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Bayesian spatio-temporal analysis of mesothelioma incidence in the Veneto Region (Italy) applied to circumstances of asbestos exposure

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The outline

Introduction

The past use of asbestos results in a worldwide epidemic of asbestos-related diseases. The malignant pleural mesothelioma is the main disease associated to the asbestos. Without asbestos exposures it's an extremely rare cancer. It primarily develops in the lining of the lungs.

It mainly occurs after an asbestos exposure and a long latency since the first exposure (>20-30 years).

The inhalation of asbestos fibres explains up the 98% of the male pleural mesothelioma cases and up 90% of female cases [Rushton et al. (2010)].

Following the other european countries, in Italy the use and the commercialization of asbestos **has been banned** since 1992.

Introduction

Nowaday
in Italy, the occurrence of mesothelioma cases is reaching its maximum impact [Marinaccio et al. (2005)].

After the asbestos
ban (1992) in Italy has been created a National Registry of Mesothelioma cases (*RENAM*) active since 1993.

In the Veneto
Region (north-east Italy - 4.5 million inhabitants) since 2001, the Regional Operative Center (COR) is responsible for the collection and investigation of each new mesothelioma case.

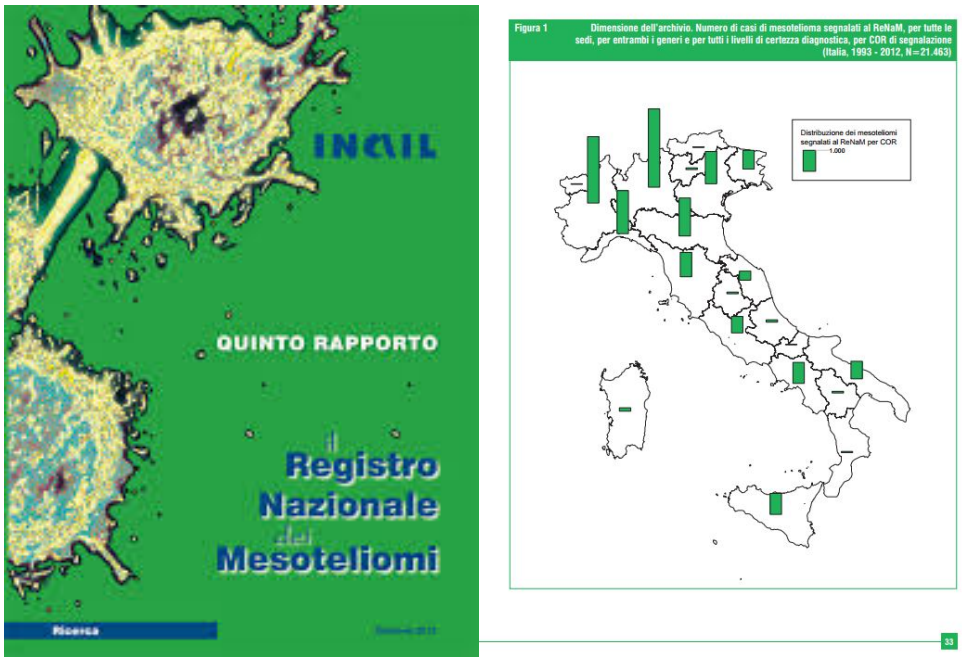
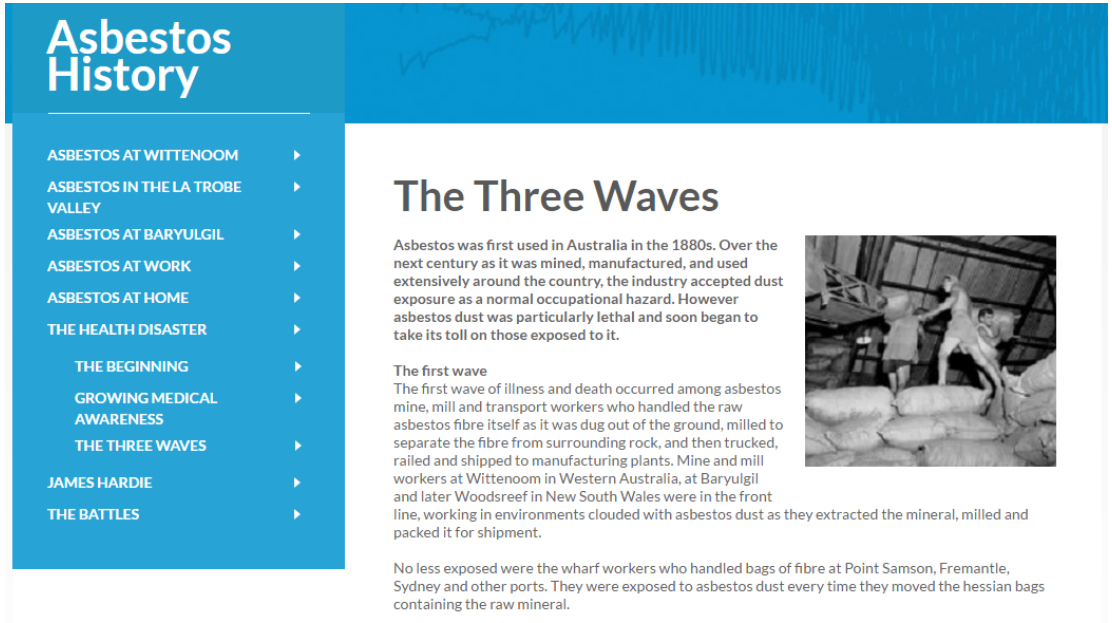


Figure: RENAM book, IV edition

Aim of the study



Asbestos History

ASBESTOS AT WITTENOOM
ASBESTOS IN THE LA TROBE VALLEY
ASBESTOS AT BARYULGIL
ASBESTOS AT WORK
ASBESTOS AT HOME
THE HEALTH DISASTER
THE BEGINNING
GROWING MEDICAL AWARENESS
THE THREE WAVES
JAMES HARDIE
THE BATTLES

The Three Waves

Asbestos was first used in Australia in the 1880s. Over the next century as it was mined, manufactured, and used extensively around the country, the industry accepted dust exposure as a normal occupational hazard. However asbestos dust was particularly lethal and soon began to take its toll on those exposed to it.

