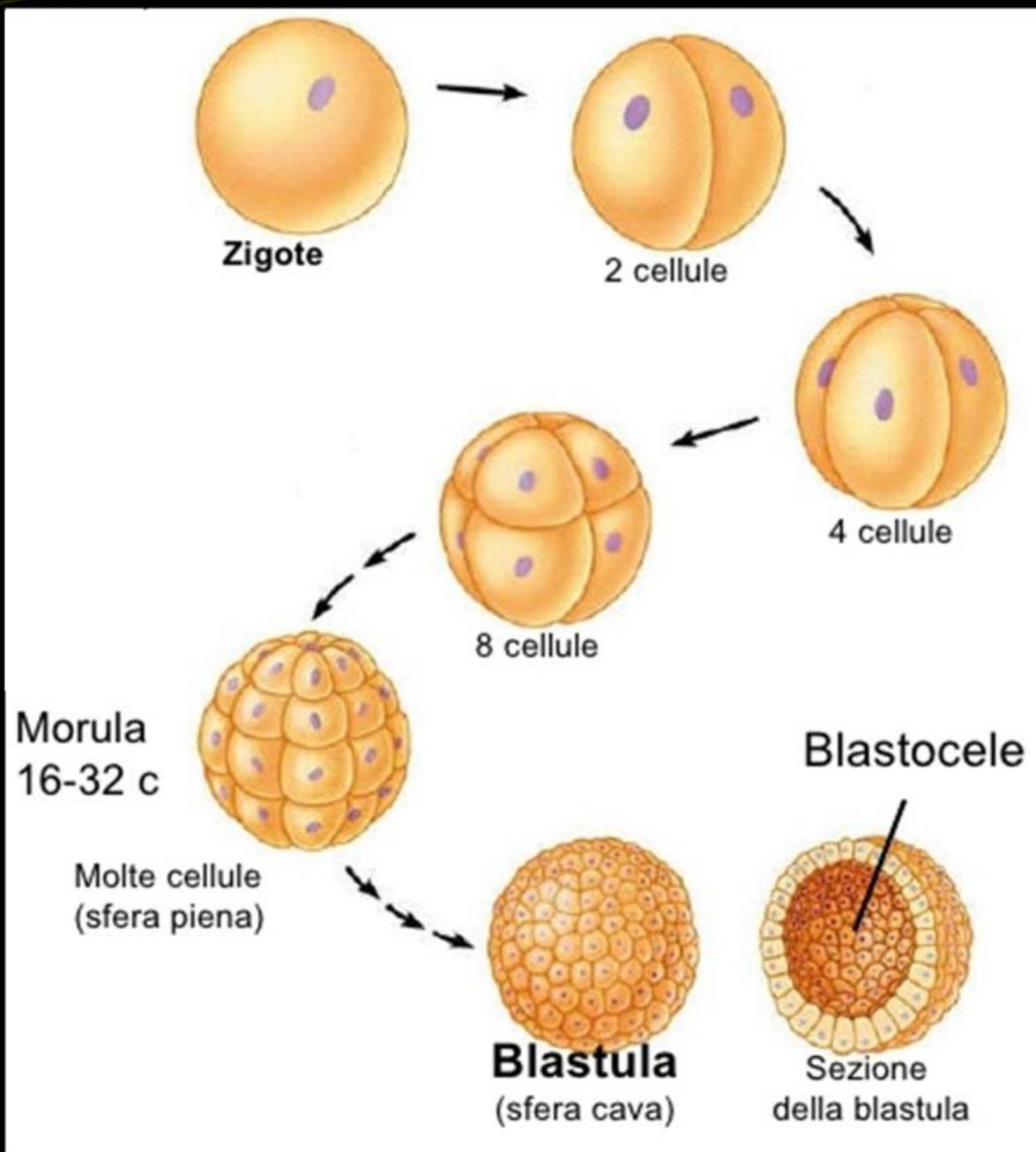


Inquinamento e tumori

Alberto Bottini, Humanitas Research Hospital, Rozzano

Pietro Cavalli, Humanitas Research Hospital, Rozzano

CORPO UMANO
95.000 MILIARDI DI
CELLULE



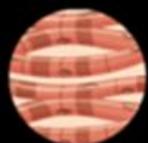
Totipotent embryonic stem cell



Pluripotent embryonic stem cells



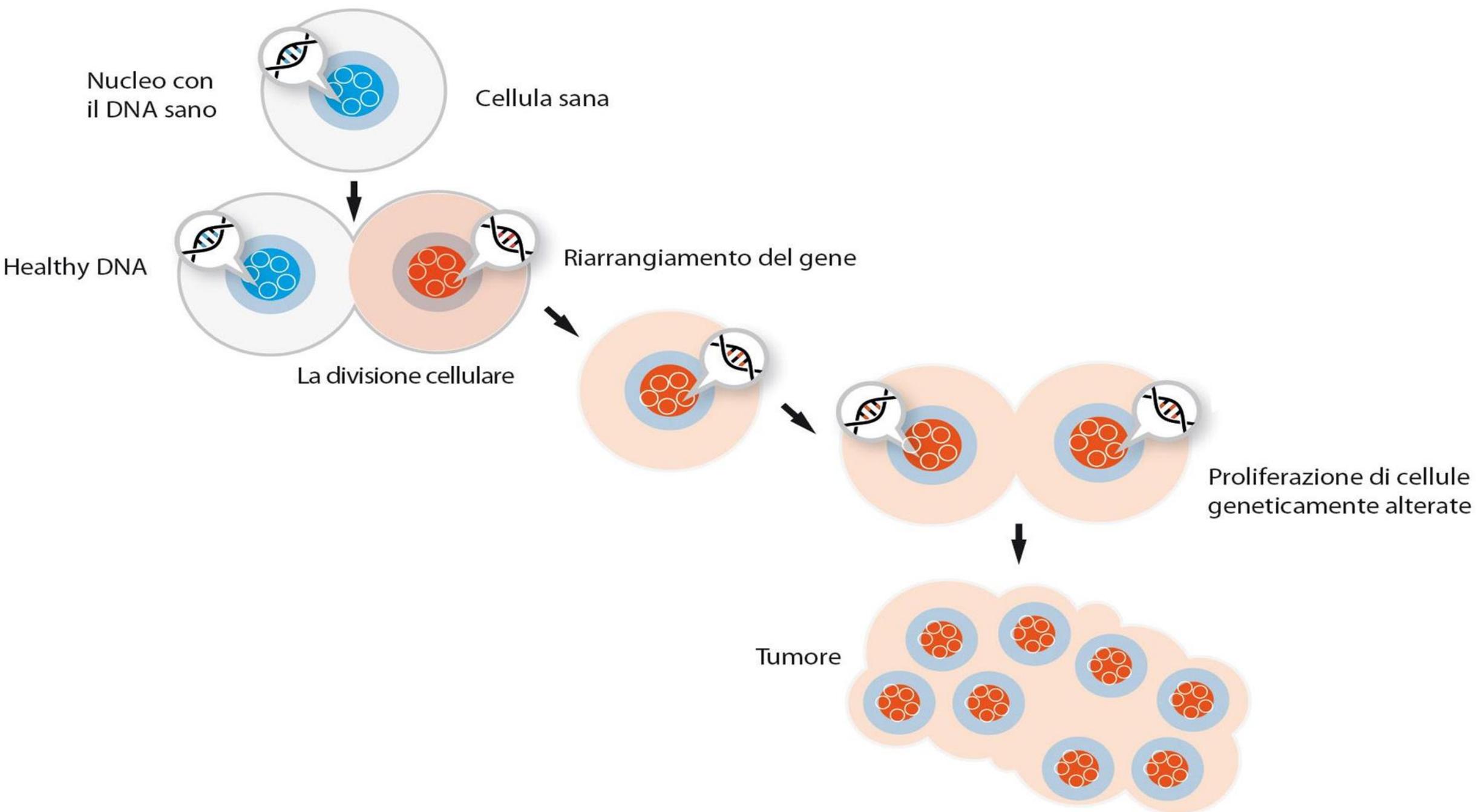
Multipotent stem cells



PROLIFERAZIONE

DIFFERENZIAZIONE







Il cancro è il risultato di graduali accumuli di mutazioni genetiche 'DRIVER' che aumentano la proliferazione cellulare.

