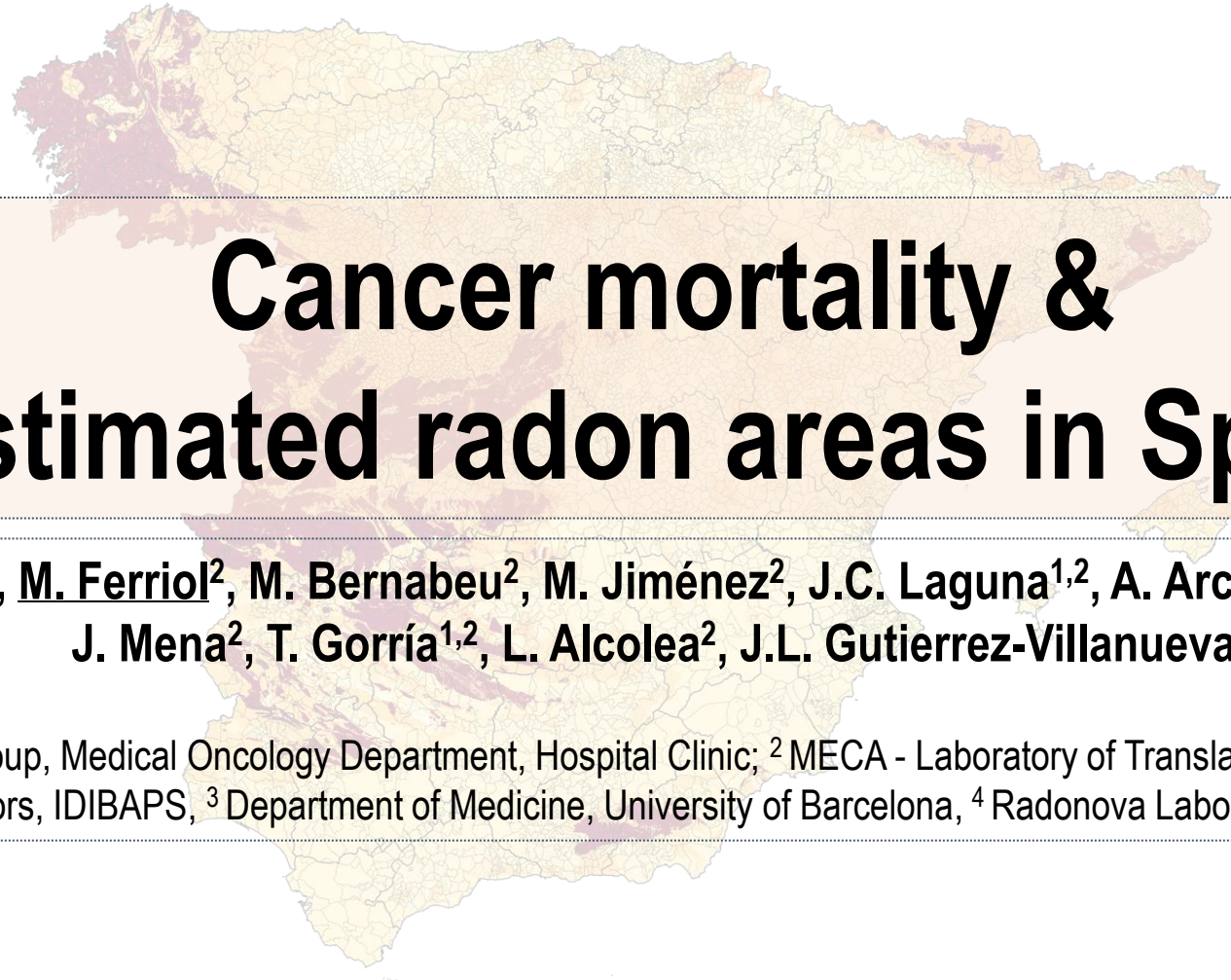

Cancer mortality & estimated radon areas in Spain

L. Mezquita[1,2,3], M. Ferriol[2], M. Bernabeu[2], M. Jiménez[2], J.C. Laguna[1,2], A. Arcocha[2], D. Delgado[2], J. Mena[2], T. Gorría[1,2], L. Alcolea[2], J.L. Gutierrez-Villanueva[4]