The first wave
The first wave of illness and death occurred among asbestos mine, mill and transport workers who handled the raw asbestos fibre itself as it was dug out of the ground, milled to separate the fibre from surrounding rock, and then trucked, railed and shipped to manufacturing plants. Mine and mill workers at Wittenoom in Western Australia, at Baryulgil and later Woodsreef in New South Wales were in the front line, working in environments clouded with asbestos dust as they extracted the mineral, milled and packed it for shipment.

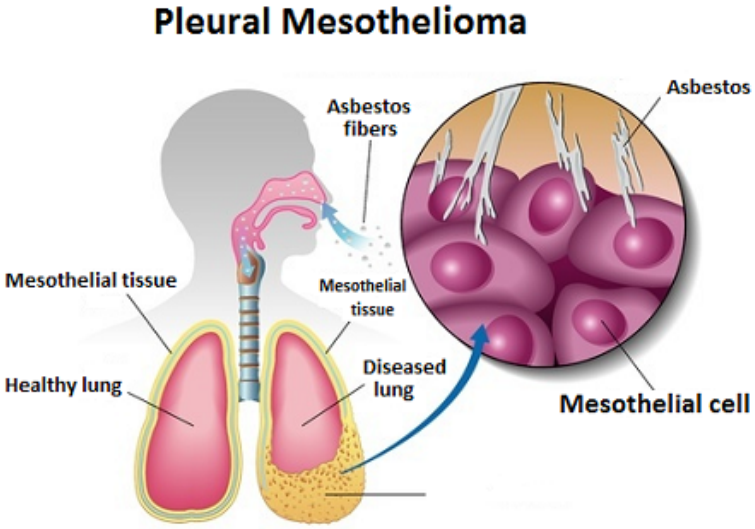
No less exposed were the wharf workers who handled bags of fibre at Point Samson, Fremantle, Sydney and other ports. They were exposed to asbestos dust every time they moved the hessian bags containing the raw mineral.

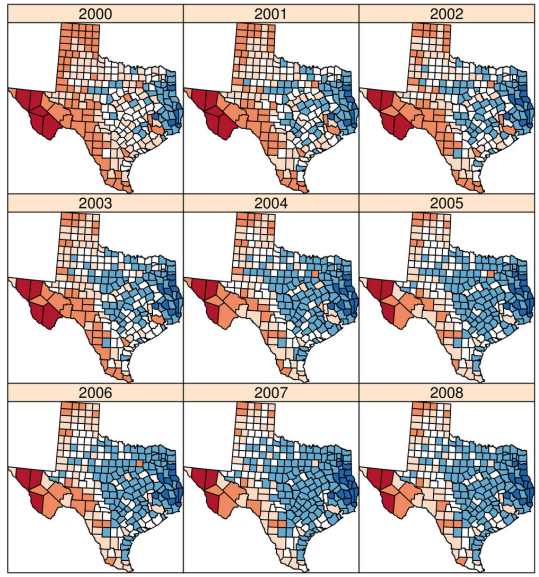
The Australian Asbestos Network predicted the presence of 3 waves of mesothelioma cases.

1. a **first** wave among miners and producers of asbestos fibres;
2. a **second** wave among workers at the asbestos factories or where the asbestos was used at work;
3. a **third** wave among the general population exposed to asbestos in contaminated workplaces or environment.

Aim of the study

The Malignant Pleural Mesothelioma (MPM) is so associated to the asbestos exposure that may be defined as a marker of asbestos contamination.





The **goal of the study** is to analyse the **spatio-temporal distribution of MPM incidence** by circumstance of asbestos exposure in the Veneto Region.
In order to obtain robust and reliable risk estimation [Lawson et al. (2000)] we use **Bayesian hierarchical model**.

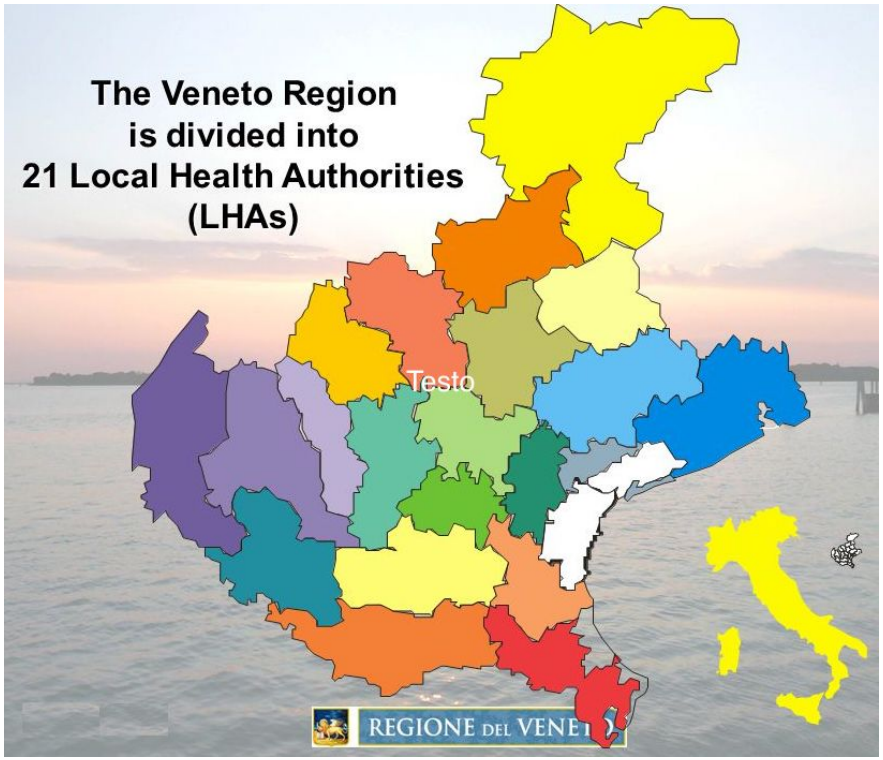
The Dataset

Dataset

1770 Malignant Pleural Mesotheliomas (MPM, ICD-9 code 163) were occurred between 1988 and 2012 in the Veneto Region and had been aggregated at the local health authority level (21 Local Health Authorities LHA).