Cancer Genome Landscapes

29 MARCH 2013 VOL 339 SCIENCE www.sciencemag.org

Bert Vogelstein et. al

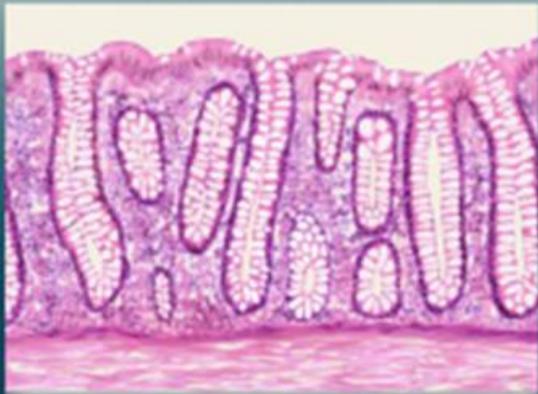
ESEMPIO DI SOMMAZIONE DI MUTAZIONI SOMATICHE

Pathways

APC

RAS

PI3K
Cell Cycle/Apoptosis
TGF- β



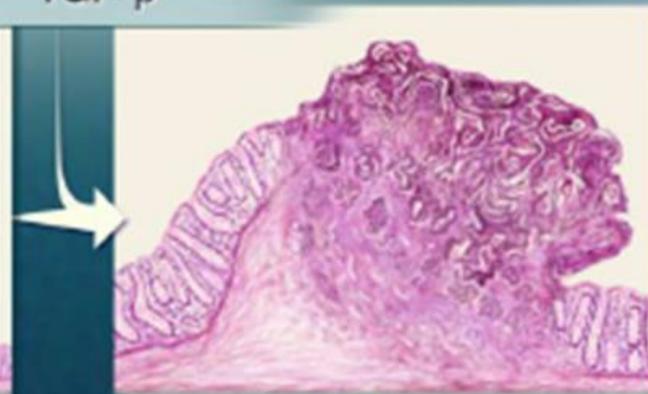
Normal colonic epithelium



Small adenoma



Large adenoma



Carcinoma

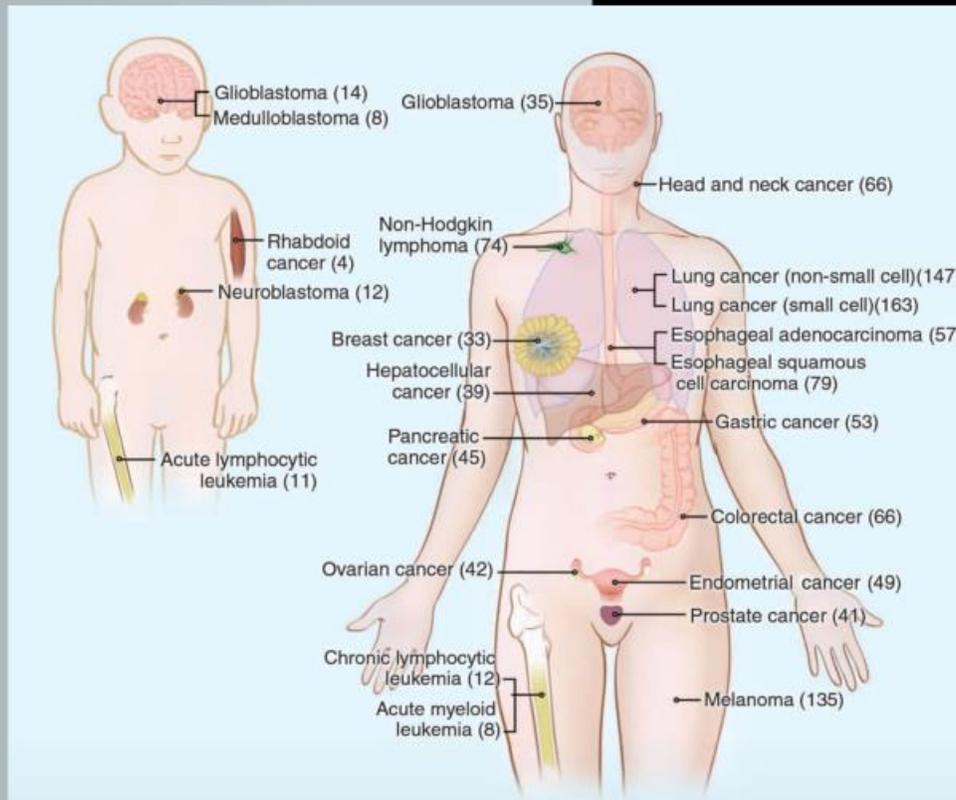
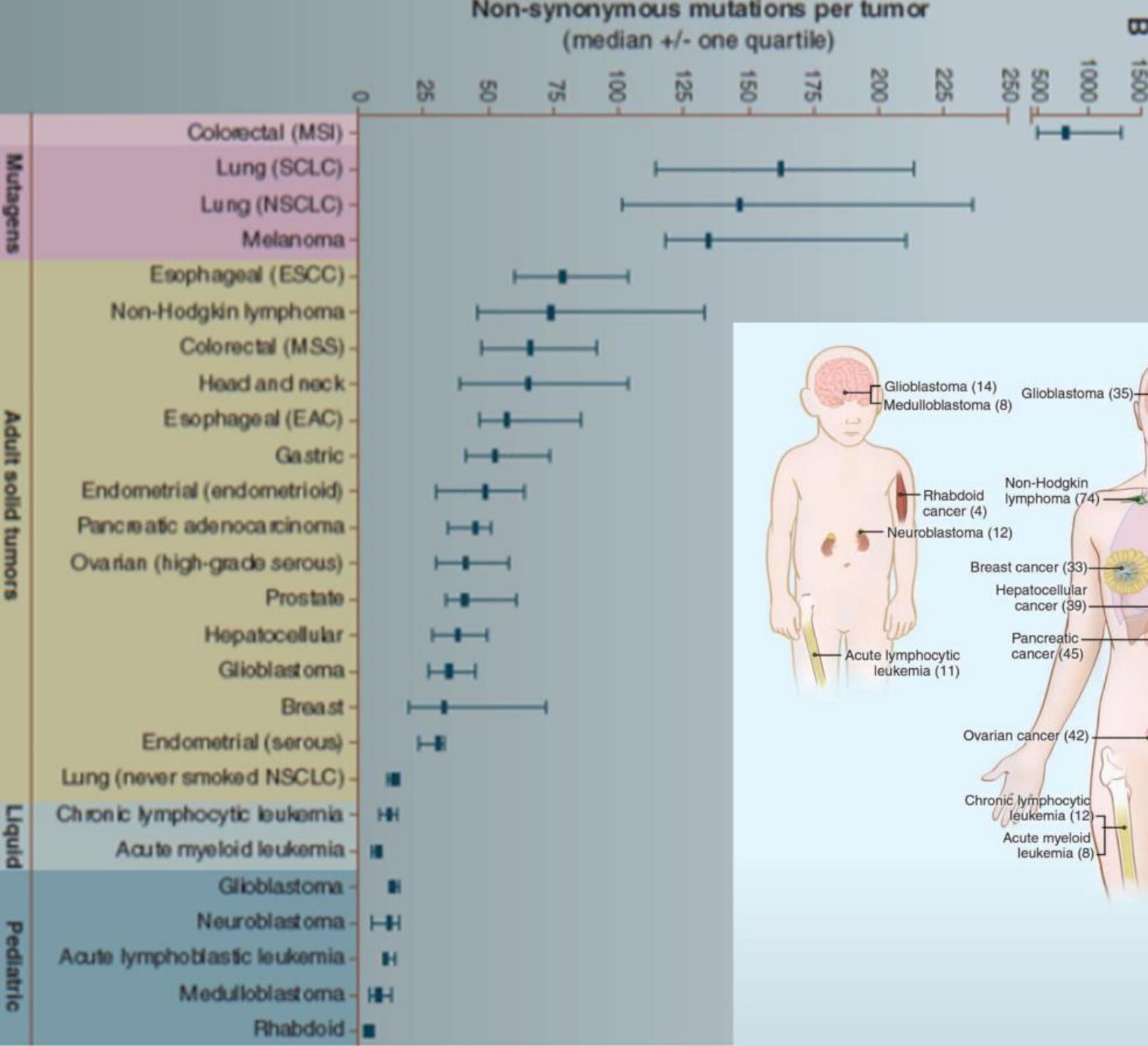


Cosa provoca le mutazioni?

