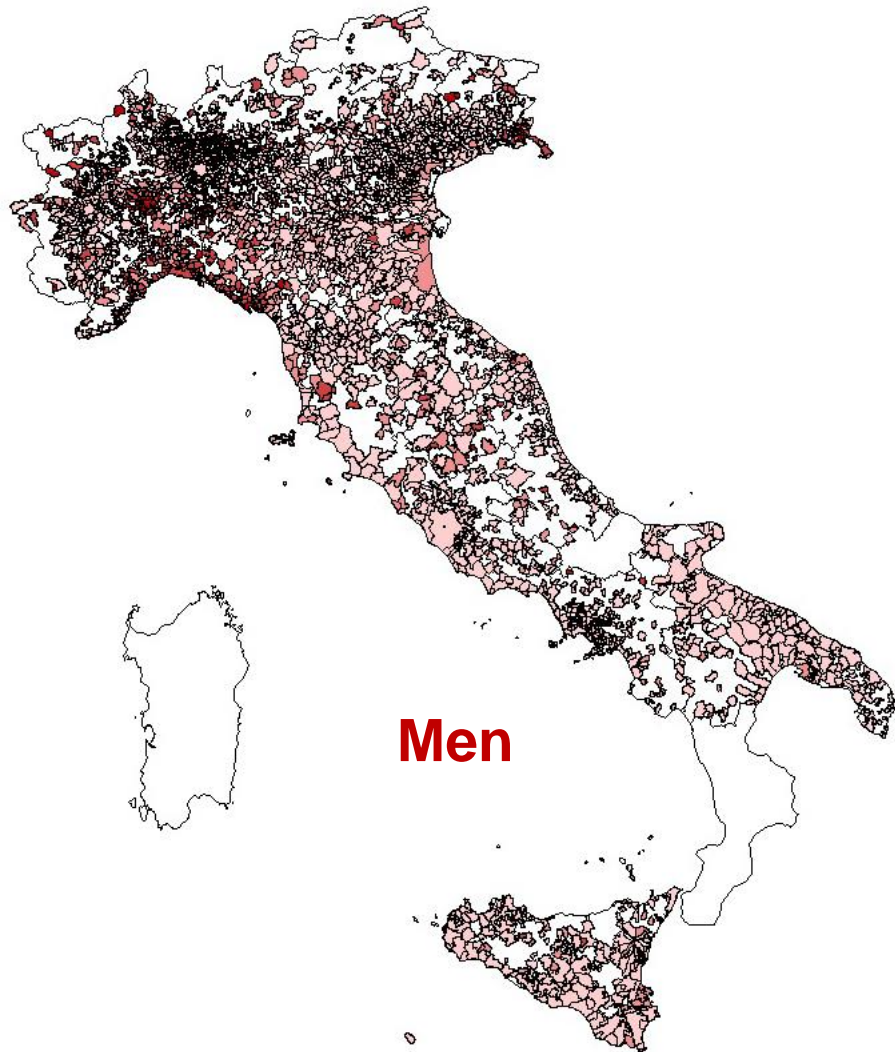
Figura 1 Dimensione dell'archivio. Numero di casi di mesotelioma segnalati al ReNaM, per tutte le sedi, per entrambi i generi e per tutti i livelli di certezza diagnostica, per COR di segnalazione (Italia, 1993 - 2012, N=21.463)
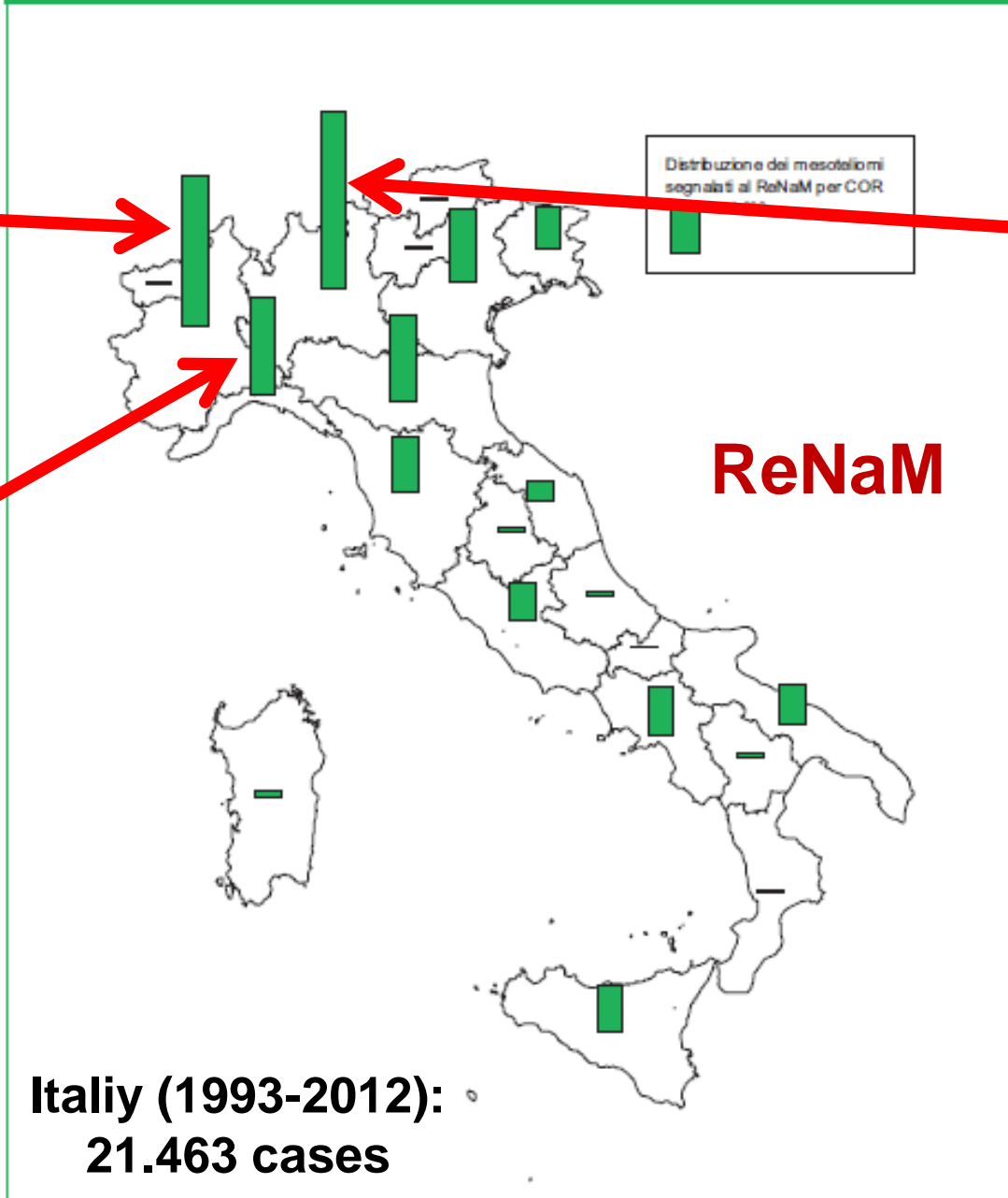
Distribuzione dei mesoteliomi segnalati al ReNaM per COR

ReNaM

Piedmont, the region of Casale Monferrato (1993-2011) 3.560 cases

Liguria (1994-2012) 2.314 cases

Lombardy (2000-2012) 4.215 cases

Italiy (1993-2012): 21.463 cases

QUINTO RAPPORTO

INAIL

il Registro Nazionale dei Mesoteliomi

Ricerca

Outline

- National Mesothelioma Registry (ReNaM)
- **Lombardy Mesothelioma Registry (RML)**
  - Geographical distribution
  - The asbestos-cement factory Fibronit: impact
  - Mesothelioma projections as of 2029
  - Ongoing projects
- Lung cancer and asbestos in the EAGLE case-control study

Lombardy Mesothelioma Registry (RML)