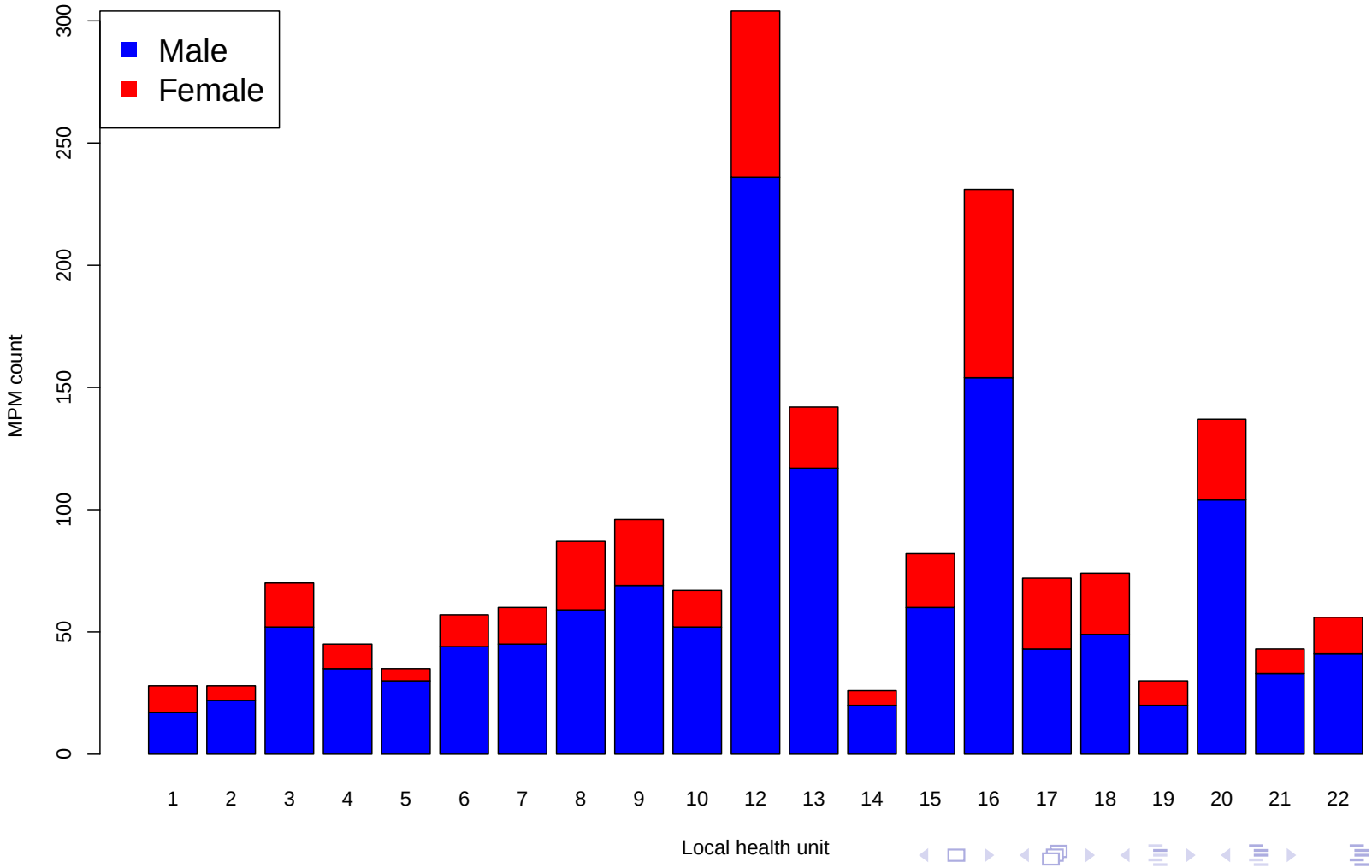
Figure: Italy and Veneto Region

Figure: Local Health Autorithies



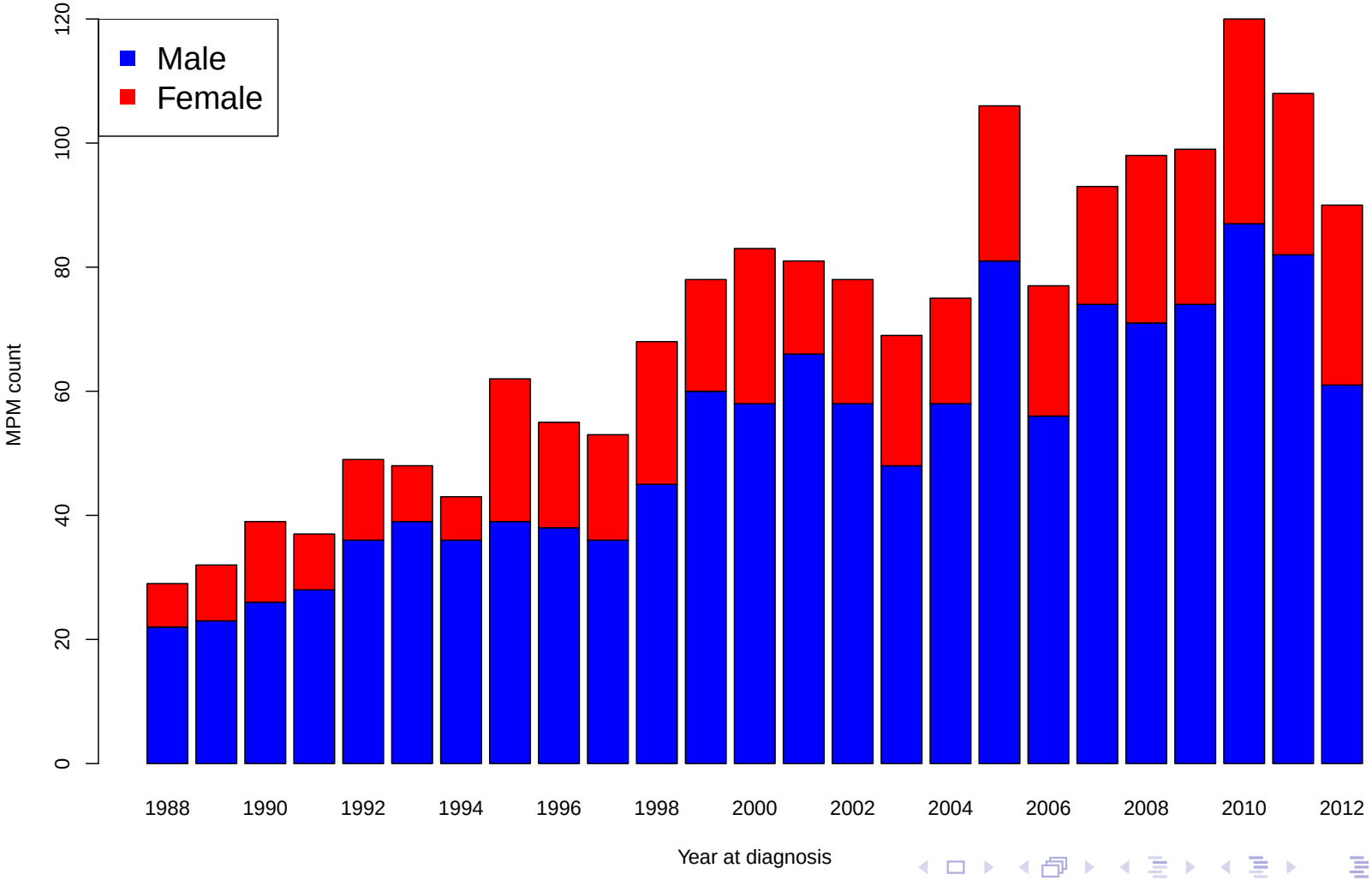
Space: Local Health Authorities (LHA)

Local Health Autorithies have different dimension and population size. MPMs mostly occured at Local Health Authority **12** (Venice), **16** (Padua) and **20** (Verona).