E (Enviromental) fattori ambientali

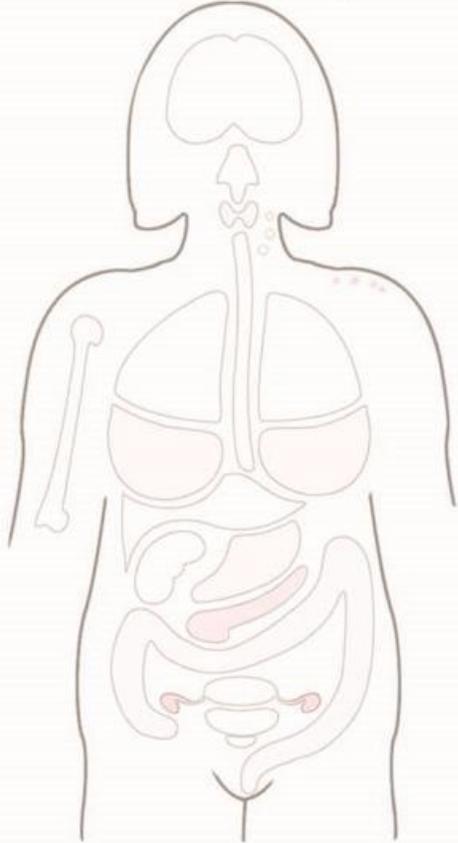
H (Ereditary) fattori ereditari

R (Replicative) fattori casuali o stocastici

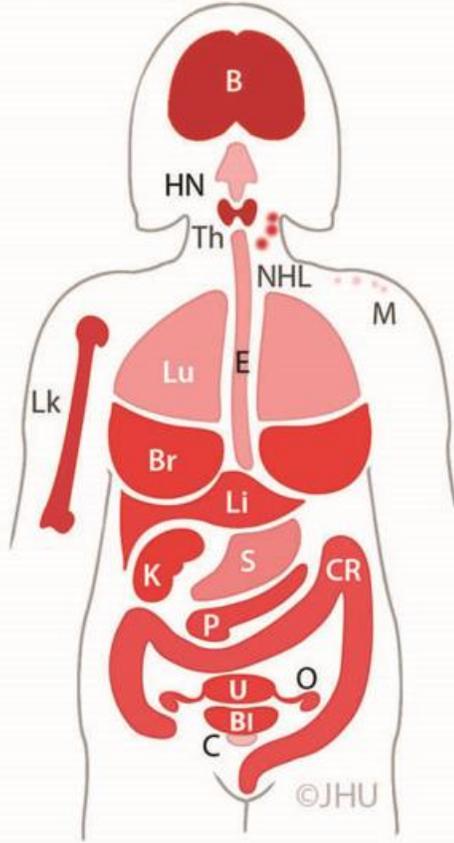


Numero di mutazioni somatiche individuate dagli studi di sequenziamento genómico

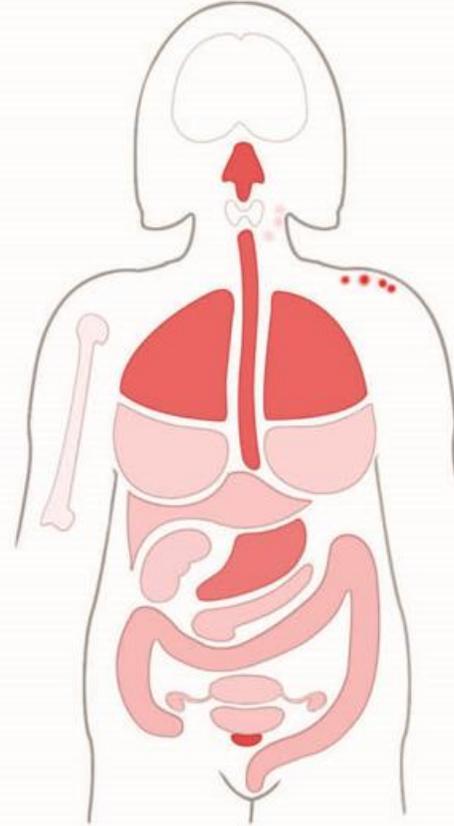
Hereditary



Replicative

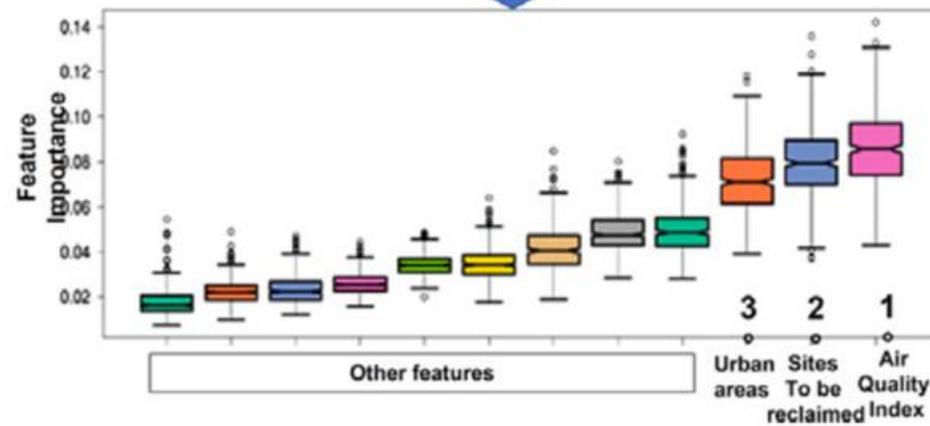
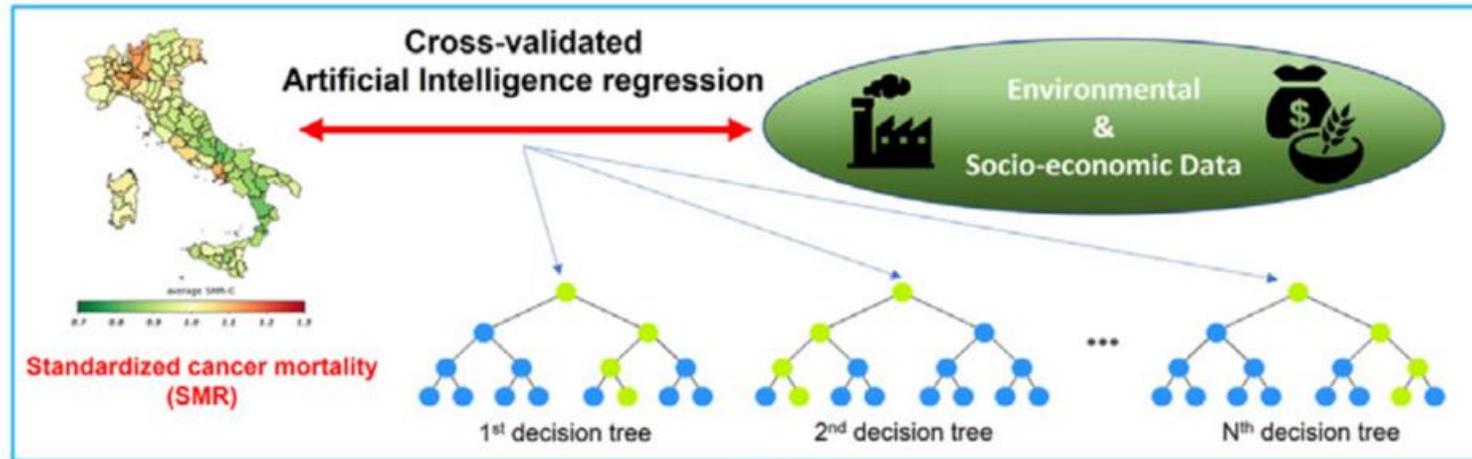


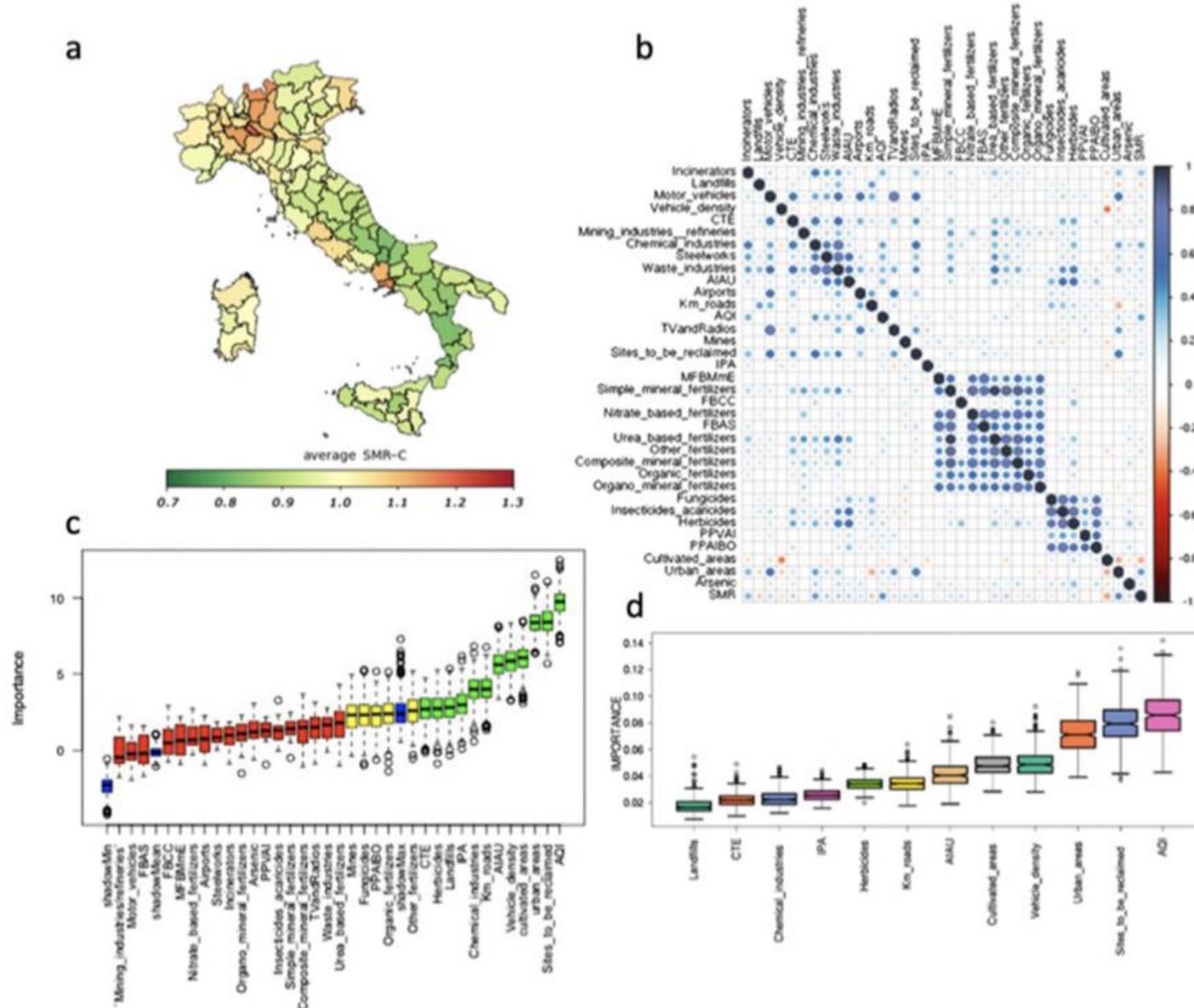
Environmental



Percentage of driver mutations attributable to each factor

GRAPHICAL ABSTRACT



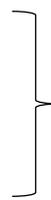


Deaths caused by malignant neoplasms, residents, 2020

	Number of deaths (number)	Share of all deaths			Standardised death rates				
		Total	Males	Females	Total	Males	Females	Persons aged < 65 years	Persons aged ≥ 65 years
		Total (%)							
EU	1 165 451.0	22.5%	24.9%	20.0%	242.2	318.3	188.1	68.8	958.3
Belgium	26 106.0	20.7%	23.3%	18.3%	223.2	286.6	178.2	57.0	909.2
Bulgaria	18 415.0	15.0%	16.3%	13.5%	245.3	340.3	181.9	93.4	872.5
Czechia	28 067.0	21.7%	23.4%	20.0%	267.2	355.5	207.8	70.8	1 078.2
Denmark	15 784.0	28.9%	30.0%	27.7%	271.0	327.1	231.9	59.8	1 143.0
Germany	231 552.0	23.4%	25.5%	21.4%	240.3	303.1	195.0	64.2	967.2
Estonia	3 656.0	23.3%	26.4%	20.4%	265.0	412.0	190.9	79.3	1 031.8
Ireland	9 633.0	29.4%	30.2%	28.5%	255.5	300.9	219.6	59.1	1 065.9
Greece	30 166.0	23.1%	27.4%	18.6%	240.8	326.0	172.8	69.9	946.1
Spain	108 409.0	22.0%	26.1%	17.8%	214.5	300.6	150.5	62.2	843.3
France	163 340.0	24.4%	27.5%	21.4%	226.6	303.4	171.8	68.6	878.7
Croatia	13 281.0	23.3%	27.1%	19.5%	303.9	429.3	221.8	89.0	1 190.8
Italy	167 576.0	22.5%	25.6%	19.7%	227.0	294.5	179.1	57.6	926.4
Cyprus	1 521.0	23.3%	26.5%	19.7%	205.6	270.9	152.1	62.1	797.9
Latvia	5 998.0	20.9%	23.2%	19.0%	296.5	451.3	221.9	95.0	1 128.4
Lithuania	8 160.0	18.9%	21.3%	16.7%	276.5	430.6	195.9	92.9	1 034.3
Luxembourg	1 009.0	22.7%	23.3%	22.0%	203.1	247.8	173.5	42.7	865.2
Hungary	31 605.0	22.4%	24.5%	20.5%	320.9	432.4	251.9	114.0	1 175.0
Malta	1 010.0	24.7%	27.3%	21.9%	212.5	275.4	166.9	54.1	866.3
Netherlands	45 188.0	26.9%	29.1%	24.7%	261.3	319.5	220.6	62.9	1 080.2
Austria	21 021.0	23.3%	25.7%	21.0%	230.5	295.0	185.5	58.1	942.6
Poland	99 923.0	20.9%	21.7%	20.0%	279.7	382.6	216.1	84.0	1 087.5
Portugal	28 354.0	22.9%	27.3%	18.7%	240.5	346.4	167.1	76.3	918.3
Romania	49 476.0	16.7%	18.4%	14.8%	260.3	360.7	188.6	104.0	905.8
Slovenia	6 404.0	27.0%	31.1%	23.2%	290.7	399.2	219.7	66.2	1 217.4
Slovakia	14 186.0	24.1%	26.0%	22.0%	301.8	421.7	227.7	85.9	1 193.2
Finland	12 996.0	23.5%	25.0%	22.0%	211.4	266.5	173.6	49.9	878.0
Sweden	22 615.0	22.9%	23.9%	21.8%	214.1	254.0	186.9	43.9	916.8
Iceland	623.0	27.3%	28.2%	26.5%	224.9	257.4	201.9	50.7	944.1
Liechtenstein	64.0	20.6%	18.5%	22.7%	182.9	180.1	177.0	36.9	785.4
Norway	10 871.0	27.2%	29.8%	24.7%	223.5	275.2	188.9	47.5	950.0
Switzerland	16 947.0	22.3%	24.6%	20.0%	196.2	248.1	160.3	45.8	817.1
Serbia	20 788.0	17.8%	19.3%	16.3%	283.0	359.6	225.5	105.8	1 014.4



Dati EUROSTAT
2024





TUMORI MALIGNI

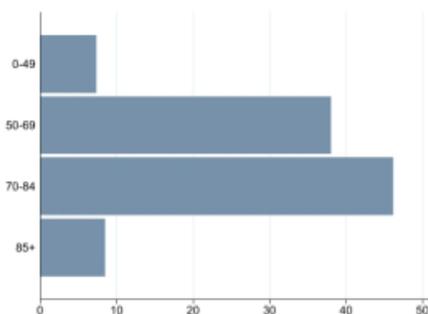
INCIDENZA: Icd10: C00-C97, D090, D414
 (esclusi carcinomi della cute)
 MORTALITA': Icd10: C00-C97

Periodo 2014 - 2018	Numero medio casi/anno	Numero soggetti che è necessario seguire da 0 a 84 anni per trovarne 1 che sviluppi un tumore	Tasso Standardizzato (x 100.000) pop. EU13	Rank
Incidenza	2594	2	674,2	n.a.
Mortalità	1207	n.a.	344,2	n.a.