Lombardy, N-W Italy, 23,864 km^2, 10 million people, highly industrialized
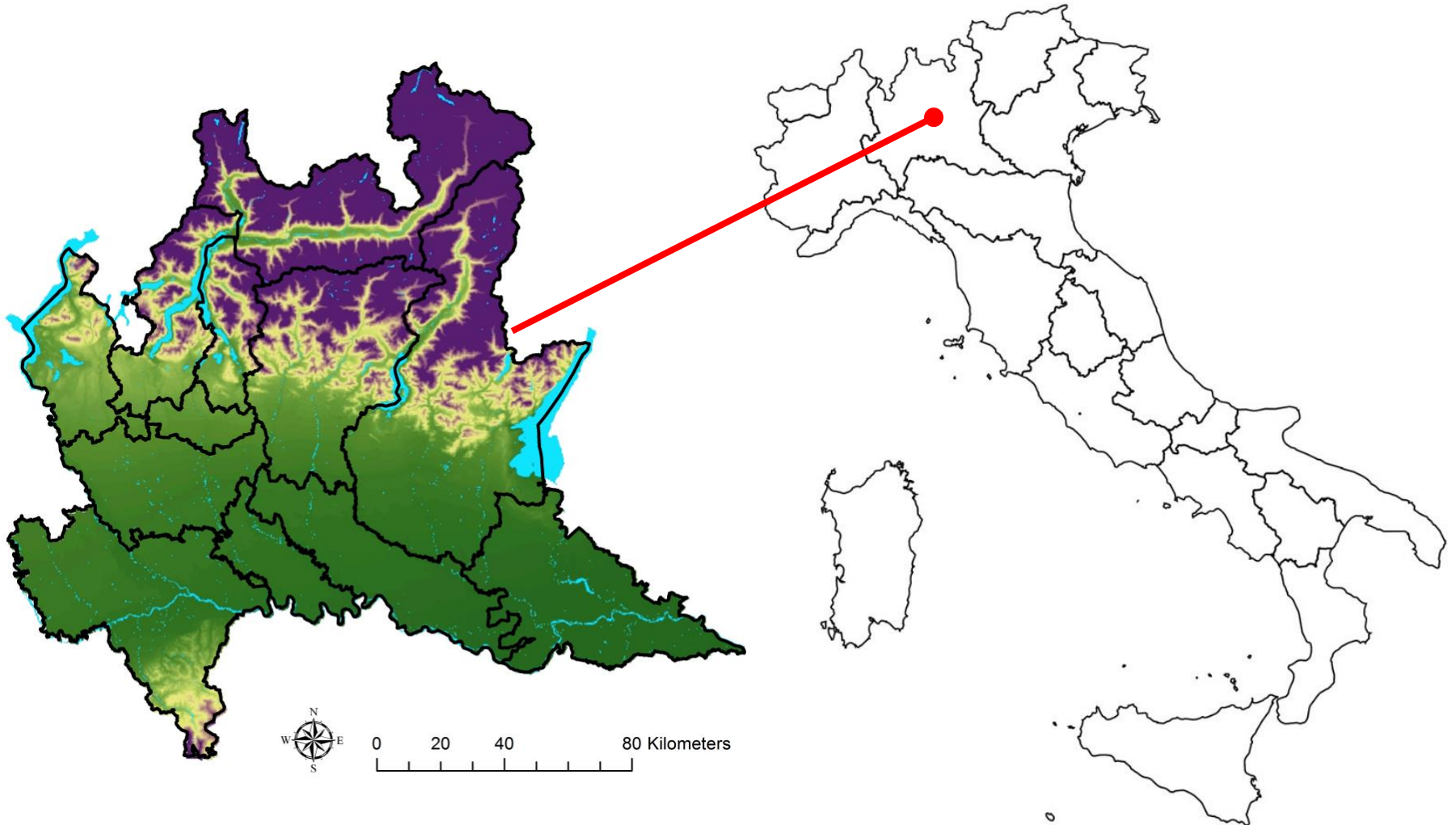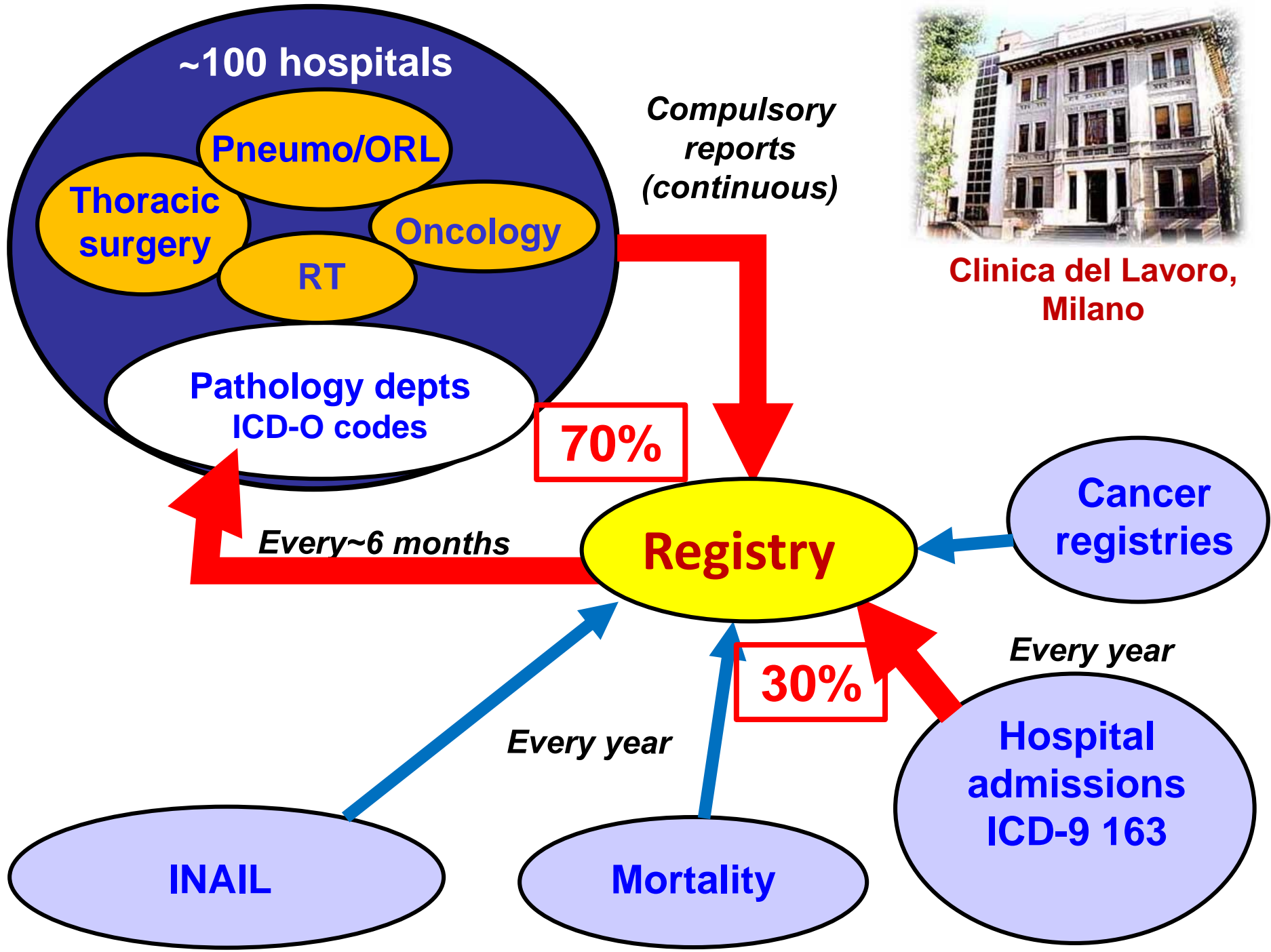
Diagnostic evaluation

Review af all clinical documentation

- **Definite**: histology + immunohistochemistry **80%**
- **Probable**: histology   **8%**
- **Possible**: imaging   **12%**

Asbestos exposure

Verified cases interviewed: **94%** (95% M, 91% F)
Patients: 54% (59% M, 45% F)

- Occupational (definite, probable, possible)
- Familiar
- Domestic
- Environmental
- Unknown (no evidence of asbestos exposure)
- Unlikely
- Undefined (interview not informative)

Validation of the diagnosis of mesothelioma and BAP1 protein expression in a cohort of asbestos textile workers from Northern Italy

P. Boffetta[1*], L. Righi[2], C. Ciocan[3], C. Pelucchi[4], C. La Vecchia[4], C. Romano[3], M. Papotti[2] & E. Pira[3]

A total of 76 of the 127 cases were also listed in the Regional Mesothelioma Registry of Piedmont: among them 56 were classified by the Registry as certain mesothelioma, 19 as probable or possible mesothelioma, and 1 as non-mesothelioma. If we consider our diagnostic validation as gold standard, the sensitivity of the classification of the Registry (certain confirmed mesothelioma versus other) was 83% and the specificity 34% (results not shown in detail).

**False positive rate = 66%,
but results not shown in detail!
This sentence is simply <u>FALSE</u>**

Disclosure

The authors have declared no conflicts of interest.

but in the same year…

J Glob Oncol 00. © 2017 by American Society of Clinical Oncology

interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

Paolo Boffetta
Consulting or Advisory Role: Edison

Matteo Malvezzi
No relationship to disclose

Enrico Pira
Other Relationship: Law offices

Eva Negri
No relationship to disclose

Carlo La Vecchia
Consulting or Advisory Role: Enel, Edison, Pirelli, Michelin

They are working for the companies in many asbestos criminal trials

Outline

- National Mesothelioma Registry (ReNaM)
- **Lombardy Mesothelioma Registry (RML)**
  - **Geographical distribution**
  - The asbestos-cement factory Fibronit: impact
  - Mesothelioma projections as of 2029
  - Ongoing projects
- Lung cancer and asbestos in the EAGLE case-control study

Geographical patterns of mesothelioma incidence and asbestos exposure in Lombardy, Italy

Carolina Mensi*, Sara De Matteis**, Dolores Catelan***, Barbara Dallari*,
Luciano Riboldi*, Angela Cecilia Pesatori*, ****, Dario Consonni*

* Department of Preventive Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
** National Heart & Lung Institute, Respiratory Epidemiology, Occupational Medicine and Public Health, Imperial College London, London, UK
*** Department of Statistics, Computer Science, Applications "Giuseppe Parenti", University of Florence, Florence, Italy
**** Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy

Results 2000-2012: 4,442 cases

	M	F
Pleura	**2693**	**1462**
	94.5%	91.8%
Peritoneum	**134**	**125**
	4.7%	7.9%
Pericardium	**6**	**5**
	0.2%	0.3%
Tunica Vaginalis Testis	**17**	
	0.6%	
Total	**850**	**1592**
	100%	100%