Time: 1988-2012 trend

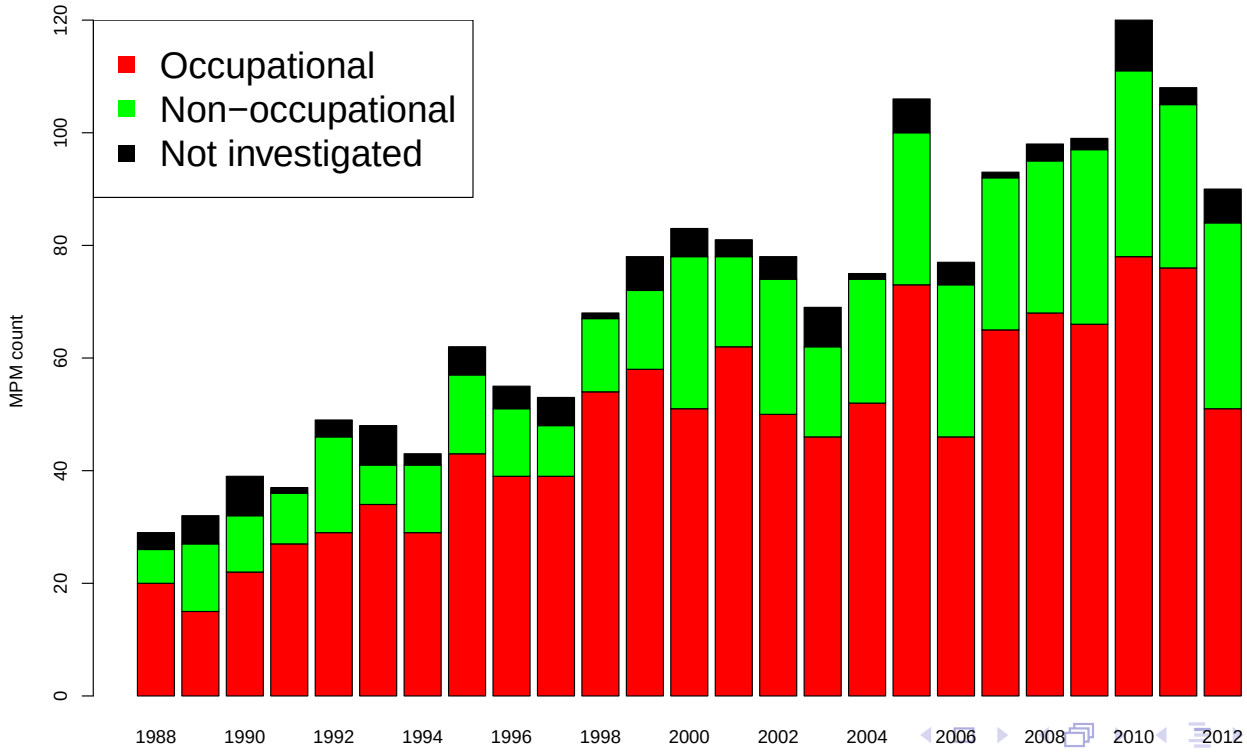
An increasing trend is observed with more than 100 MPMs in the last years.
In the last years, a higher proportion of female cases has been observed.



Exposure assessment: circumstance of exposure

The circumstance of asbestos exposures was assessed by a panel of hygienists.