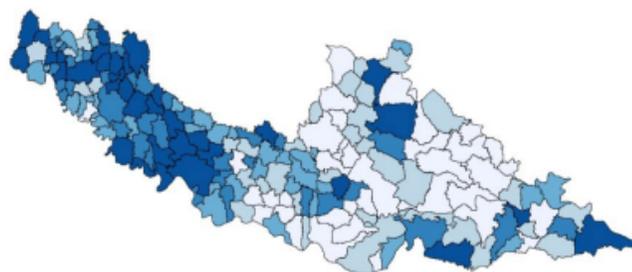
italia

294,5

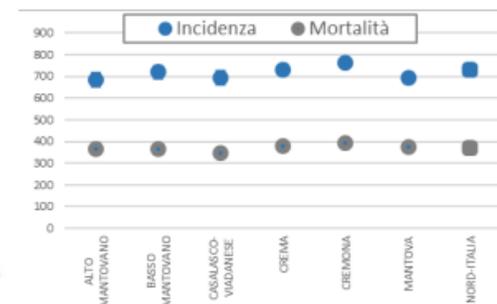
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)



Confronto tra distretti ATS e Nord Italia (2010-2015)



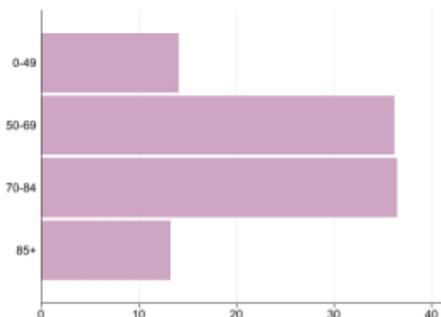
TUMORI MALIGNI

INCIDENZA: Icd10: C00-C80, D090, D414
 (esclusi carcinomi della cute)
 MORTALITA': Icd10: C00-C80

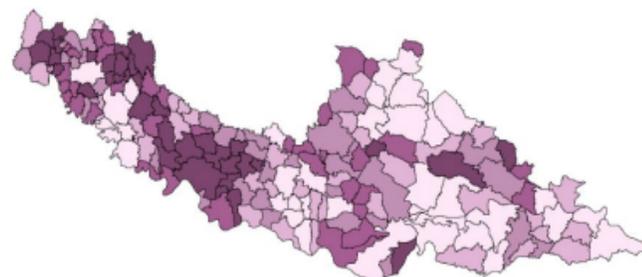
Periodo 2014 - 2018	Numero medio casi/anno	Numero soggetti che è necessario seguire da 0 a 84 anni per trovarne 1 che sviluppi un tumore	Tasso Standardizzato (x 100.000) pop. EU13	Rank
Incidenza	2417	3	515,6	n.a.
Mortalità	970	n.a.	201,1	n.a.

179,1

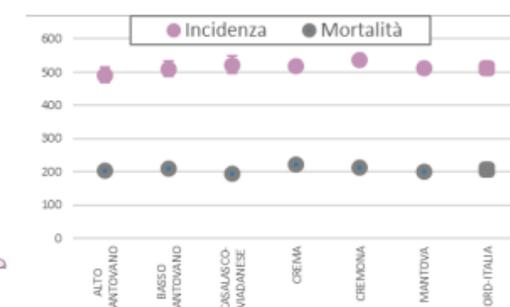
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)

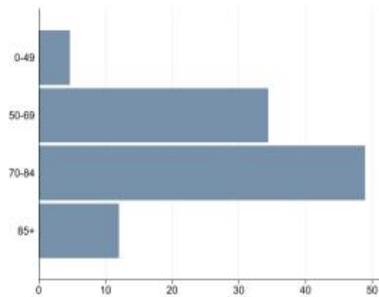


Confronto tra distretti ATS e Nord Italia (2010-2015)

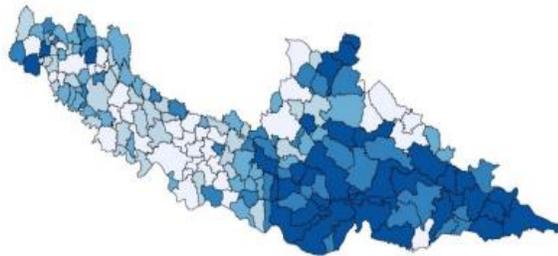


	Cremona	Lombardia	Italia
K colon retto			
incidenza			
maschi	82,1	62,1	67,4
femmine	49,9	41,0	43,6
mortalità			
maschi	35,5	18,4	19,9
femmine	19,2	11,5	12,3

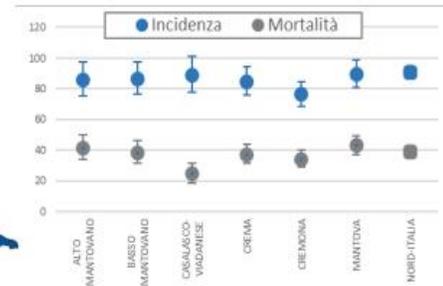
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)

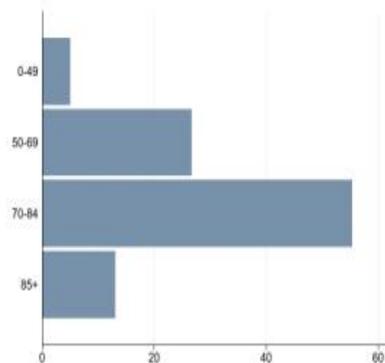


Confronto tra distretti ATS e Nord Italia (2010-2015)

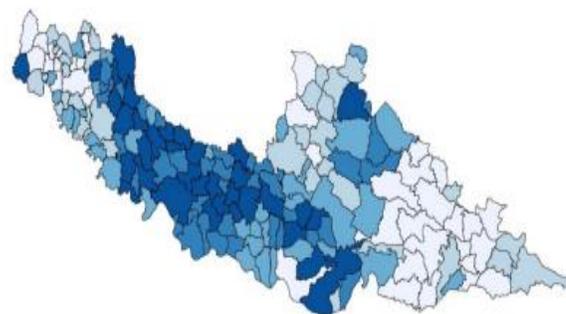


	Cremona	Italia	Piacenza
K stomaco			
incidenza			
maschi	37 (41)	35,9 (nord) – 28 (sud)	
femmine	18,1 (28)		
mortalità			
maschi	29,1	21,2	37
femmine	11,5	14,5	19,6

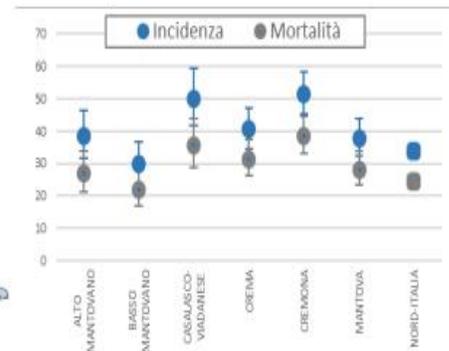
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)

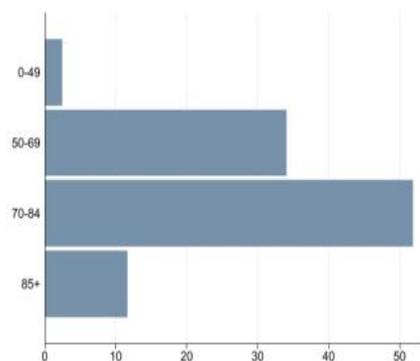


Confronto tra distretti ATS e Nord Italia (2010-2015)

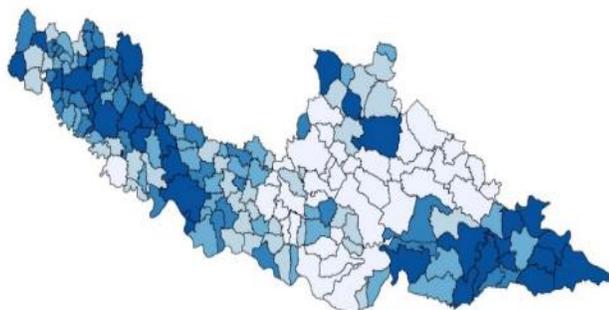


	cremona	Italia	europa
K polmone			
incidenza			
maschi	92,6	34,5	42,4
femmine	36,2	16,2	17,9
mortalità			
maschi	84,2	25,9	32,6
femmine	27,8	11,6	12,4

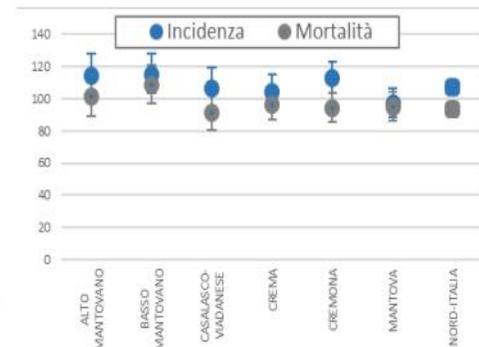
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)

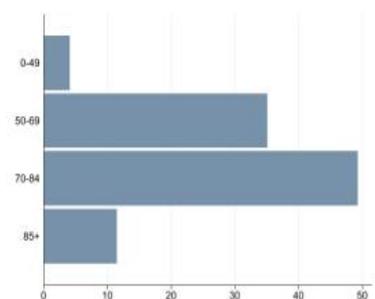


Confronto tra distretti ATS e Nord Italia (2010-2015)

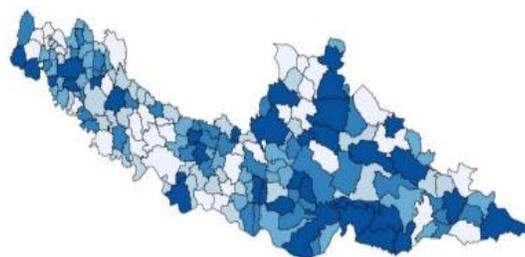


	cremona	italia	europa
K pancreas			
incidenza			
maschi	24,8	9	9,5
femmine	18,7	7	6,7
mortalità			
maschi	22,8	8,2	8,8
femmine	16,9	6,3	5,9

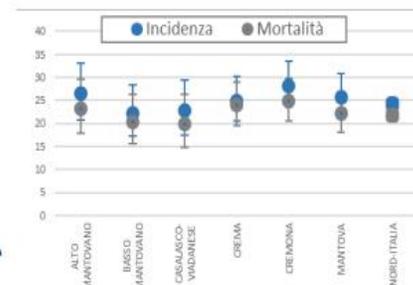
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)

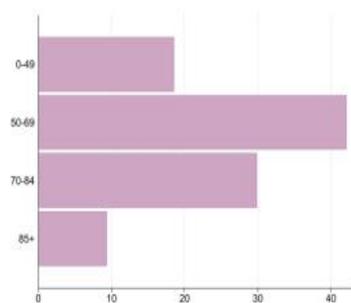


Confronto tra distretti ATS e Nord Italia (2010-2015)