[1] Thoracic Oncology Group, Medical Oncology Department, Hospital Clinic; [2] MECA - Laboratory of Translational Genomics and Targeted Therapies in Solid Tumors, IDIBAPS, [3] Department of Medicine, University of Barcelona, [4] Radonova Laboratories AB, Uppsala, Sweden

BACKGROUND

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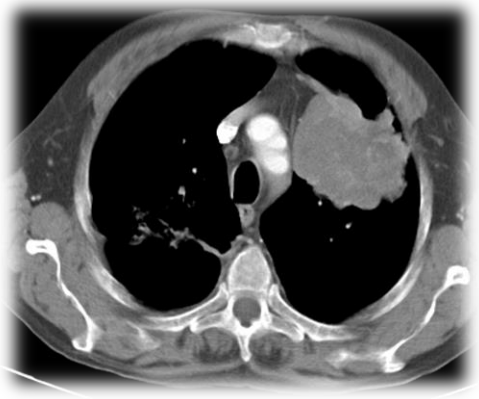
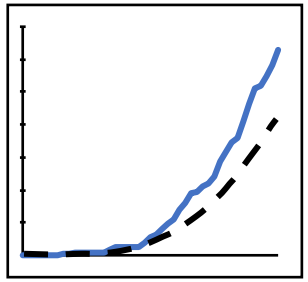
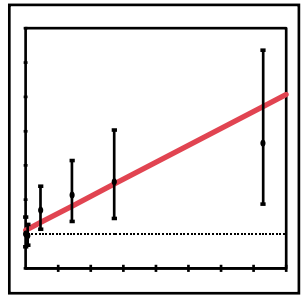
- Radon gas is a **Group 1 carcinogen**, leading cause of lung cancer in non-smokers; 2nd one in smokers
- **3-14% of lung cancer cases** depending on:
  - Smoking prevalence
  - Area





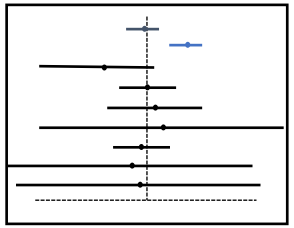
Excess lung cancer mortality



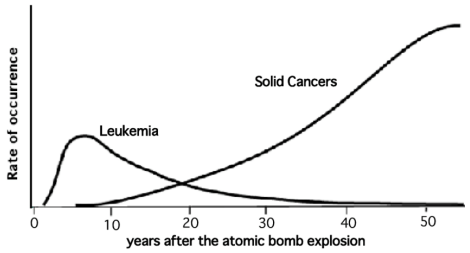
Exposure-risk relationship between radon & lung cancer

- Role of radon gas in **other solid tumors remains uncertain**
- **Epidemiological data:**
  - Uranium Miners, recent evidence
  - Indoor radon, no consistent data
- **Ionizing radiation** – Group 1 carcinogen for other solid tumors

Epidemiological data



No consistent data for other solid tumors



Miners, PUMA cohort

Fenske N, Radonorm Meeting Poland 2023, Mezquita L, Radonorm meeting Poland 2023; Shin E, Front. Genet. 2020, Radon WHO 2009, Ferriol M, ESMO 2024; manuscript in preparation