	F	M	Total
Occupational exposure	133 (28%)	1060 (81%)	1193 (67%)
Non-occupational exposure	279 (60%)	195 (15%)	474 (27%)
Impossibile to investigate	56 (12%)	47 (4%)	103 (6%)
Total	468 (26%)	1302 (74%)	1770 (100%)



Spatio temporal analysis with R-INLA

We modelled MPM cases by means of a BYM (Besag, York and Mollié) model using an Integrated Nested Laplace Approximation (INLA).

Starting phase

For the i-th LHA (*space*) at the year t (*time*):

- the observed number of MPM, y_{it}, was modelled as:

$$y_{it} \sim Poisson(\lambda_{it}) \text{ with } i = 1, \ldots, 21 \text{ and } t = 1988, \ldots, 2012;$$

- expected number of MPMs cases (E_{it}) by means of Regional Rates for Mesothelioma.

R-INLA phase: BYM model

We modelled the ratio $\frac{\lambda_{it}}{E_{it}}$, called Standardized Incidence Ratio (SIR), with a BYM model including temporal covariates:

$$log(SIR) = log(\tfrac{\lambda_{it}}{E_{it}}) = \alpha + \mu_i + \nu_i + \gamma_t + \phi_t,$$

where α is the intercept and:

space μ_i and ν_i are two area specific effects with normal distribution modelled using an intrinsic conditional autoregressive structure (iCAR);

time $\gamma_t \sim RW2$ are the coefficients related to the random walk process and to the time $t = 1988, \ldots, 2012$; $\phi_t \sim N(0, \tau_t^{-1})$ are the temporal specific random errors.

Spatio temporal analysis with R-INLA

R-INLA phase: interaction inclusion

In order to permit a flexible estimation, we included in the model a spatio-temporal interaction of TYPE IV [Blangiardo et al. (2013)]

Table 7.1 Interaction types: parameter interacting and rank of $\boldsymbol{R}_\delta$.

Interaction	Parameter interacting	Rank
I	v_i and ϕ_t	nT
II	v_i and γ_t	$n(T-1)$ for RW1 $n(T-2)$ for RW2
III	ϕ_t and u_i	$(n-1)T$
IV	u_i and γ_t	$(n-1)(T-1)$ for RW1 $(n-1)(T-2)$ for RW2

The Type IV is the most complex type of interaction, assuming the spatial and the temporal structured effects μ_i and γ_t interact. The model becames:

$$log(SIR_{it}) = log(\frac{\lambda_{it}}{E_{it}}) = \alpha + \mu_i + \nu_i + \gamma_t + \phi_t + \mu_i * \gamma_t$$

Spatio temporal analysis with R-INLA

R-INLA phase: 4 spatio-temporal models.

Four different R-INLA models have been estimated as the product of the combination of:

- circumstance of exposure (occupational vs. non occupational);
- gender (men vs. women).

R-INLA results: Interpreting the results
We evaluated the effects of the spatial and the temporal component by means of the Incidence Rate Ratio (IRR) obtained by an exponential trasformation of the spatial (μ_i) and temporal (γ_t) coefficients.

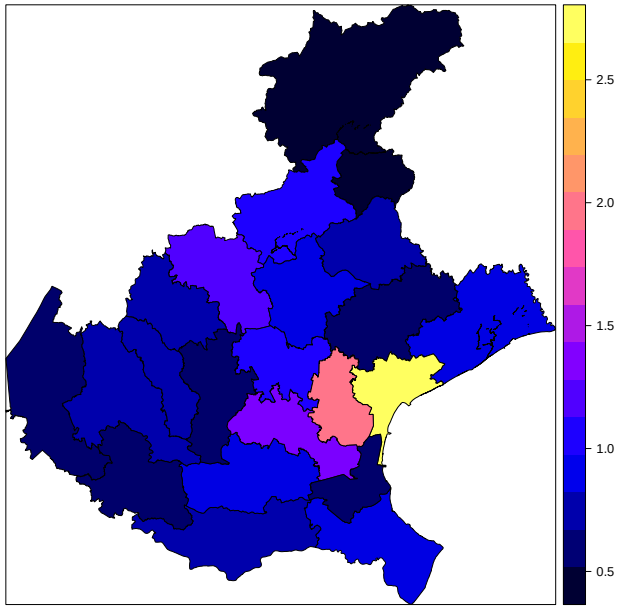
- $IRR > 1$: MPM risk is greater than the Regional reference;
- IRR $\simeq 0$: MPM is risk equal to the Regional reference;
- $IRR < 1$: MPM risk is greater than the Regional reference.

The analysis were performed by means of R software (R 3.4) and R-INLA and other several R packages.

Results

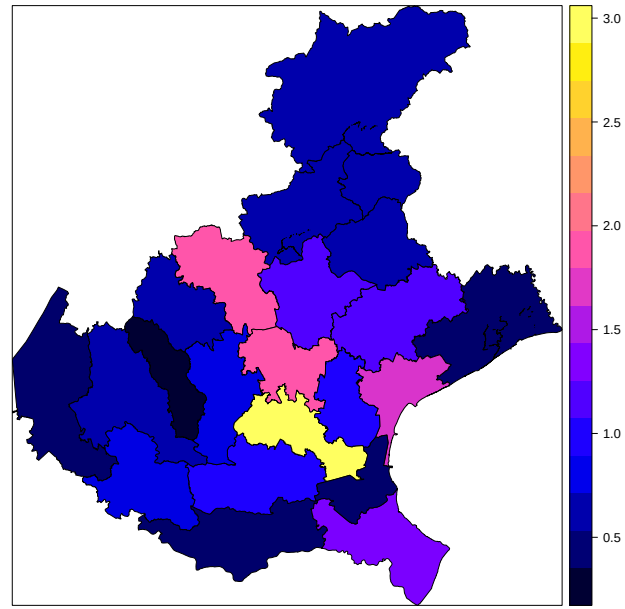
Occupational exposures - Spatial MPM Risk