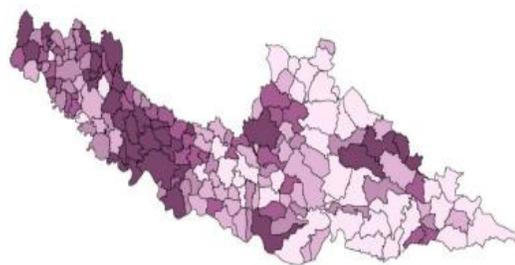


	Cremona	Italia	Europa
K mammella			
incidenza	172,7	87	75,6
mortalità	19,2	14,8	14,6

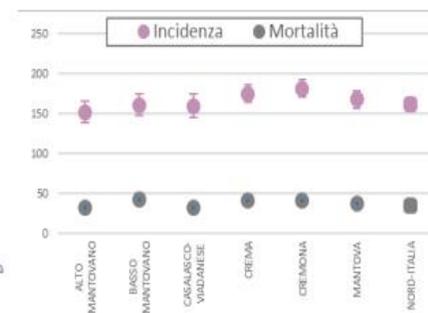
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)



Confronto tra distretti ATS e Nord Italia (2010-2015)



Dati ATS Valpadana

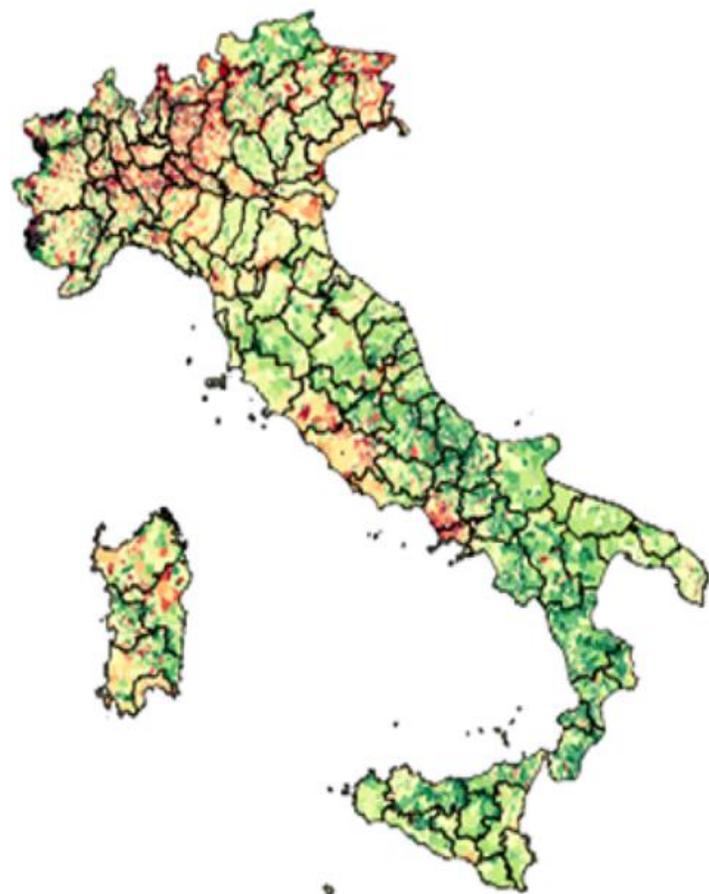
Dati IARC – WHO

Dati <https://zenodo.org/records/6924899>

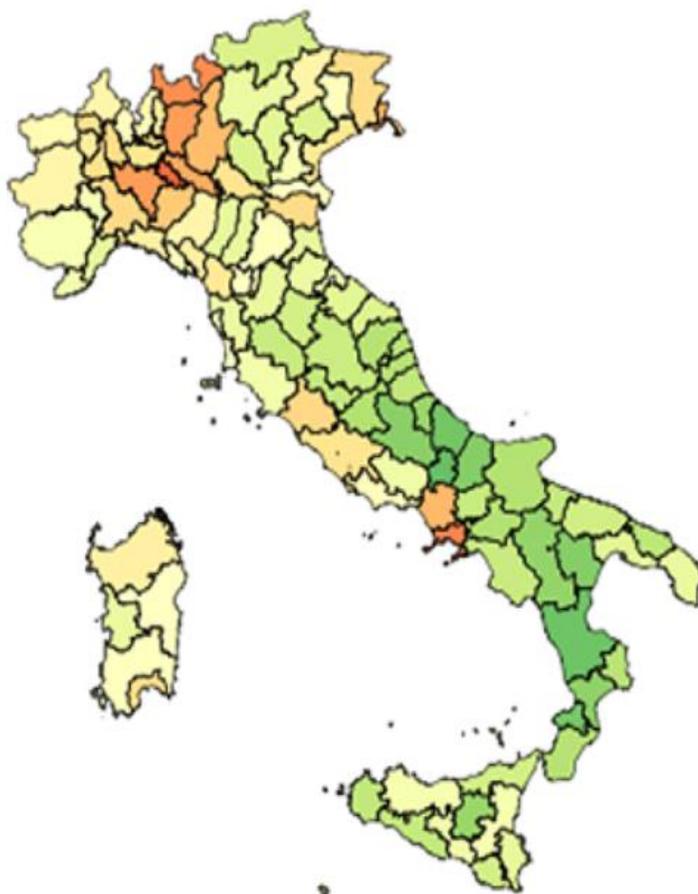
Dati <https://doi.org/10.1016/j.scitotenv.2022.158439>

Dati https://ec.europa.eu/eurostat/statistics-explained/index.php?title=File:Deaths_caused_by_malignant_neoplasms,_residents,_2020V3.png

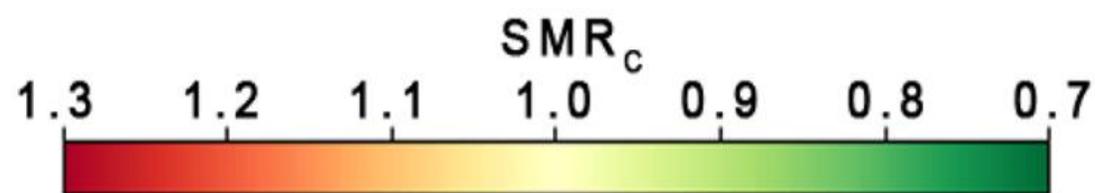
municipal level



provincial level



regional level



Età media popolazione

Lodi 46,2

Napoli 43. 6

Bergamo 45

Pavia 47,2

Sondrio 46,1

Cremona 47,9

Gorizia 48.3

Caserta 42,8

Brescia 44,3

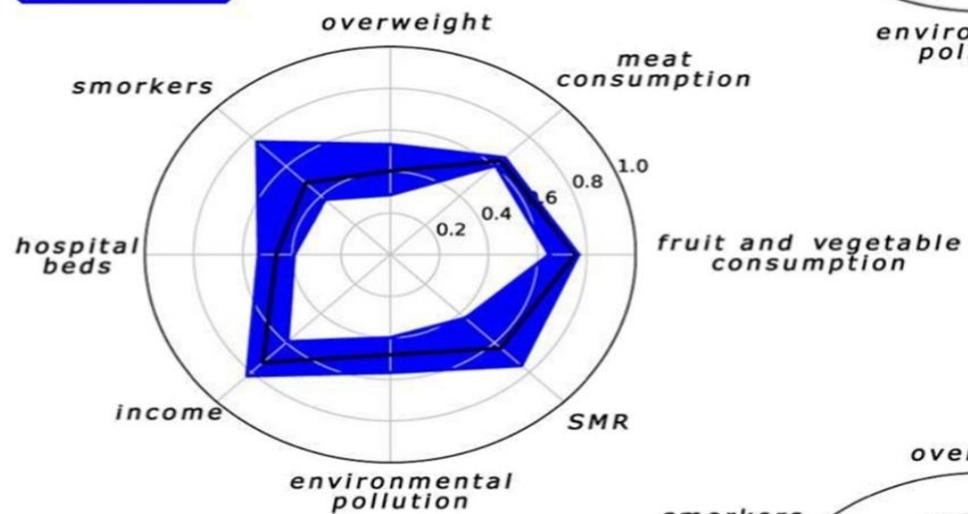
Piacenza 46,3

Fumo
Sovrappeso
Consumo di carne
Consumo frutta e verdura

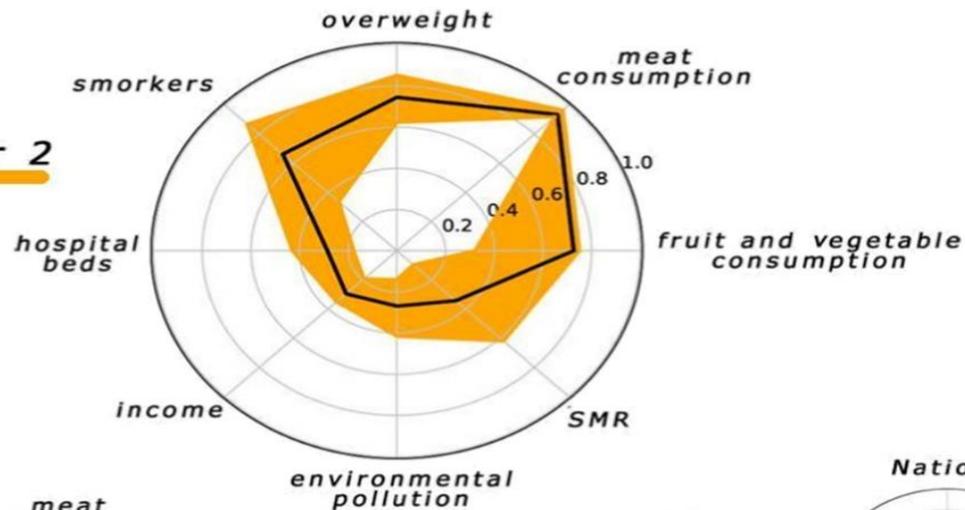
Reddito
Letti ospedalieri

Inquinamento ambientale
SMR

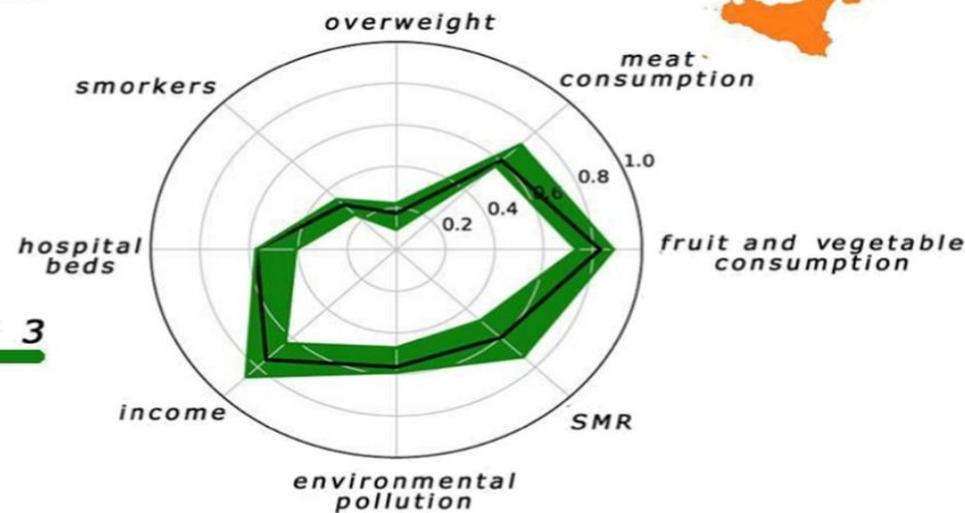
cluster 1



cluster 2



cluster 3

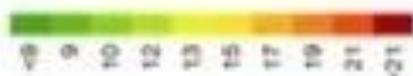


Prime 10 posizioni delle Province italiane per mortalità da tutti i tumori (10 anni: 2009-2018) e presenza di fonti d'inquinamento (associate significativamente alla mortalità da tumori) da *Cazzolla Gatti et al. (2022), The spatial association between environmental pollution and long-term cancer mortality in Italy, Science of The Total Environment, 158439* <https://doi.org/10.1016/j.scitotenv.2022.158439>