M/F Ratio: 2850/1592 = 1.8

Asbestos exposure

- No interview
- Unknown
- 17%
- Extra 4%
- 74%
- Occupational
- 39%
- Extra 14%
- 38%

M   F

Cases by Sector

Metal-mechanic, metallurgy

Construction

Non-asbestos textile

Asbestos-cement

■ M   ■ F

800
700
600
500
400
300
200
100
0

MMM | Edilizia | Tessile | Auto | Chimica | Alimentare | Militare | Trasporti | Gomma | Cemento-amianto | Ferrovie | Energia | Socio-sanitario
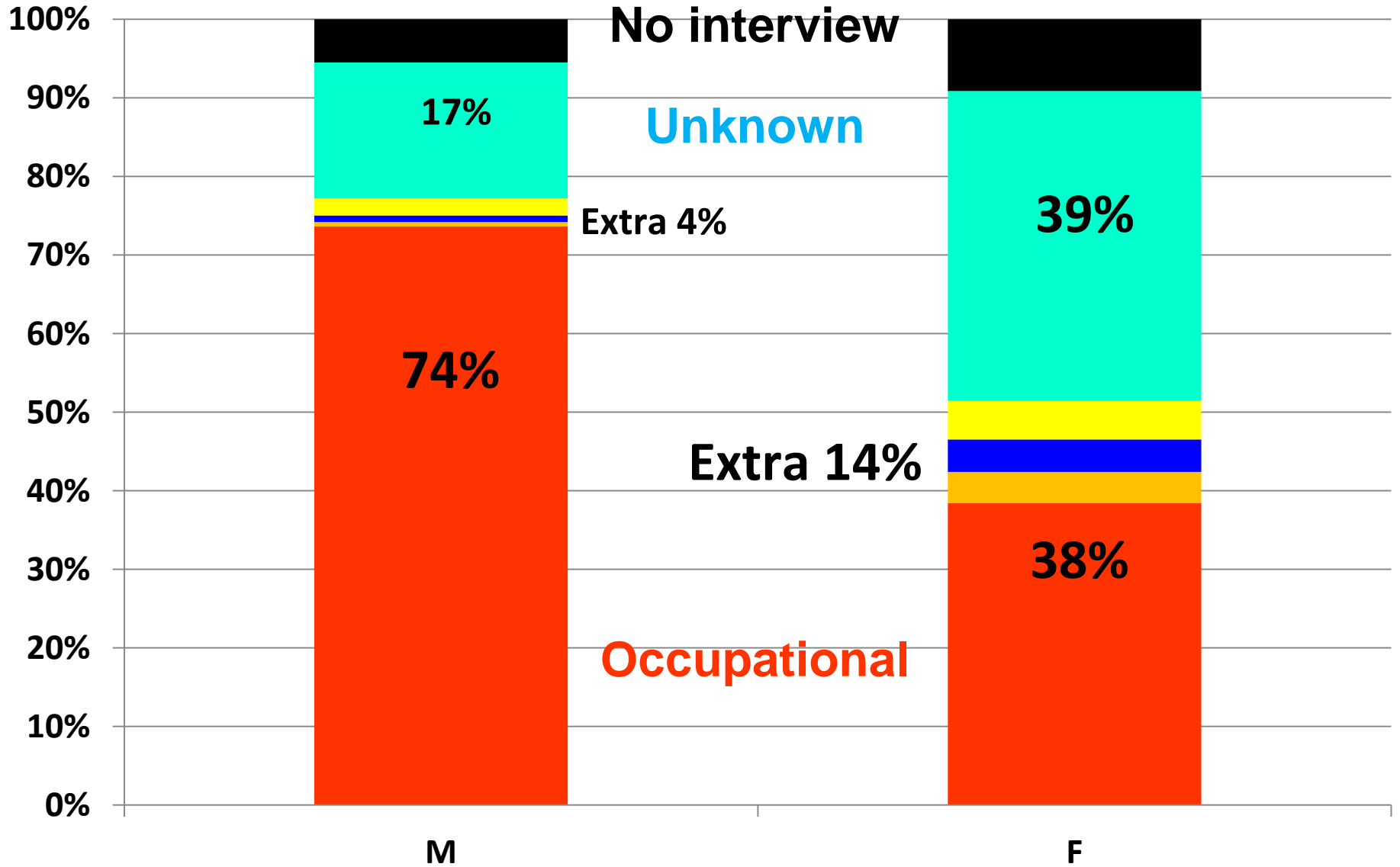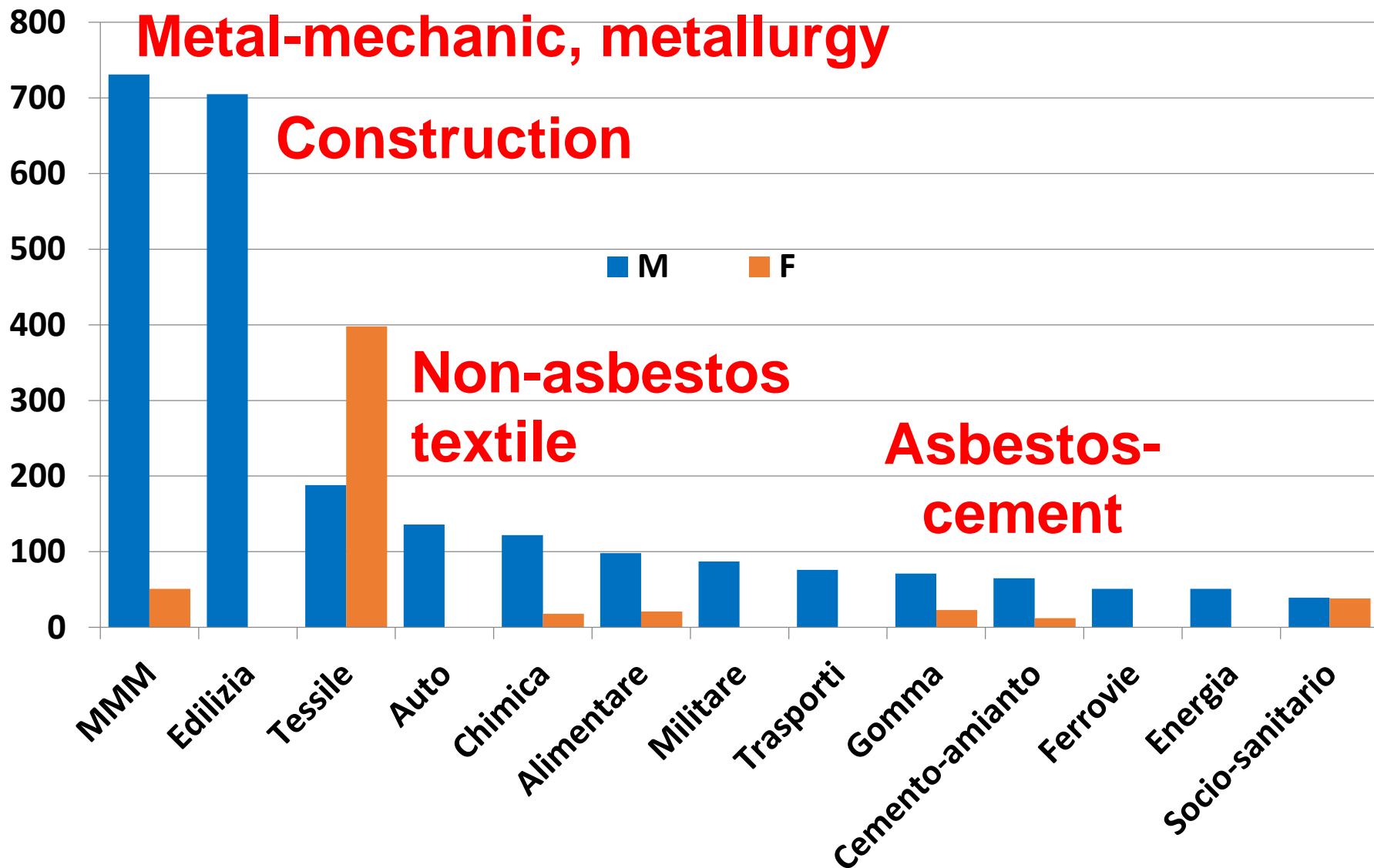
Textile industry – Asbestos in ceilings, walls, brakes
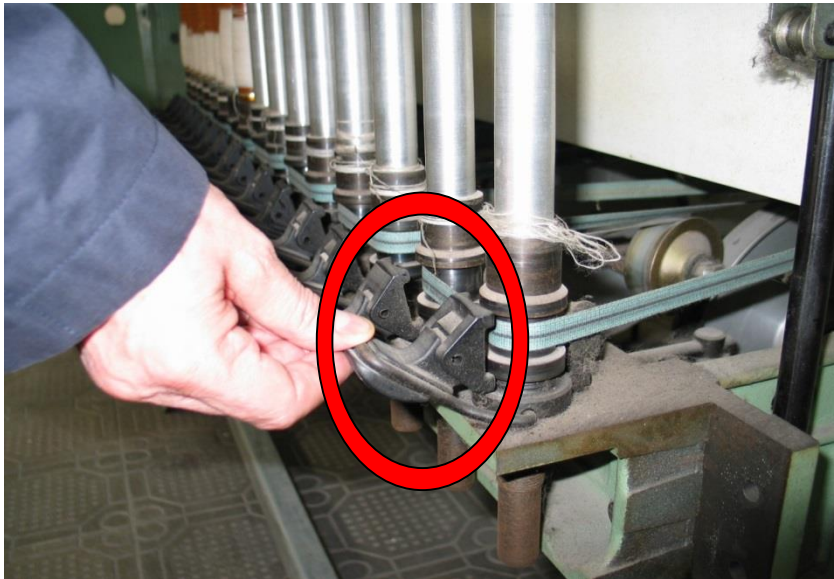
Il rischio amianto nel settore tessile: indicazioni dal Registro Mesoteliomi Lombardia e definitiva conferma