BACKGROUND: Clinical observations

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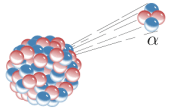
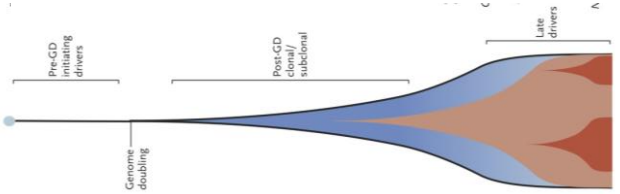
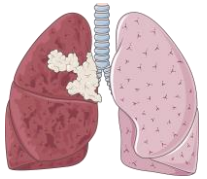
MAIN Hypothesis:

1. Radon is associated with molecular profile of lung cancer
2. Identify a radon-associated signature in cancer
3. Improve Biomarkers & Precision Medicine of radon-related cancer

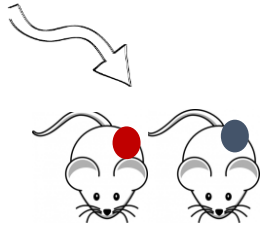


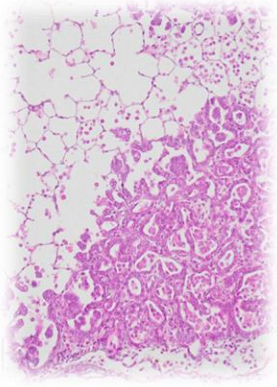




Preclinical models

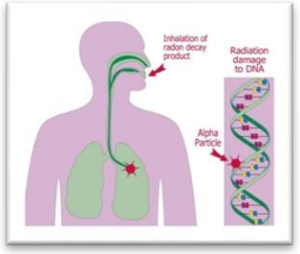
Radon inhaled



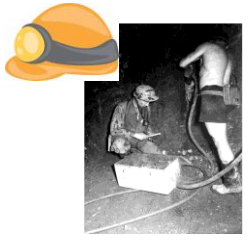


- Molecular profile of radon-induced lung cancer
- Also → other solid tumors induced by radon

Clinical studies



Uranium-workers

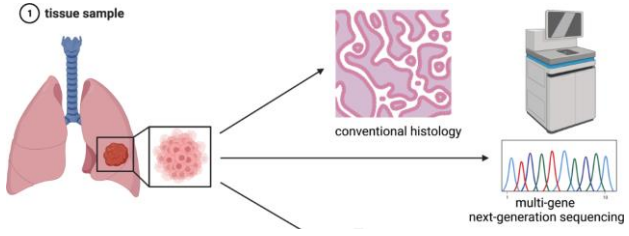


Patients – indoor Rn

EORTC European Organisation for Research and Treatment of Cancer
The future of cancer therapy
mc ca Grupo de Medioambiente y Cáncer
ICAPEM

BIORADON (EU) – 975 pts
MIRROR (ES) – 670 pts

- Molecular profile of radon-induced lung cancer
- Differences – sex (female) & age
- Also → similarities with other solid tumors



Comprehensive genomic profiling

BACKGROUND: Ecological studies

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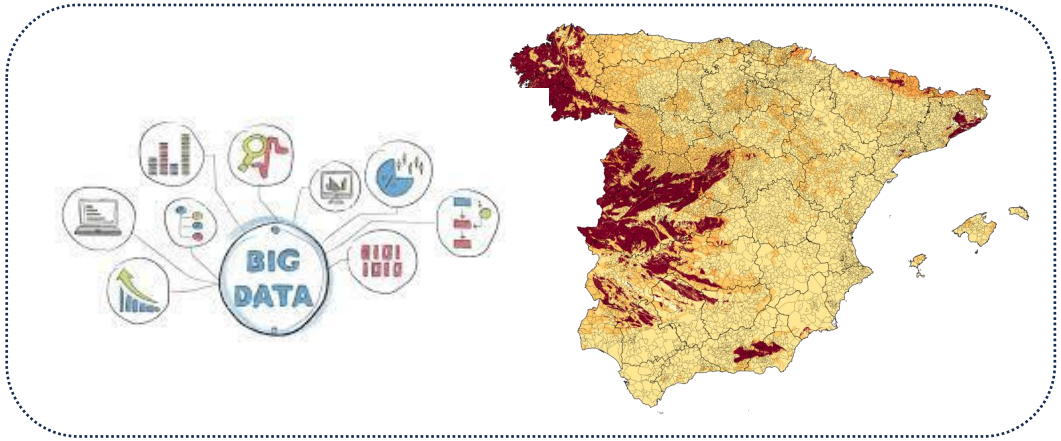
- **ECOLOGICAL study:**
  - **To generate hypothesis** - ↓ level of evidence
  - ↑ **Big data** – to study correlations
  - **Limitations:** mobility, cofounding factors (smoking), pop level reflects patient level?