Posizione In Italia	Mortalità tumori 10 anni	Qualità dell'aria	Siti da bonificare	Aree urbane	Densità veicoli	Aree coltivate	Siti industriali	Km di strade	Erbicidi	Indice allergie pollini	Industrie chimiche	Impianti energia termica	Discariche
1	Lodi	Ragusa	Milano	Napoli	Aosta	Cremona	Verona	Cuneo	Verona	Lecco	Milano	Torino	Taranto
2	Napoli	★ Cremona	Roma	Monza-Brianza	Trento	★ Campobasso	Brescia	Foggia	Ferrara	Perugia	Bergamo	Milano	Torino
3	Bergamo	Monza-Brianza	Massa-Carrara	Milano	Bolzano	Fermo	Mantova	Torino	Pavia	Arezzo	Venezia	Venezia	Alessandria
4	Pavia	Milano	Napoli	Varese	Isernia	Ancona	Forli-Cesena	Salerno	Ravenna	Trento	Varese	Mantova	Perugia
5	Sondrio	Como	Firenze	Trieste	Firenze	Mantova	★ Cremona	Perugia	Bari	Firenze	Pavia	Roma	Brescia
6	Cremona	Mantova	Genova	Prato	Catania	Avellino	Cuneo	Sassari	Cuneo	Bolzano	Vicenza	Ravenna	Agrigento
7	Gorizia	Bergamo	Torino	Roma	Biella	Viterbo	Vicenza	Roma	Vercelli	Catanzaro	Torino	Livorno	Bolzano
8	Caserta	Brescia	Livorno	Gorizia	Perugia	Pavia	Padova	Palermo	BAT	Reggio Calabria	Novara	Ferrara	Chieti
9	Brescia	Lodi	Monza-Brianza	Bergamo	Cuneo	Lodi	Bergamo	Trento	★ Cremona	Cosenza	Verona	Bologna	Cuneo
10	Piacenza	Pavia	Trieste	Treviso	Frosinone	Pesaro-Urbino	Treviso	Lecce	Foggia	Crotone	Monza-Brianza	Terni	Cosenza



PM_{2,5}



PM₁₀



NO₂



O₃ (MAG-OTT)



Figura 1. Concentrazioni medie annue (PM₁₀, PM_{2,5} e NO₂, µg/m³) e dei mesi maggio-ottobre (O₃, µg/m³), anno 2018.

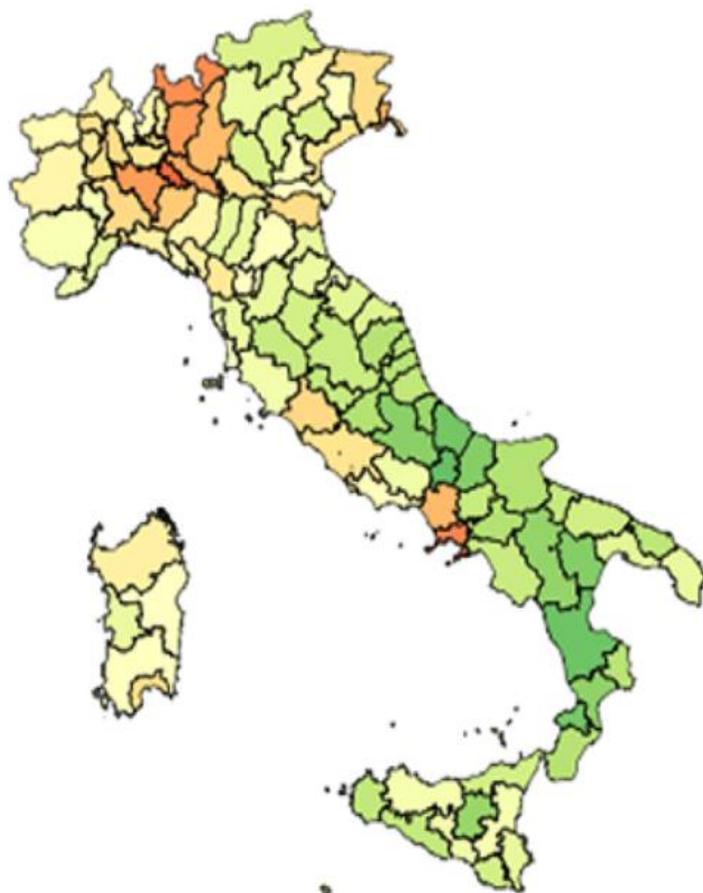
Figure 1. Annual mean concentrations (PM₁₀, PM_{2,5}, and NO₂, µg/m³) and mean of the months May-October (O₃, µg/m³), year 2018.

<https://greenreport.it/rubriche/inquinamento-atmosferico-in-pianura-padana-ecco-quali-sono-gli-impatti-sulla-salute/>

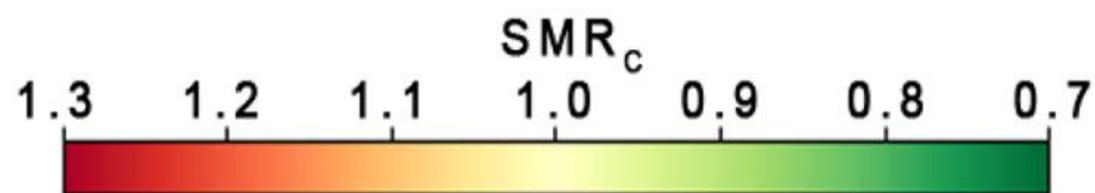
municipal level

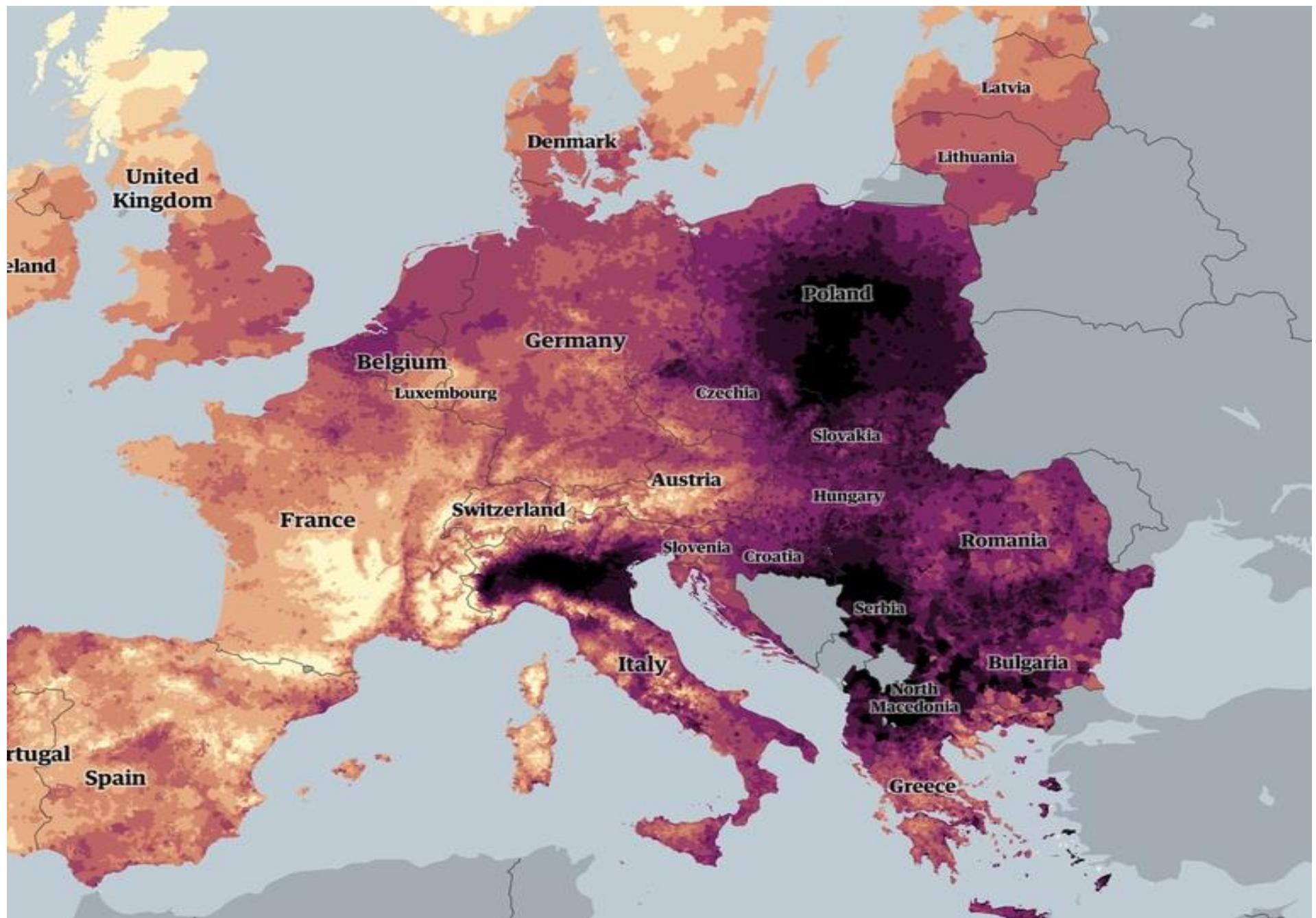


provincial level



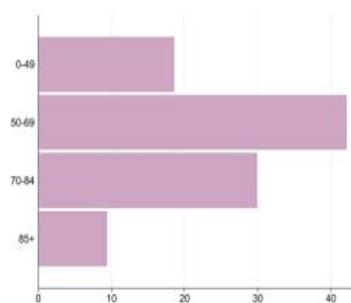
regional level



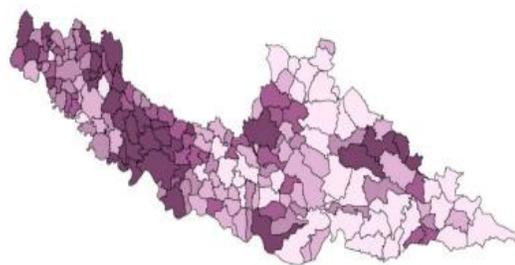


	Cremona	Italia	Europa
K mammella			
incidenza	172,7	87	75,6
mortalità	19,2	14,8	14,6