G. Chiappino, C. Mensi*, L. Riboldi, G. Rivolta

Centro Studi Effetti Biologici Polveri Inalate - Dipartimento di Medicina del Lavoro - Milano
* Responsabile Registro Mesoteliomi Lombardia

Rates by Province
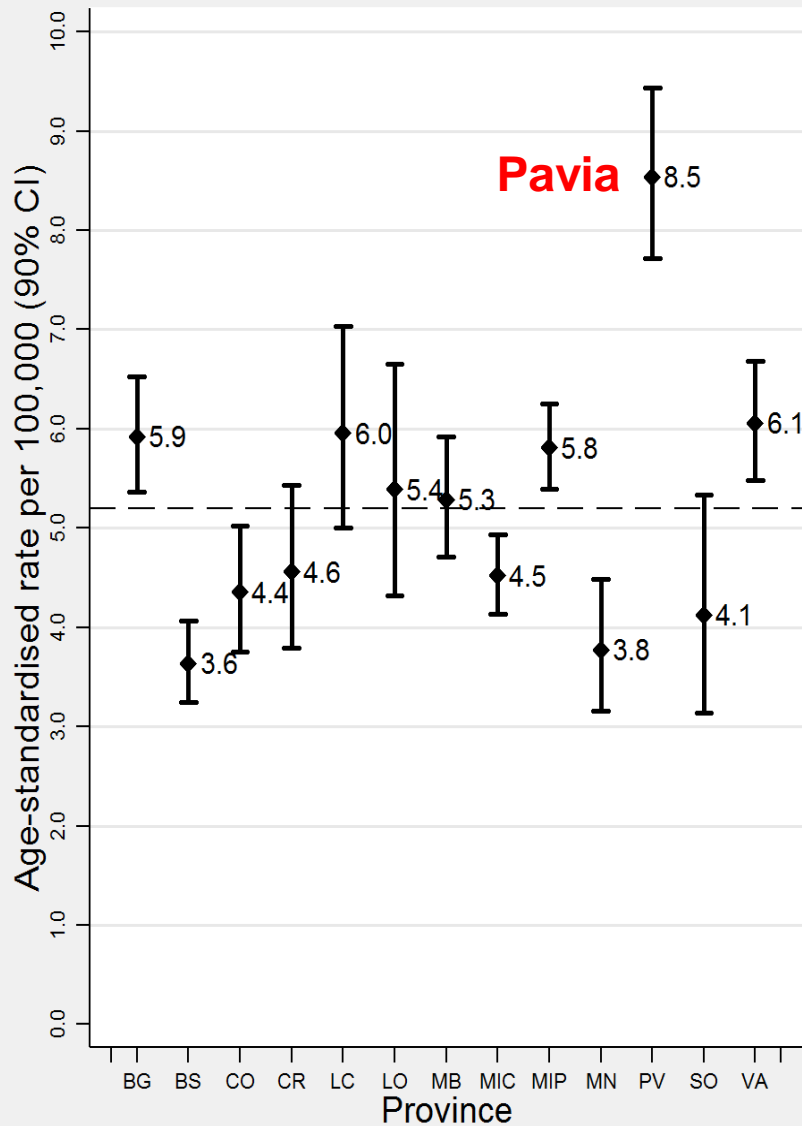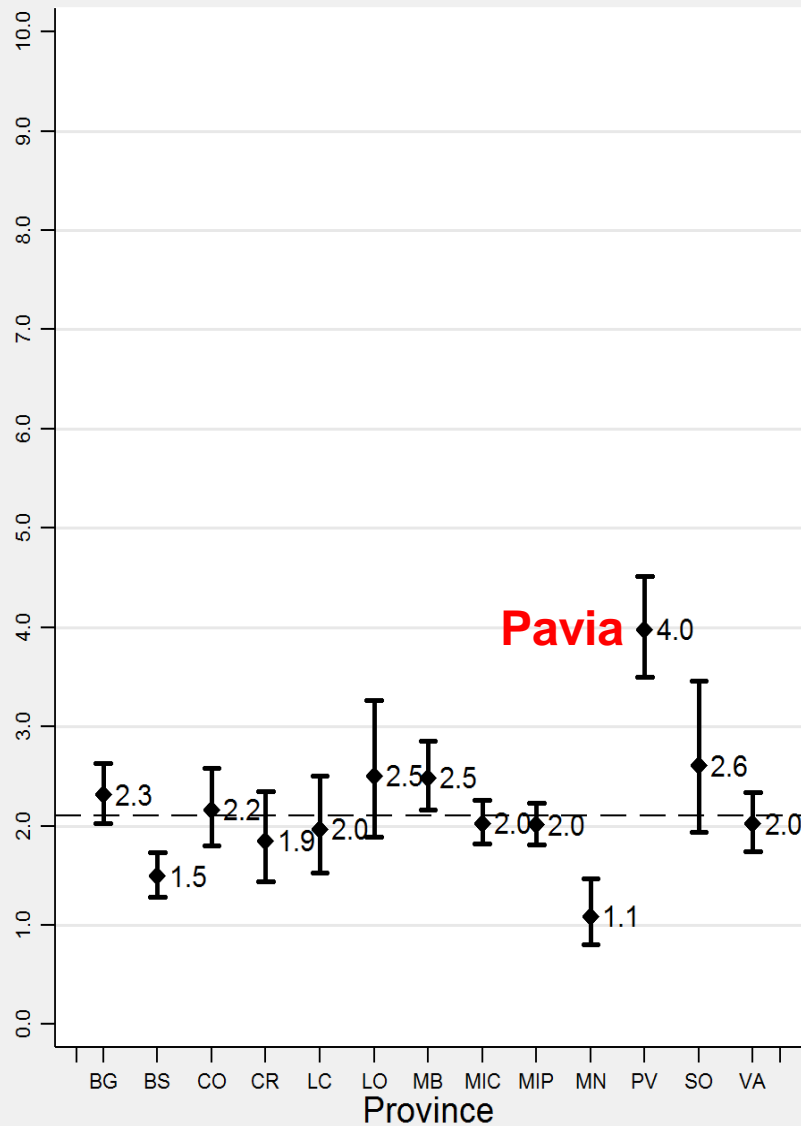
Cases by Province

Rates by Municipality

Crude rates (per 100,000) - Men

(10,150]
(5,10]
(4,5]
(3,4]
(2,3]
(1,2]
[0,1]

Crude rates (per 100,000) - Women

(10,150]
(5,10]
(4,5]
(3,4]
(2,3]
(1,2]
[0,1]

BYM crude rates (per 100,000) - Men

M4   M5
M3
M2
M1   M7   M6

(10,150]
(5,10]
(4,5]
(3,4]
(2,3]
(1,2]
[0,1]