- **BIG question –** "integrating our clinical perspective"



AIM: To explore the link between **cancer mortality** and estimated **Radon risk areas** in Spain to identfiy priority areas for cancer prevention (focus on radon)

METHODS

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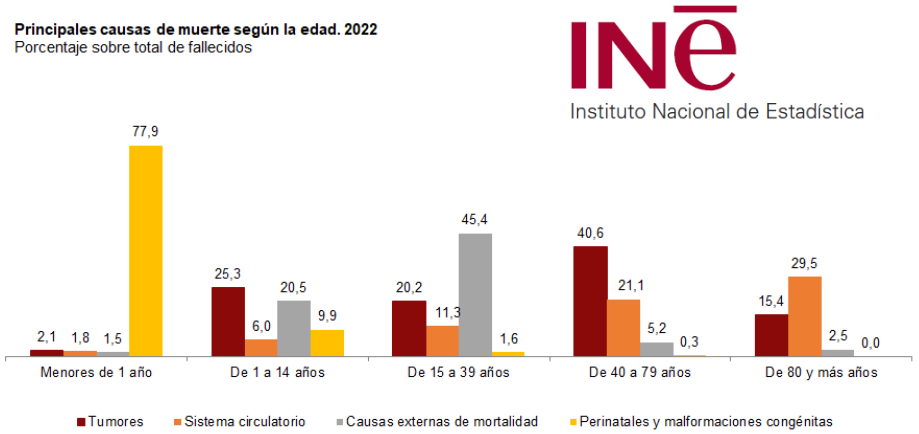
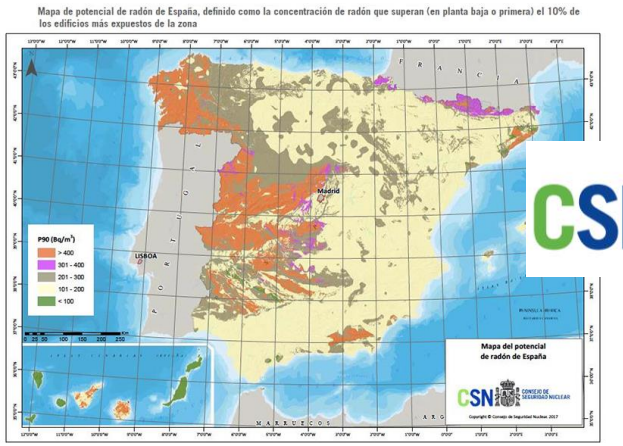
- **Retrospective analysis** of **mortality cases** recorded in the National Mortality Registry (INE) between 1999-2021 (22 years – period)

- We analyzed **age-standardized rates**, considering **age & sex**, using the ICD-10 classification, in municipalities with >10,000 inhabitants (overall, and the P25 of municipalities with higher rates)

- **Radon classification:** Municipalities grouped into **3 levels** (CSN):
  - Low: Aggregated very-low and low
  - Medium: Moderate
  - High: Aggregated high and very-high

- **Correlation Analysis:**
  - Used the area of each radon risk category within municipalities
  - Calculated Pearson correlation for each municipality & province
  - Selected results with p-value < 0.05 for significance