Men



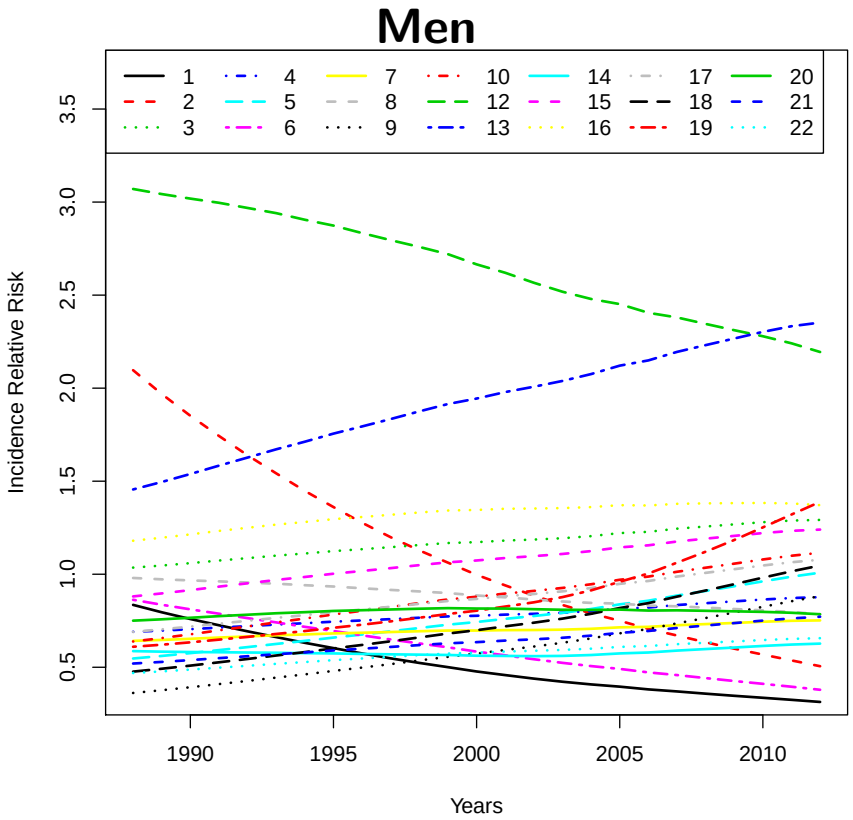
High IRRs in correspondence with LHA 12 and 13 (Venice and Mirano) due to the presence of shipyards and chemical companies.

Women

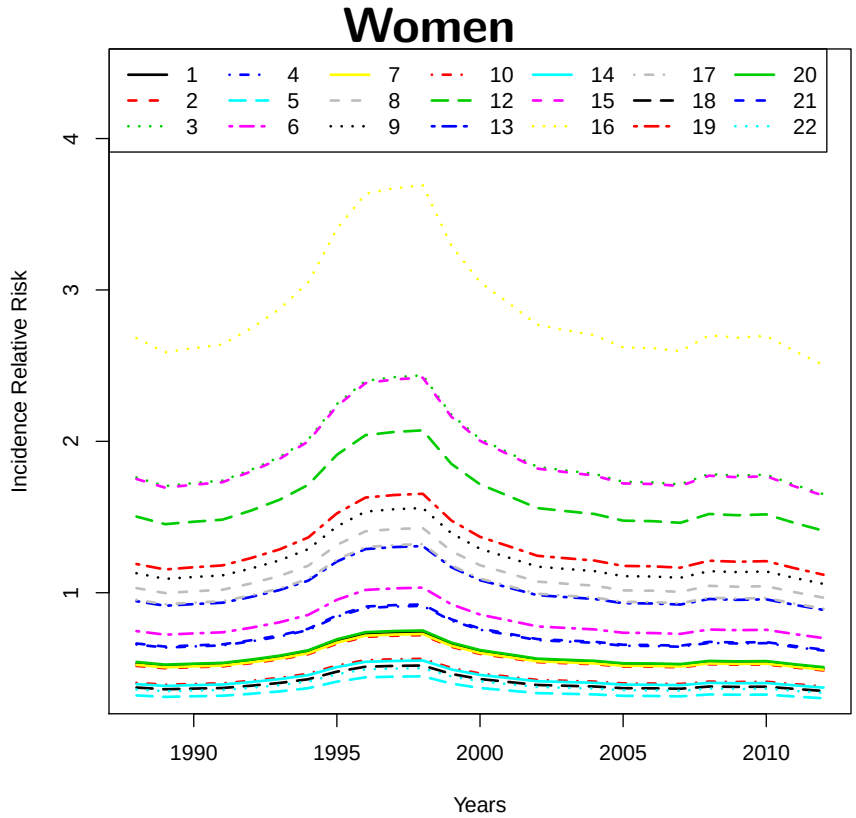


High IRRs in correspondence with LHA 15 and 16 (Padua and Cittadella) due the past presence of asbestos-cement industries.

Occupational exposures - Temporal MPM Risk



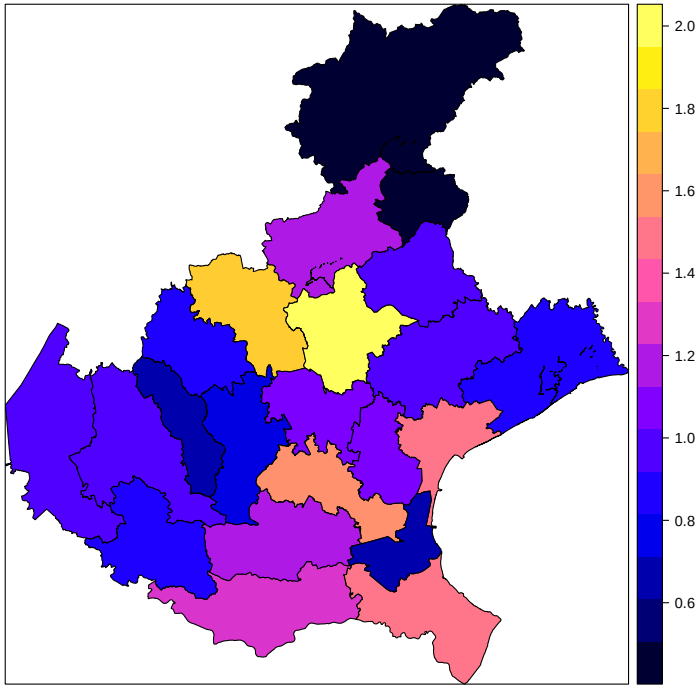
Venice shows the highest IRR in the first period with a a decreasing trend. Mirano reports an increasing trend overhelming Venice.