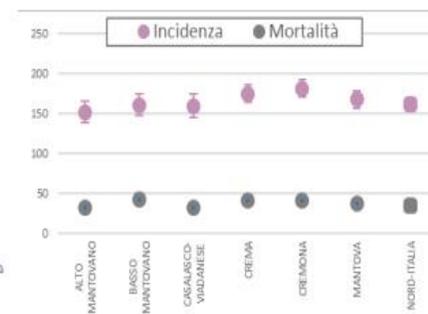
Distribuzione % nuovi casi per classi di età (2014-2018)



Disease mapping (2014-2018)



Confronto tra distretti ATS e Nord Italia (2010-2015)



POLVERI SOTTILI

Particelle di dimensione inferiore ai 2micron in diametro aerodinamico PM2.5

Derivano da numerose sorgenti (scarico dei veicoli a motore, processi di combustione di olio, carbone, fumo di piante, incendi ed emissioni industriali)

Classificate come **carcinogeni** umani dall'agenzia internazionale per la ricerca sul cancro

Sono misture complesse ed eterogenee di «polluzioni aeree» comprendenti metalli (sodio e nickel), metalloidi (silicone), componenti organici (idrocarburi aromatici policilici, ammonio, nitrati, ozono e solfati). Molti di questi componenti hanno proprietà disturbanti del sistema endocrino (breast K)

sources

JNCI: <https://doi.org/10.1093/jnci/djad170>

	Cases/controls	Model ^a	Model ^b
		OR (95% CI)	OR (95% CI)
PM_{2.5} (for an increment of 10 µg/m³)	2419/2984	1.28 (1.00, 1.63)	1.28 (1.00, 1.64)
PM ₁₀ (for an increment of 10 µg/m ³)	2419/2984	1.09 (0.92, 1.30)	1.10 (0.92, 1.31)
NO ₂ (for an increment of 10 µg/m ³)	2419/2984	1.05 (0.97, 1.13)	1.05 (0.97, 1.13)

Statistically-significant increased BC risk for a 10 µg/m³ increase of the 1990-2011 average PM_{2.5} concentration estimates.

No difference by hormone receptor status, nor effect modification by menopausal status were observed.

OR, Odds ratio; 95% CI, 95% confidence intervals; PM_{2.5}, particulate matters with a diameter < 2.5 µg/m³; PM₁₀, particulate matters with a diameter < 10 µg/m³; NO₂, nitrogen dioxide.

^a Adjusted for matching variables (age at inclusion or at blood collection, date of return of inclusion questionnaire or at blood collection, menopausal status at inclusion or at blood collection, department of residence at inclusion or at blood collection, availability of a salivary sample), and level of education and urban/rural status of birthplace and follow-up duration.

^b Adjusted for matching variables (age at inclusion or at blood collection, date of return of inclusion questionnaire or at blood collection, menopausal status at inclusion or at blood collection, department of residence at inclusion or at blood collection, availability of a salivary sample), and physical activity, body mass index, alcohol intake, smoking status, oral contraceptive use, menopausal hormone therapy use, mammography, parity, age at first full-term pregnancy, breastfeeding and follow-up duration.

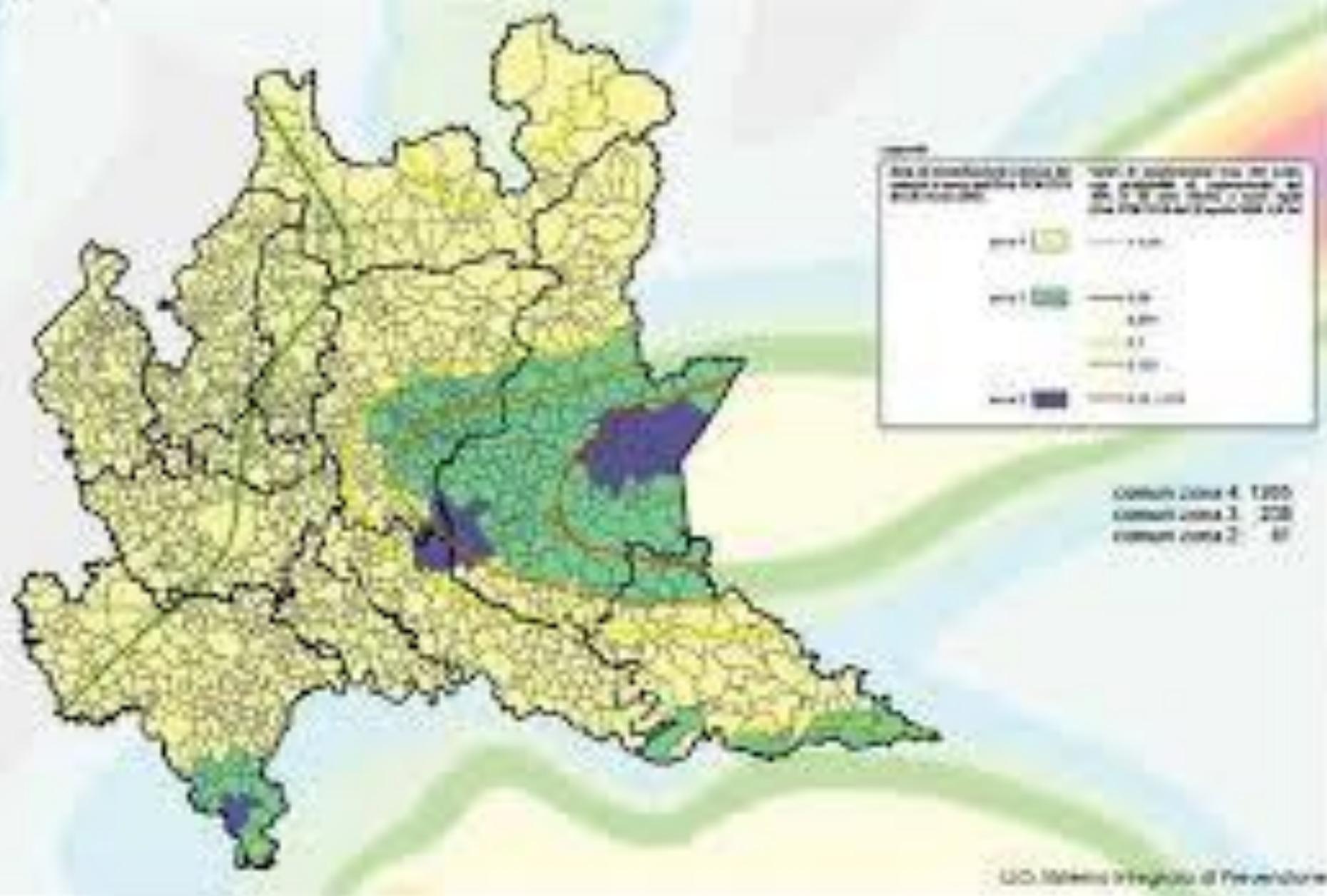
Results: With follow-up of participants through 2017, a total of 15 870 breast cancer cases were identified. A 10 ug/m³ increase in PM_{2.5} was statistically significantly associated with overall breast cancer incidence (HR ¼ 1.08, 95% CI ¼ 1.02 to 1.13). The association was evident for estrogen receptor–positive (HR ¼ 1.10, 95% CI ¼ 1.04 to 1.17) but not estrogen receptor–negative tumors (HR ¼ 0.97, 95% CI ¼ 0.84 to 1.13; Pheterogeneity ¼ .3). Overall breast cancer hazard ratios were more than 1 across the catchment areas, ranging from a **hazard ratio of 1.26 (95% CI ¼ 0.96 to 1.64)** for North Carolina to a hazard ratio of 1.04 (95% CI ¼ 0.68 to 1.57) for Louisiana (Pheterogeneity ¼ .9).

JNCI: Journal of the National Cancer Institute, 2024, 116(1), 53–60

<https://doi.org/10.1093/jnci/djad170> Advance Access Publication Date: September 11, 2023

Grazie per l'attenzione

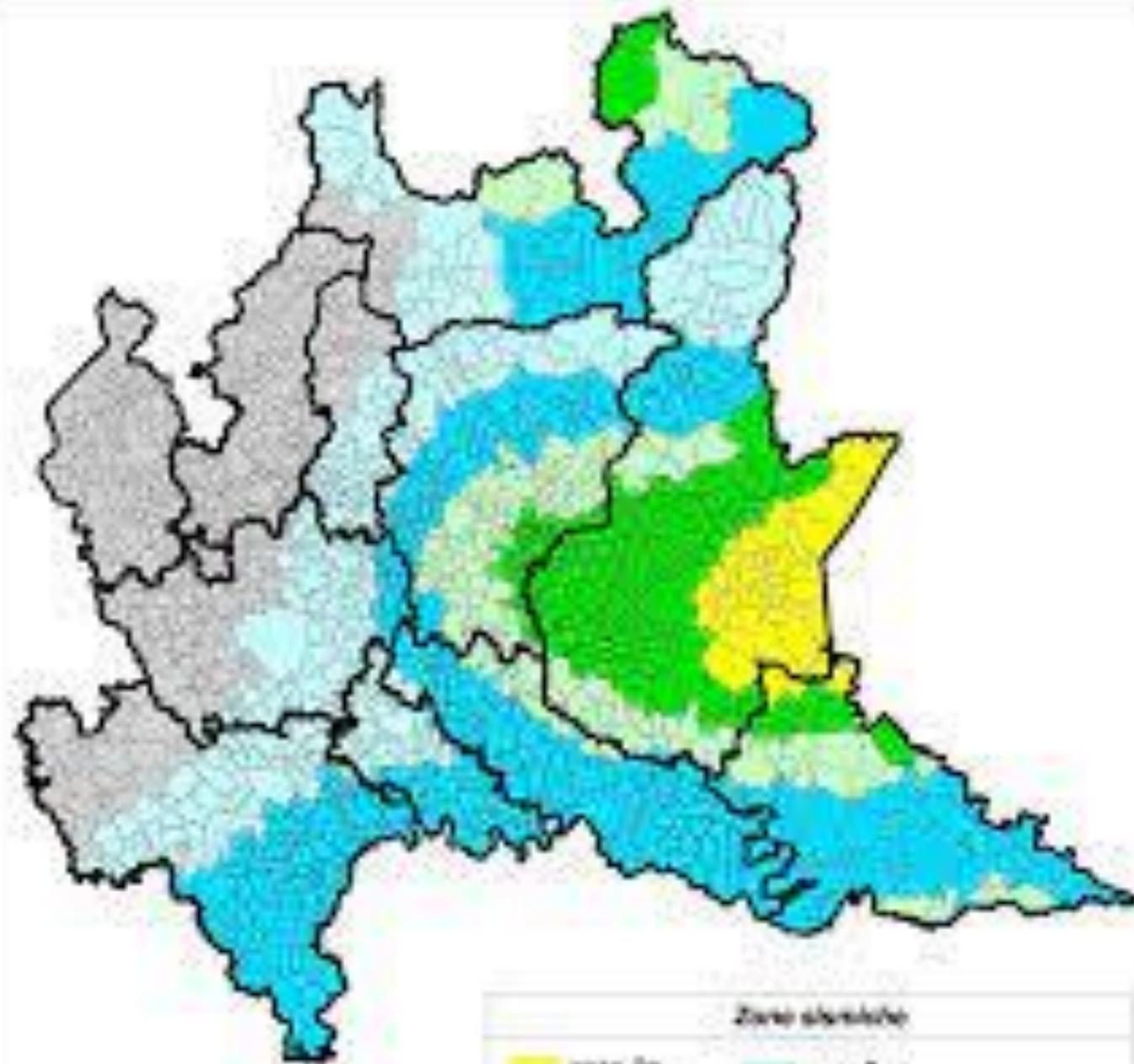
Mapa di pericolosità sismica e classificazione dei comuni lombardi in base all'OPCM 3276/2003