CSN CONSEJO DE SEGURIDAD NUCLEAR

https://www.ine.es/dyngs/INEbase/es/; https://www.csn.es/mapa-del-potencial-de-radon-en-espana

Ferriol M, ESMO 2024; manuscript in preparation

METHODS: Radon Map

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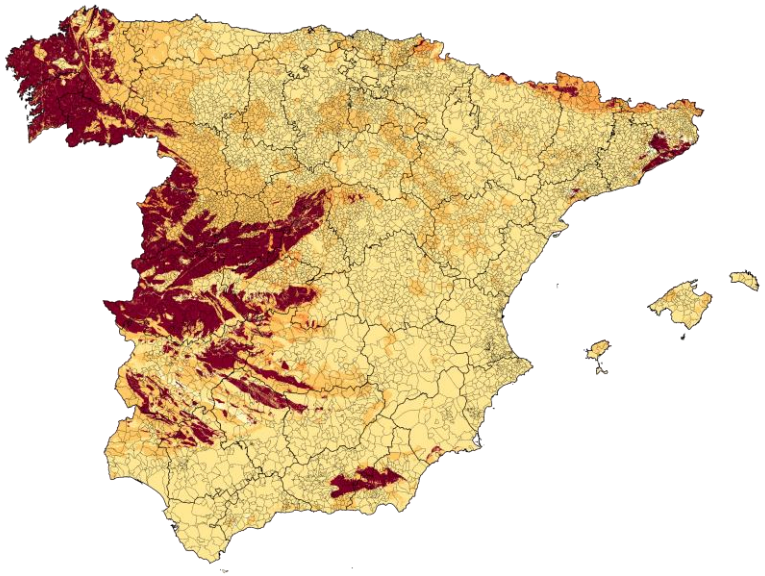
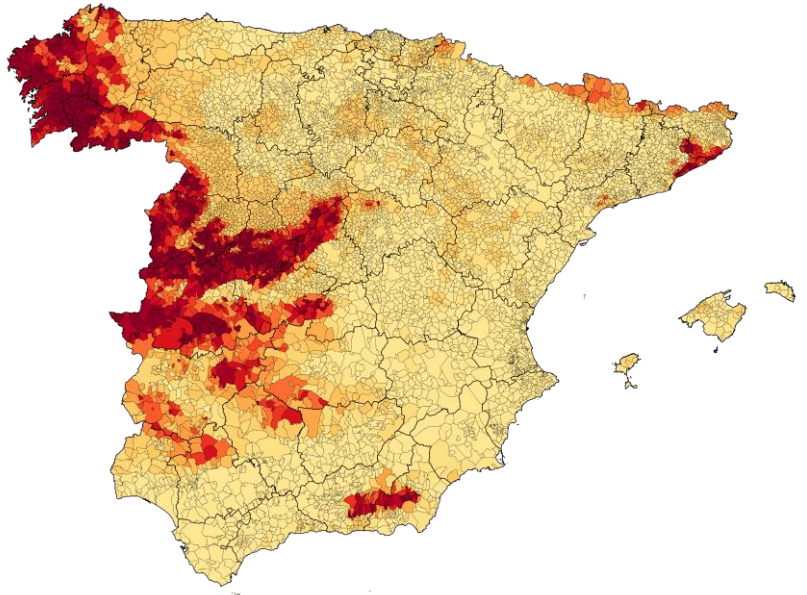
CSN Map



Radon Map by municipality



- **Data Source:** CSN
- **Geographic Scope:** All Spain except Canary Islands
- **Geographic Level:** Municipality
- **Radon Levels:** Averaged using areas of 5 categories
- **Category Mean:** Based on CSN-provided means