BYM crude rates (per 100,000) - Women

F4   F5
F3
F2
F1

(10,150]
(5,10]
(4,5]
(3,4]
(2,3]
(1,2]
[0,1]
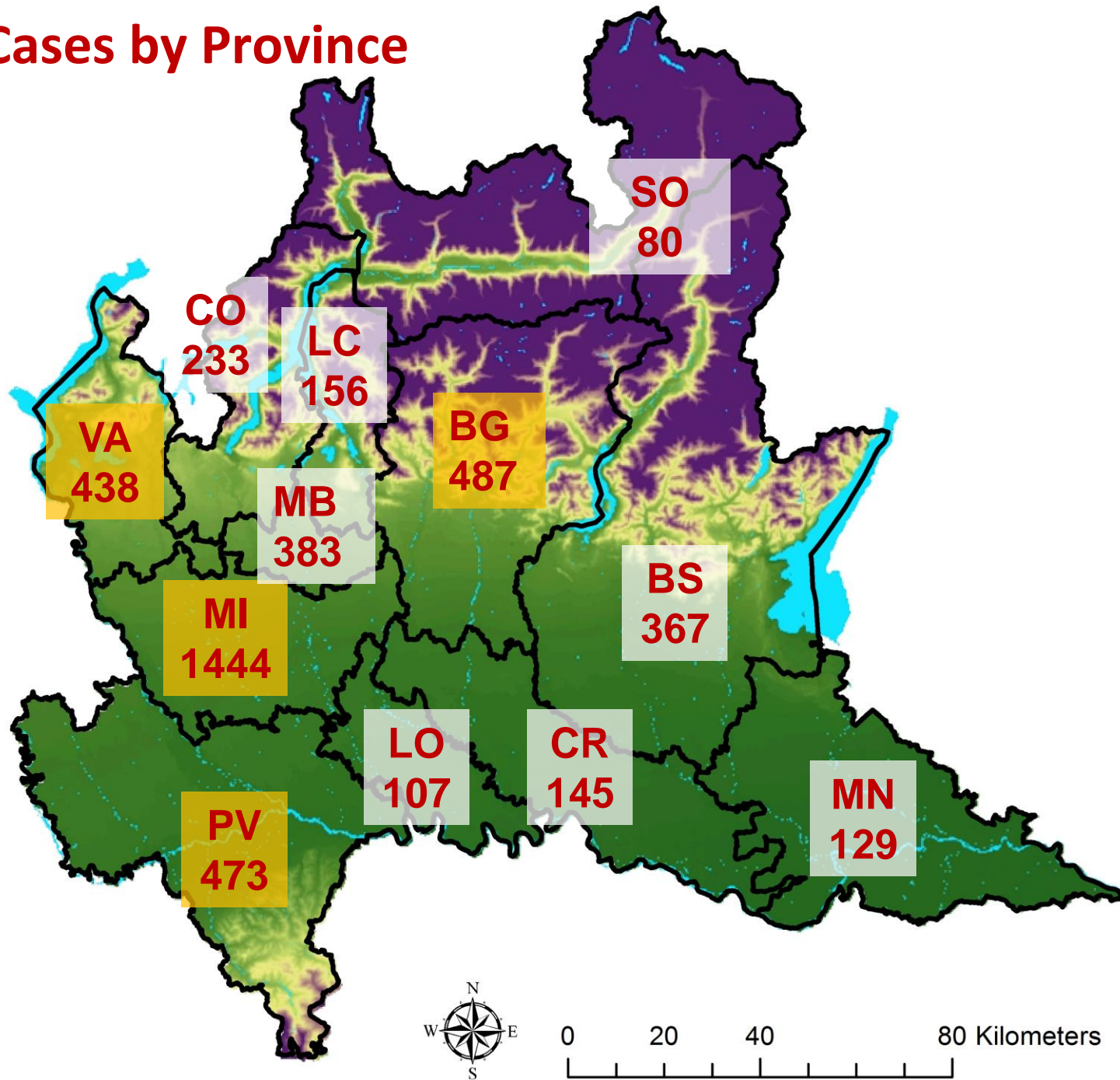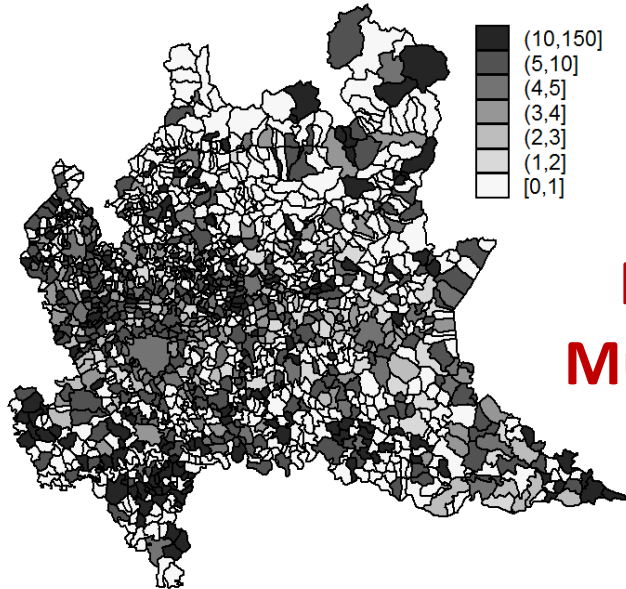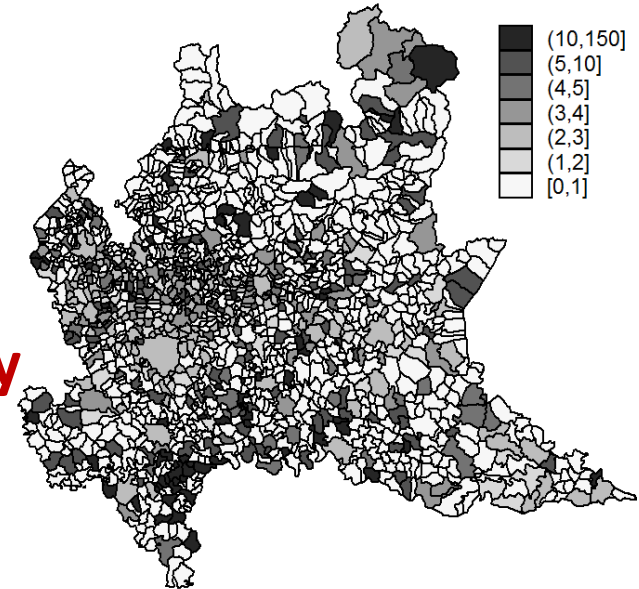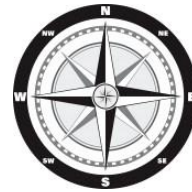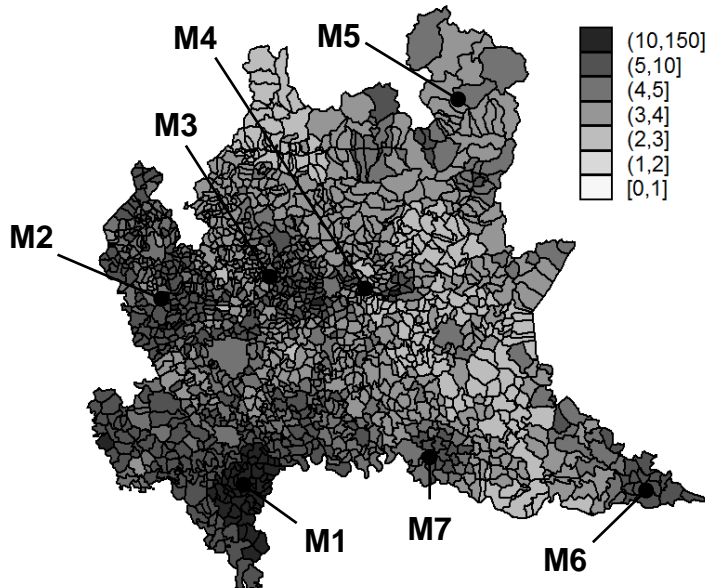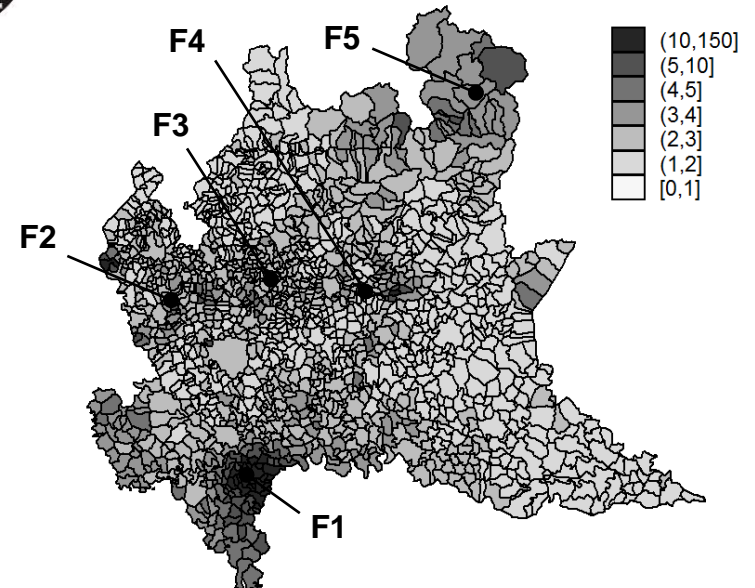
M1/F1 - Pavia

- **Asbestos-cement factory (Fibronit) in Broni (1932-92)**

- **Broni rates:**   **M: 100.0 (57 cases), F: 68.4 (44 cases)**

- **Stradella rates: M: 33.6   (23 cases); F: 43.5 (33 cases)**

- **(Borni < 10,000 people; Stadella 11,600 people)**
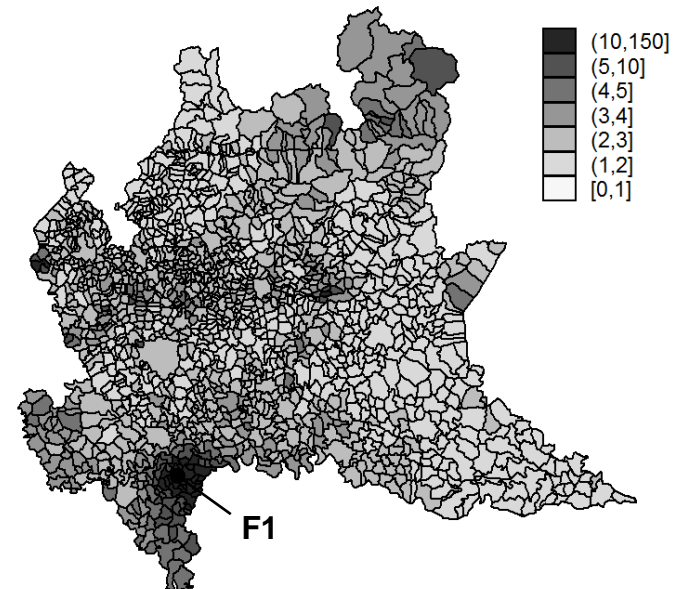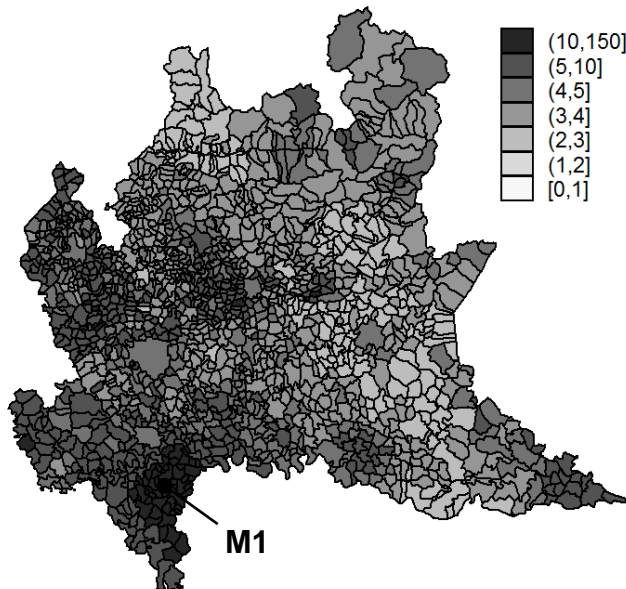
Outline