All LHAs have a peak of MPM risk in the years 1995-2000 followed by a slight decreasing trend.

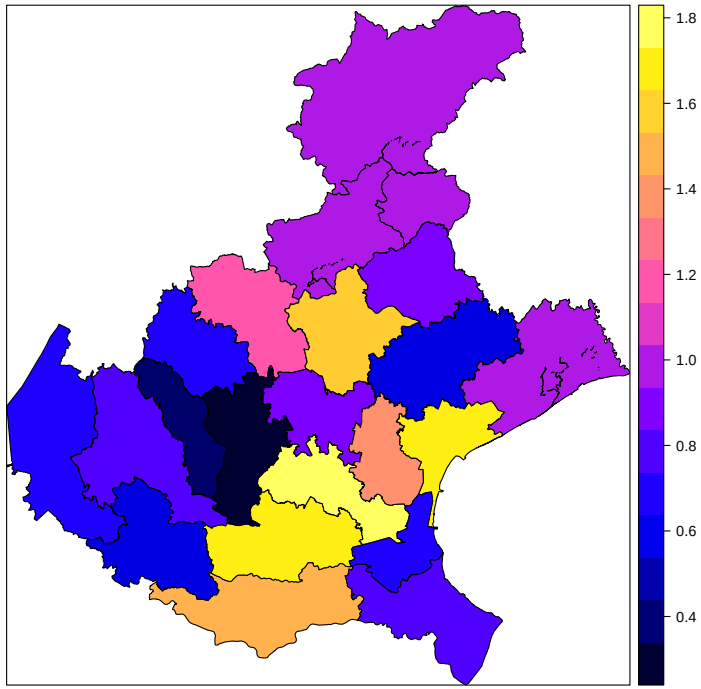
Non-occupational exposures - Spatial MPM Risk

Men



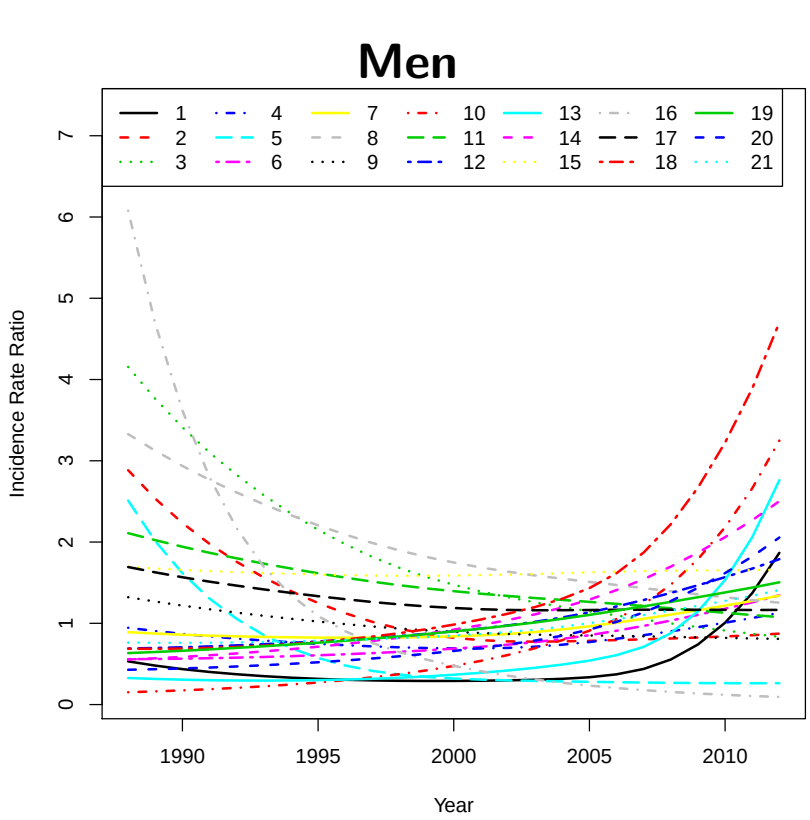
High IRRs in LHA 8 (*Asolo*). A suspected environmental contamination due to the presence of a single railway carriage factory has been assessed.