Ferriol M, ESMO 2024; manuscript in preparation

Radon Map by regions

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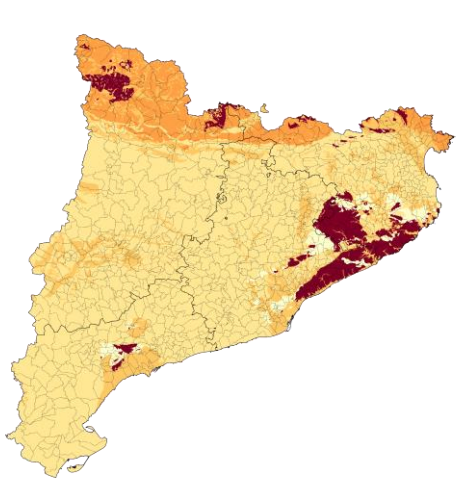
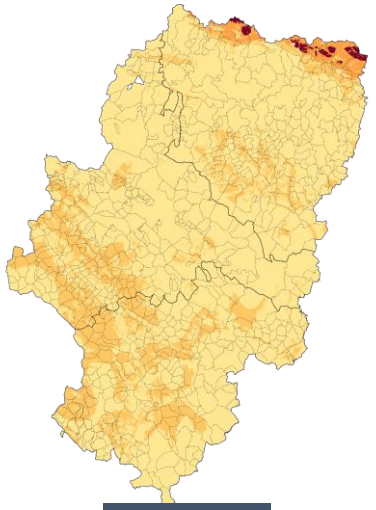
CSN Map