Zone di classificazione sismica dei
comuni ai sensi dell'Ord. PCM 3274
del 20 marzo 2003.

	n° comuni
zona 1	440
zona 2	1028
zona 3	57



Zona shpirtërore

zona 2a
zona 2b
zona 2c
zona 2d

zona 3a
zona 3b
zona 3c
zona 3d

zona 4

Valutazione d'impatto sanitario mediante calcolo dei decessi attribuibili alle polveri sottili nel Distretto di Cremona (dati sino al 2019)

Dal presente documento emerge come una quota compresa tra **lo 0.6 e il 13.4% dei decessi** (rifacendosi alle stime del 2019) sia attribuibile e quindi prevenibile applicando interventi, sia a livello individuale che a livello di popolazione, che abbiano l'obiettivo di ridurre le emissioni degli inquinanti in atmosfera.

Associazione tra inquinamento atmosferico e patologie respiratorie nella popolazione pediatrica del distretto di Cremona

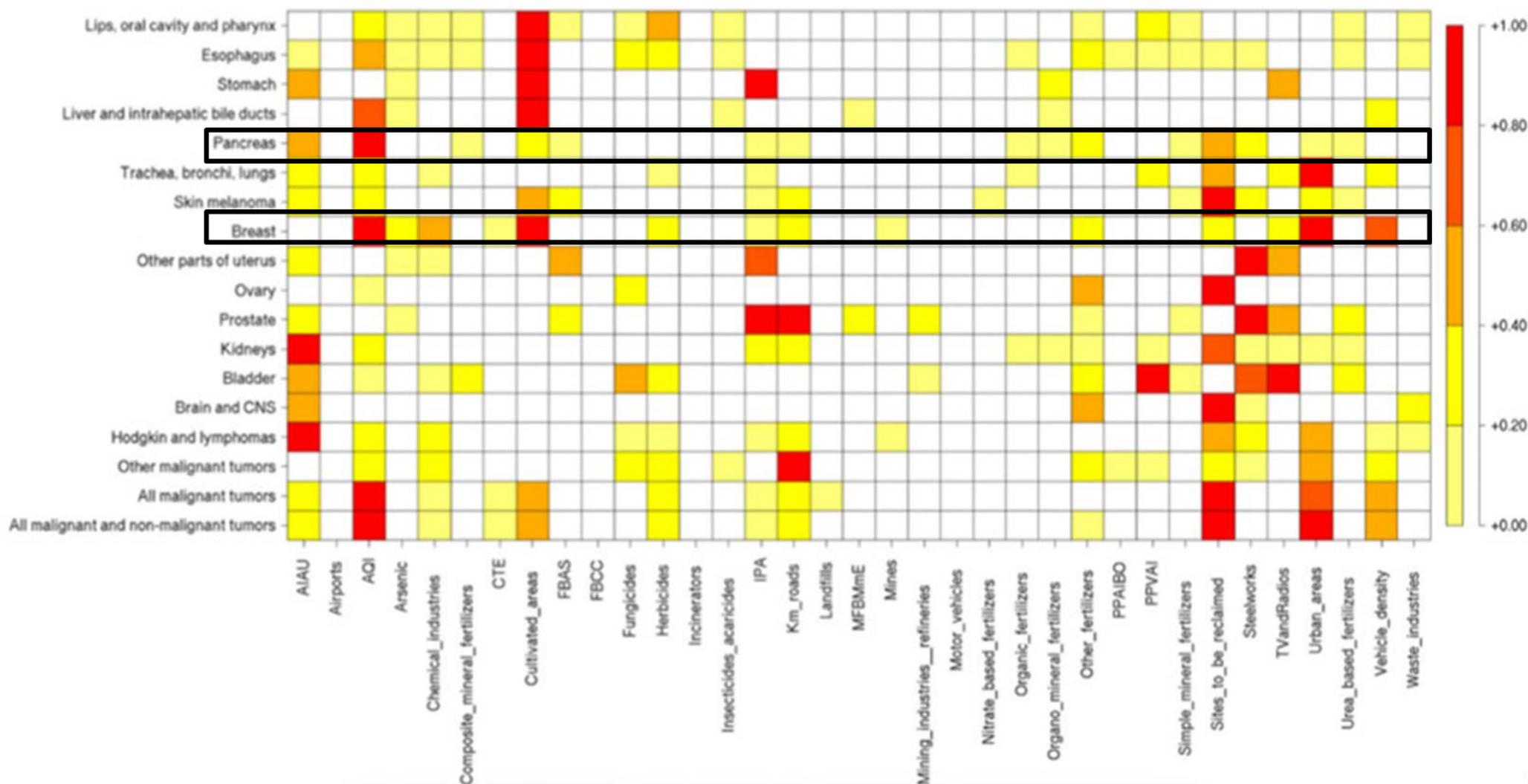
Il nostro studio conferma una **possibile associazione** tra polveri sottili e asma, rilevata sia nell'analisi dei ricoveri ospedalieri, sia nell'analisi delle prescrizioni di farmaci per l'ostruzione delle vie aeree, soprattutto in relazione alle dosi assunte più che al numero dei soggetti trattati

Associazione tra inquinamento atmosferico da polveri sottili e leucemia acuta nella provincia di Cremona

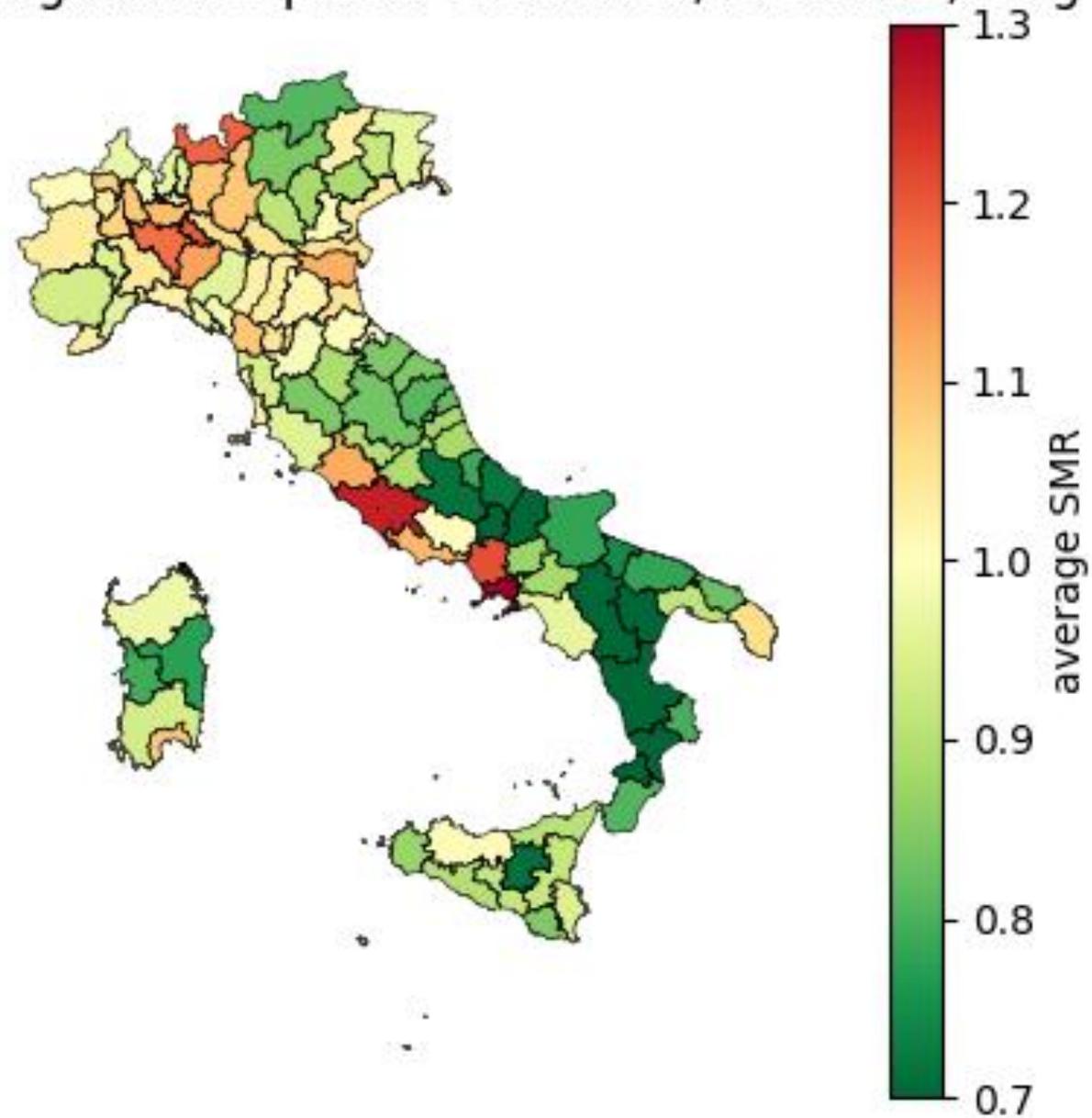
I risultati di questo studio caso-controllo condotto nella provincia di Cremona suggeriscono un **lieve aumento** di rischio di insorgenza delle leucemie acute all'aumentare della concentrazione di PM10, in particolar modo per quanto riguarda le leucemie mieloidi e il sesso femminile.

Associazione tra inquinamento atmosferico ed eventi avversi della riproduzione nel distretto di Cremona

Complessivamente, il nostro studio ha suggerito un'associazione tra esposizione a inquinanti aerodispersi e alcuni esiti avversi della gravidanza, seppure **di limitata entità**



of which malignant neoplasm of trachea, bronchus, lung



of which malignant neoplasm of pancreas