- National Mesothelioma Registry (ReNaM)
- **Lombardy Mesothelioma Registry (RML)**
  - Geographical distribution
  - **The asbestos-cement factory Fibronit: impact**
  - Mesothelioma projections as of 2029
  - Ongoing projects
- Lung cancer and asbestos in the EAGLE case-control study

ELSEVIER

ENVIRONMENT INTERNATIONAL

CrossMark

Impact of an asbestos cement factory on mesothelioma incidence: Global assessment of effects of occupational, familial, and environmental exposure

Carolina Mensi [a,1], Luciano Riboldi [a,1], Sara De Matteis [b,2], Pier Alberto Bertazzi [a,c,1,3], Dario Consonni [a,*]

[a] Department of Preventive Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[b] National Heart & Lung Institute, Respiratory Epidemiology, Occupational Medicine and Public Health, Imperial College London, London, UK
[c] Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy

- **Broni**: small town <10,000 people (Pavia Província)
- **Fibronit**: second largest Italian asbestos-cement factory in terms of person-years: 2.741 M, 714 F (1932-93). ~100,000 tons/year in the '60s

- Portland Cement 325 mixed with asbestos 7:1
- Chrysotile
- Crocidolite (10-15% in tiles, 30% in pipes)
- Amosite, small quantities
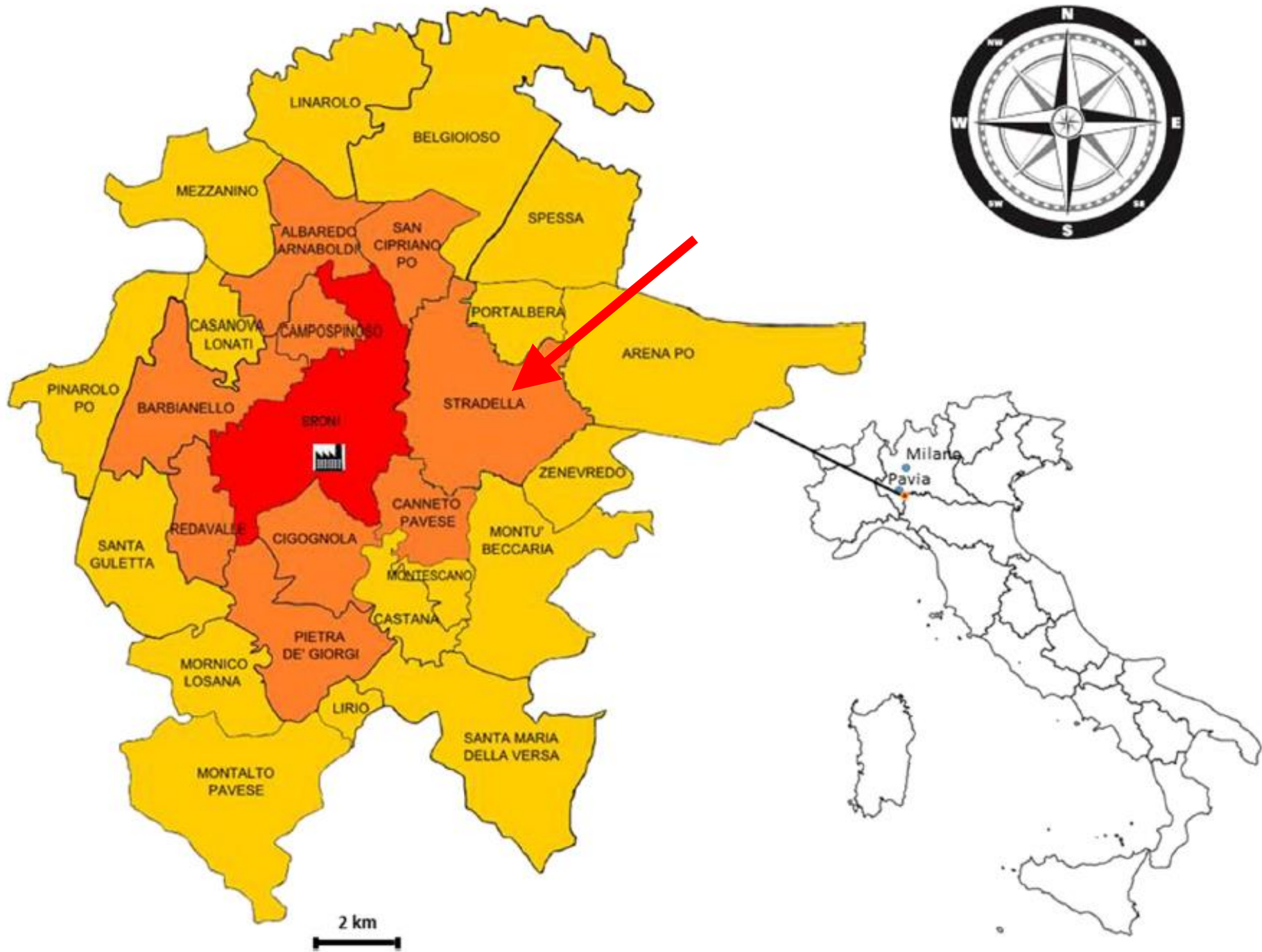
Results (2000-2011)

	Men	Women	Total
Occupational	<u>32</u>	6	38
Familiar	5	<u>32</u>	<u>37</u>
Environmental	23	<u>49</u>	<u>72</u>
-Broni	*20*	*<u>28</u>*	*48*
*-Adjacent towns**	*2*	*<u>17</u>*	*19*
-Surrounding towns	*1*	*4*	*5*
Total	**60**	**87**	147**

*Stradella (11,600 people), M: 2 cases F: 14 cases

**138 pleura, 9 peritoneum

- **147 cases** (130 more than expected in 12 years (2000-2011) caused by asbestos from Fibronit
- **Occupational** impact in **men**: 32 cases
- **Familar/Environmental** impact in **women**: 32 + 49
- **Broni** e **Stradella**: 48+16 cases

- [Not counted: 57 cases (47 M, 10 F) exposed to asbestos in other occupational contexts]

Not only Mesothelioma...

Mortality in asbestos cement workers in Pavia, Italy: A cohort study

Enrico Oddone[1,2] | Daniela Ferrante[3] | Sara Tunesi[3] | Corrado Magnani[3]

1818 workers (1663 M, 165 F) 1970-2014

Cancer site	Observed	Expected	Excess cases O – E
Pleura	74	2.8	71.1
Peritoneum	14	1.5	12.5
Lung	169	113.9	55.1
Ovary	4	1.1	2.9
Asbestosis	17	0	17
Total	278	119.3	158.7

Outline

- National Mesothelioma Registry (ReNaM)
- **Lombardy Mesothelioma Registry (RML)**
  - Geographical distribution
  - The asbestos-cement factory Fibronit: impact
  - **Mesothelioma projections as of 2029**
  - Ongoing projects
- Lung cancer and asbestos in the EAGLE case-control study

Incidence of mesothelioma in Lombardy, Italy: exposure to asbestos, time patterns and future projections

Carolina Mensi,[1] Sara De Matteis,[2] Barbara Dallari,[1] Luciano Riboldi,[1] Pier Alberto Bertazzi,[1] Dario Consonni[1]