Women

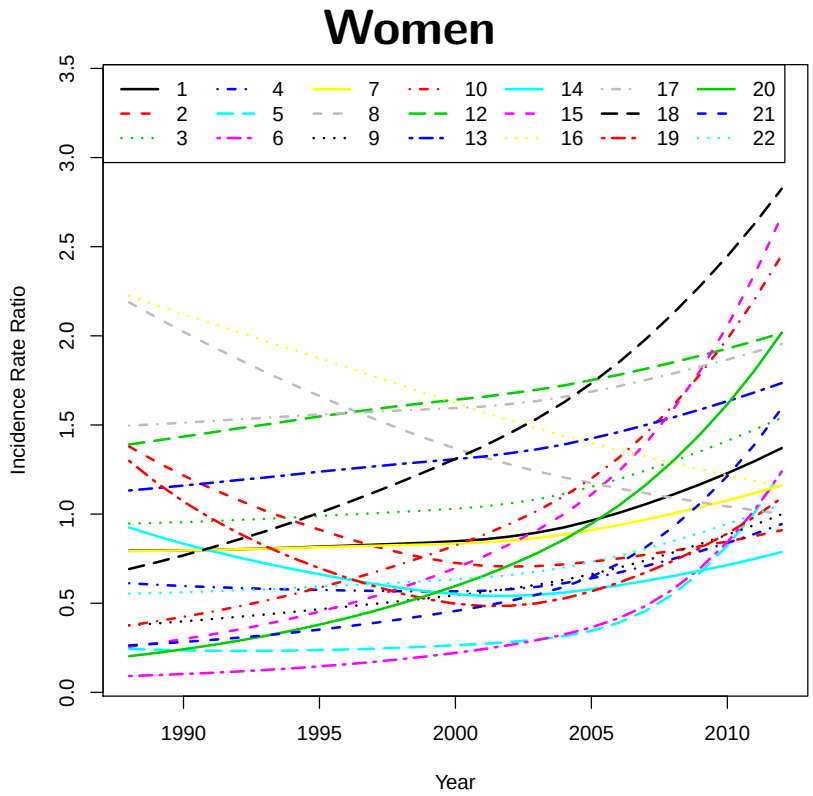


High IRRs in LHA 12, 16 and 17 (Venice, Padua and Este) due to the presence of shipyards, asbestos-cement industries, railway carriage production (i.e. wifes washed husband's contaminated clothes).

Non-occupational exposures - Temporal MPM Risk



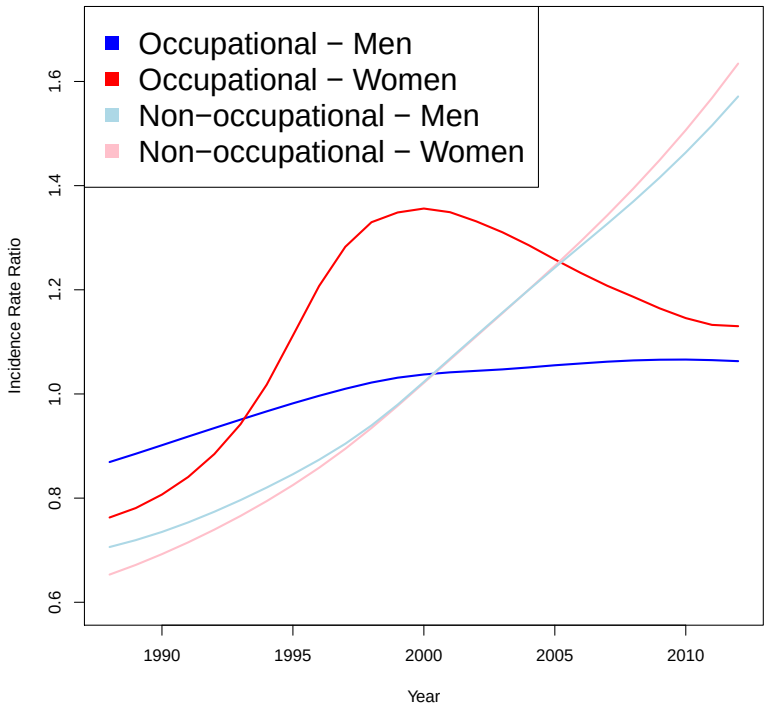
Some LHAs report a increasing trend in the last years (however based on few MPMs).



Many LHAs of the southern part of Veneto (Rovigo, Chioggia, Este) showed a increasing trend in the last years up to IRRs equal to 3.

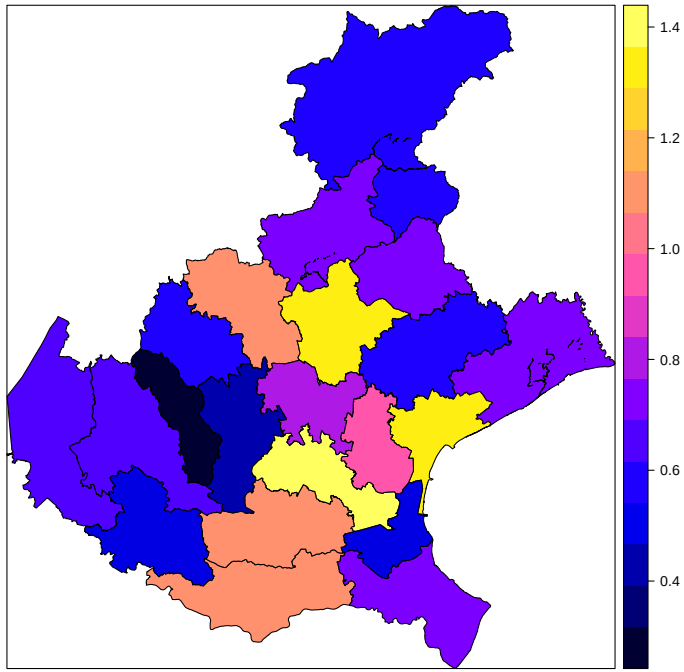
Overall - Spatio-temporal analysis

Overall temporal component



Despite the decrease of MPM risk for the occupational exposed, an increasing MPM risk due to non-occupational exposures has been observed in both gender.

Focus on the overall spatial component Non-occupational exposure



Some LHAs reports a higher MPM risks due to non occupational exposures.

Conclusions

The increasing commercial use of asbestos has determined a growing incidence of MPM with a well defined spatial pattern. Our study assesses that:

- the wave of MPM due to occupational exposures, after reached a maximum, already shows a downward trend, not homogeneous in all areas, and more marked in women;
- the wave of MPM due to non-occupational exposures is growing;
- clusters of non-occupational MPM deserve special attention, i.e. clusters of occupational MPM may be linked to clusters of non-occupational MPM.

Strengths

- Assessment of spatio-temporal dynamics applied to MPM due to occupational and non-occupational exposure;
- we perform a fast and flexible extimation through R-INLA.

Weaknesses

- interpretation of the results remains difficult;
- the rarity of disease may causes instable estimates.

Thank you for the attention

References

Blangiardo, M., Cameletti, M., Baio, G., and Rue, H. (2013). Spatial and spatio-temporal models with r-inla. *Spatial and spatio-temporal epidemiology*, 7:39–55.

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