Open Access

Cases 2000-2012

Cases: +3.6% / year
Crude rates: +2.6% / year

Cases: +3.3% / year
Crude rates: +2.5% / year

Adjusted rates by age:
65+ y: increasing
<65 y: decreasing

Men: 174, 182, 193, 209, 193, 219, 196, 227, 221, 252, 254, 255, 275

Women: 103, 99, 116, 104, 103, 120, 127, 130, 134, 107, 155, 166, 128

Year of diagnosis

—— Men   ----- Women
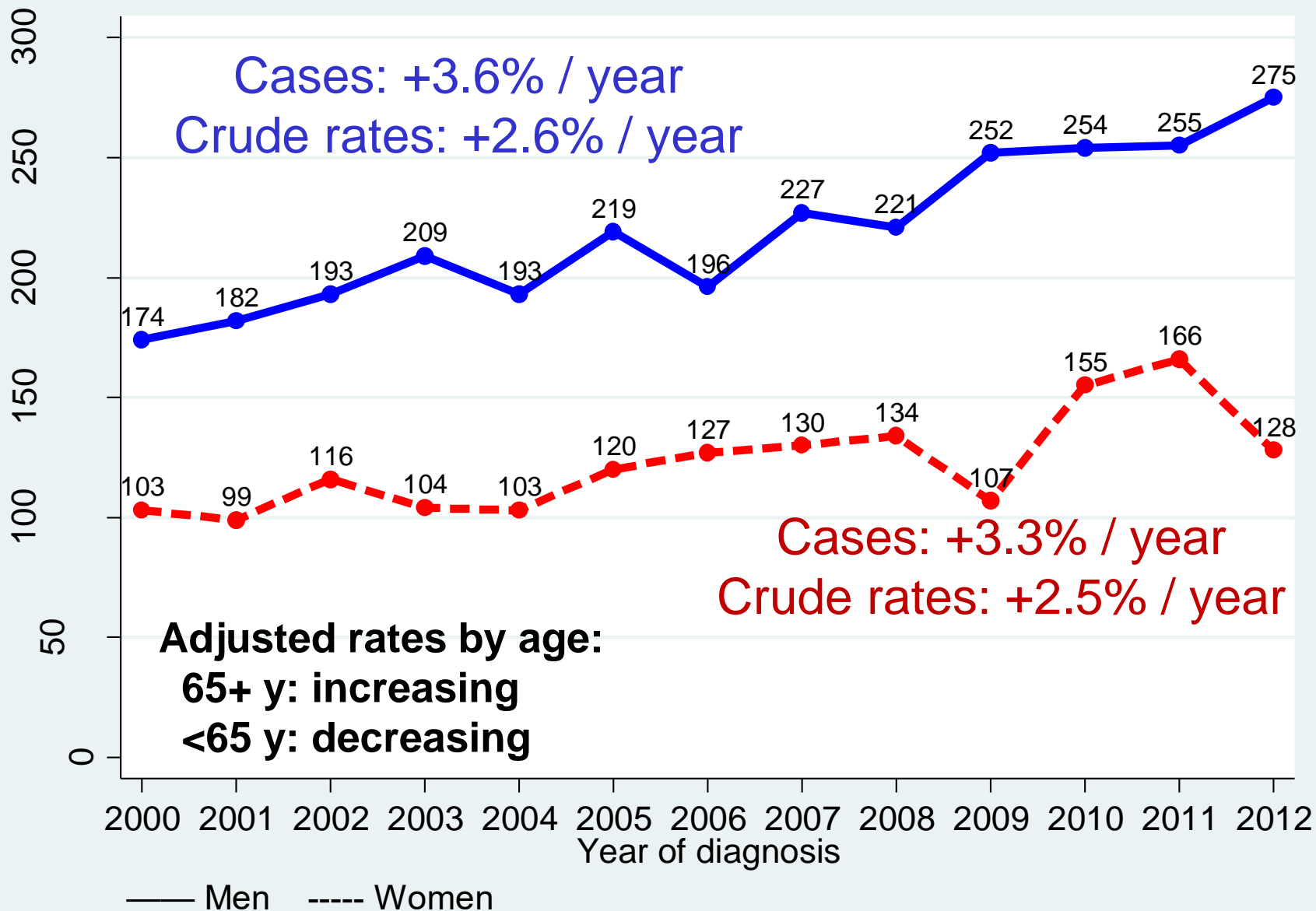
Poisson Age-Cohort model: results

Men

Women
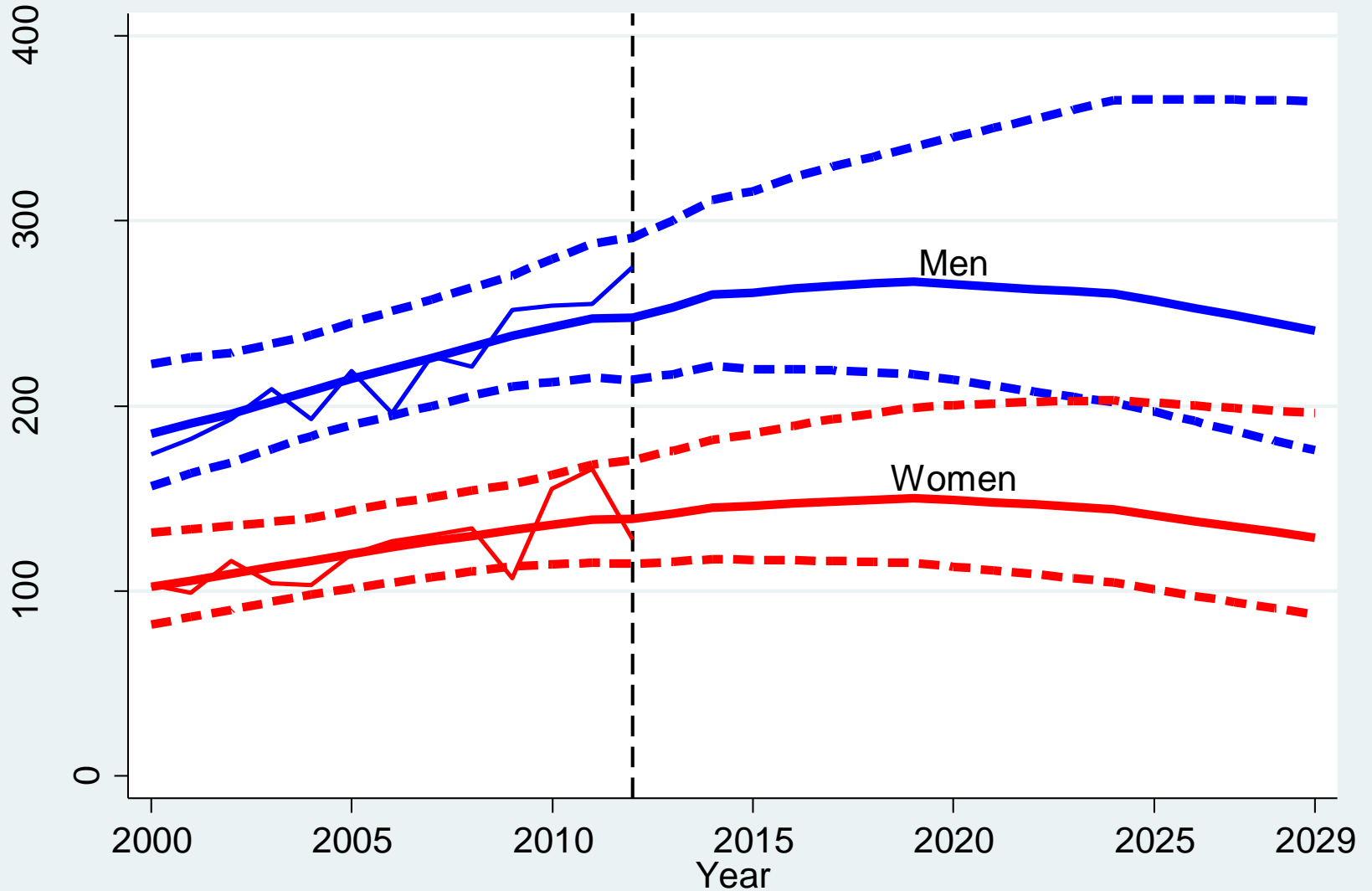
Solid lines: observed/predicted counts
Dashed lines: 90% bounds around predicted counts

- **Peak in 2019 (417 cases, 267 M, 150 F)**

- **Cases 2013-2029:**   **Total: 6832**
              M: 4397
              F: 2435

- **Cases 2000-2029:**   **Total: 11274**
              M: 7247
              F: 4027

- **Similar to Italian mortality projections** (Marinaccio IJC 2005)

- **Italy: only West European country in which asbestos consumption increased in 1975-85** (Marinaccio IJC 2015)

- **Cases are decreasing in some Regions, increasing in others** (ReNaM 2015)

Mesotheliomas in Lombardy 2000-2029
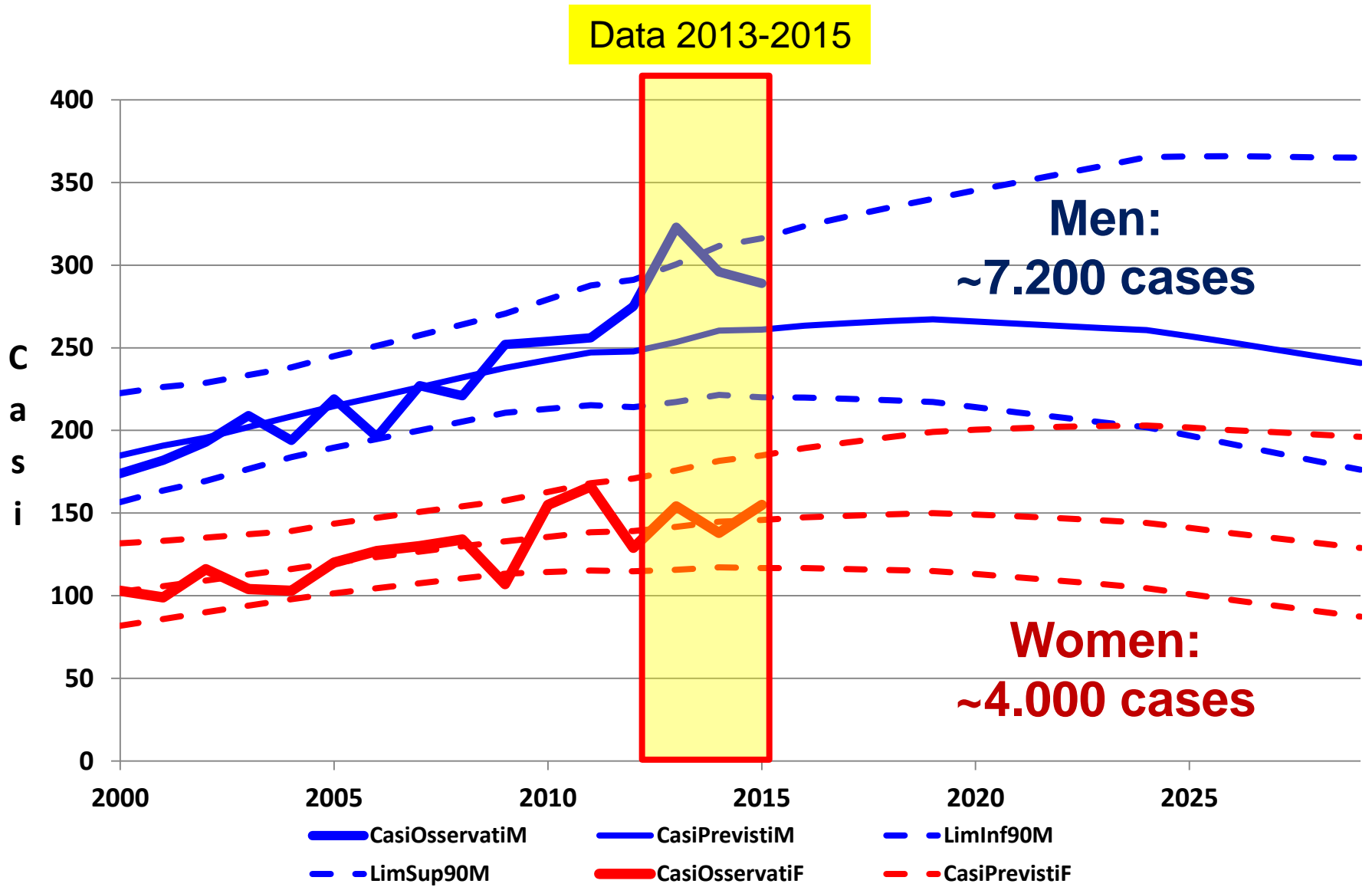
Outline

- National Mesothelioma Registry (ReNaM)
- **Lombardy Mesothelioma Registry (RML)**
  - Geographical distribution
  - The asbestos-cement factory Fibronit: impact
  - Mesothelioma projections as of 2029
  - **Ongoing projects**
- Lung cancer and asbestos in the EAGLE case-control study

Ongoing projects

- **Case-control study on pleural MM in 6 Regions**

- **Case-control study on pericardial and TVT MM in 6 Regions** (relationship with asbestos put into doubt in a recent review paper)

- **Case-control study on peritoneal MM in Lombardy**

- **Economical costs**

- **Comparison of MM cases with autopsy data in Pavia**

- **Rate Advancement Periods (RAP): M vs F**

Outline

- National Mesothelioma Registry (ReNaM)
- Lombardy Mesothelioma Registry (RML)
  - Geographical distribution
  - The asbestos-cement factory Fibronit: impact
  - Mesothelioma projections as of 2029
  - Ongoing projects

- **Lung cancer and asbestos in the EAGLE case-control study**

Not only Mesothelioma…

Impact of occupational carcinogens on lung cancer risk in a general population
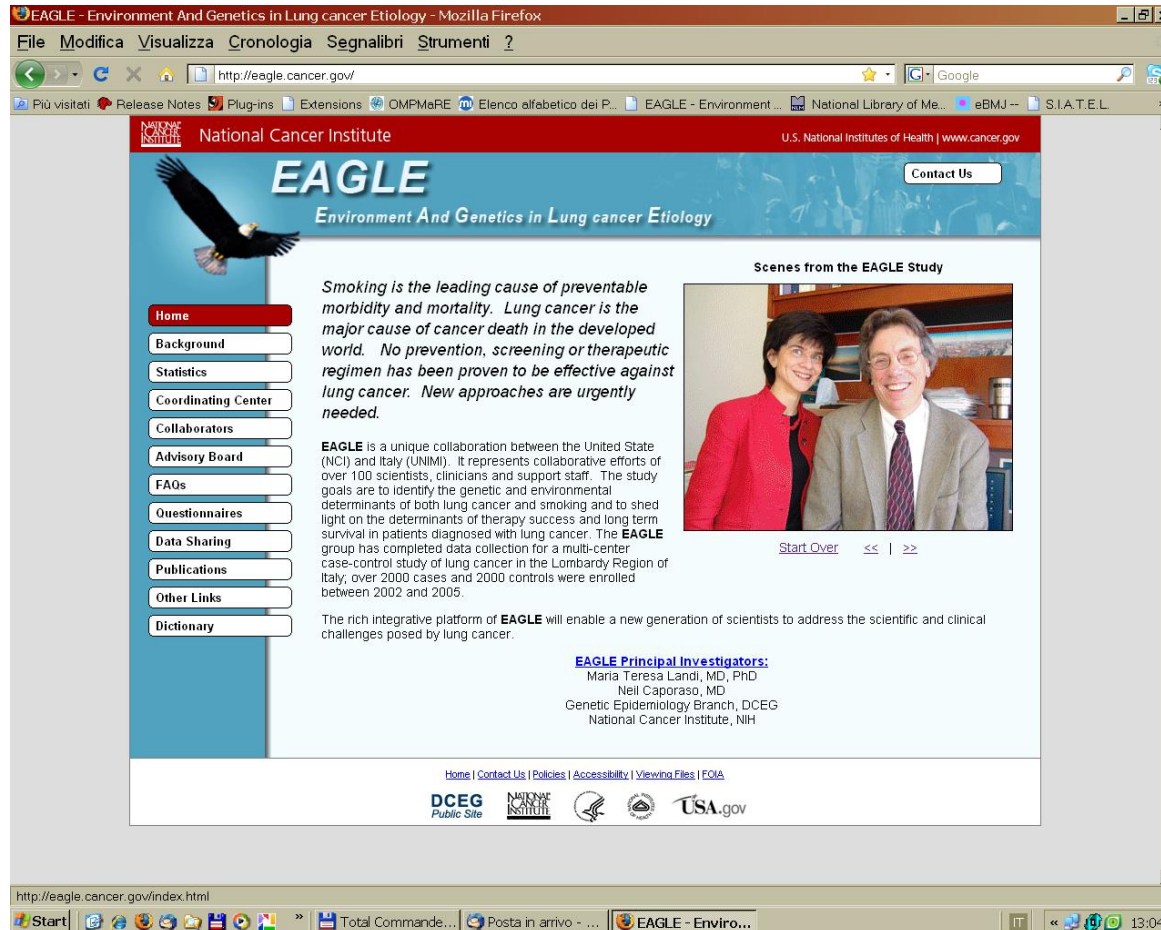
Sara De Matteis,[1,2] Dario Consonni,[1] Jay H Lubin,[2] Margaret Tucker,[2] Susan Peters,[3] Roel CH Vermeulen,[3] Hans Kromhout,[3] Pier Alberto Bertazzi,[1] Neil E Caporaso,[2] Angela C Pesatori,[1] Sholom Wacholder[2] and Maria Teresa Landi[2]*

[1]Unit of Epidemiology, Department of Preventive Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico and EPOCA Research Centre, Department of Occupational and Environmental Health, Università degli Studi di Milano, Milan, Italy, [2]Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Bethesda, MD, USA and [3]Institute for Risk Assessment Sciences, Environmental Epidemiology Division, Utrecht University, Utrecht, The Netherlands

EAGLE

- Population-based case-control study in Lombardy, 2002-05
- National Cancer Institute (Bethesda, USA), Milan University, 13 Hospitals

http://eagle.cancer.gov/

Results

Table 2 Lung cancer risk for exposure to JEM carcinogens for men in the EAGLE study, Lombardy, Italy, 2002–05[a]

Carcinogens	Cases, N (%)	Controls, N (%)	OR[b] (95% CI)	OR[c] (95% CI)	PAF[d] % (95% CI)
Asbestos					
Never[e]	905 (58.9)	1097 (67.8)	1.00	1.00	
Any	632 (41.1)	520 (32.2)	1.73 (1.43–2.09)	1.78 (1.46–2.18)	18.1 (12.6–23.3)
Low	546 (35.5)	448 (27.7)	1.68 (1.38–2.04)	1.76 (1.42–2.18)	
High	86 (5.6)	72 (4.5)	2.09 (1.39–3.13)	1.51 (0.94– 2.44)	
P-value			0.001	<0.001	

- Lung cancer risk increased **78%** in asbestos exposed (all three main histological types)
- Population Attributable Fraction: **18.1%**
- In **2005**, 4,515 lung cancer cases in Lombardy, then
- 0.181*4,515 = **817 asbestos-related lung cancer cases** in Lombardy
- (In the same year: **318 mesotheliomas**)

By applying our PAFs to the lung cancer incidence rates in males in Lombardy in 2005,[57] we estimated that 817 (95% CI: 569–1052), 257 (95% CI: 18–479), 316 (95% CI: 9–600) and 1016 (95% CI: 637–1355) lung cancer cases were attributable to occupational exposure to asbestos, silica, Ni–Cr and these three exposures combined, respectively. If we consider also the increased risk found for high exposure to PAH, corresponding to a PAF of 2.9% (95% CI: 0.1–5.9), there would be 131 additional potentially avoidable cases (95% CI: 5–266). These numbers sharply contrast with those officially reported to and compensated by the Italian Workers' Compensation Authority. For instance, in the period 1999–2004, only 399 work-related lung cancer cases (on average 66.5/year) were reported in Lombardy and about half of them compensated.[58]

Acknowledgements