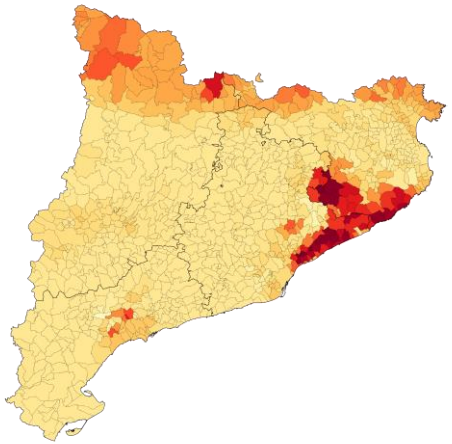


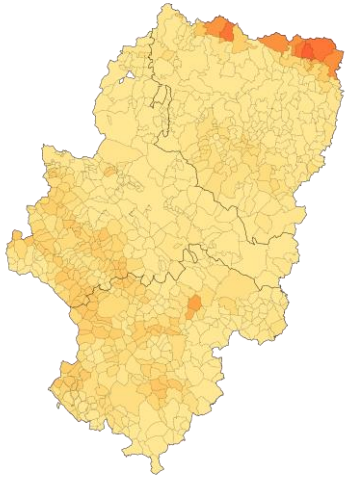
Catalonia



Aragon

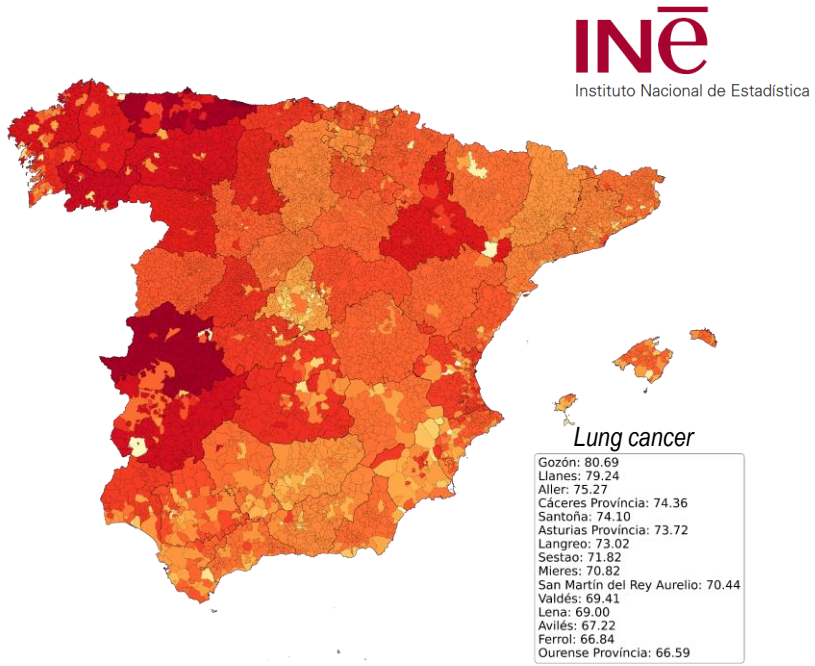
Radon Map by municipality



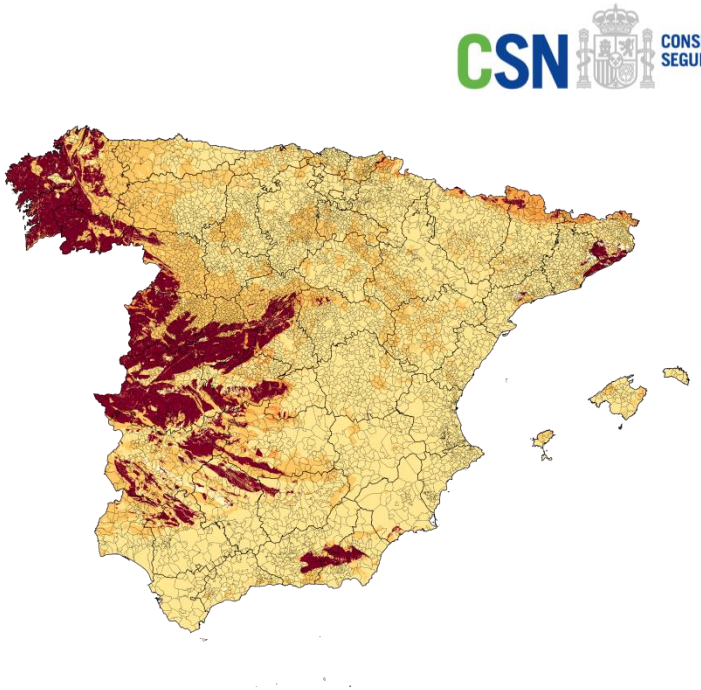


METHODS: Data sources

Clínic Barcelona | Cancer Institute and Blood Disorders



- **Data Source:** INE (1999-2021)
- **Geographic Scope:** Provinces and municipalities (>10,000)
- **Mortality Definition:** Based on ICD-10 cancer classifications
- **Age-Standardized Mortality:** Adjusted to account for age differences

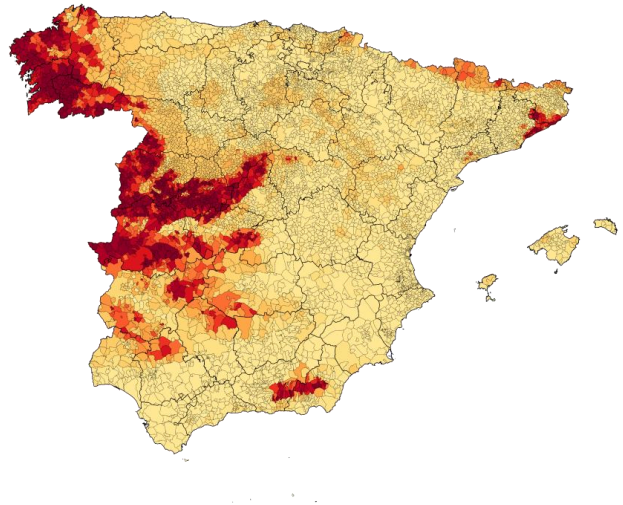


- **Data Source:** CSN
- **Geographic Scope:** All Spain except Canary Islands
- **Geographic Level:** Municipality
- **Radon Levels:** Averaged using areas of 5 categories
- **Category Mean:** Based on CSN-provided means

RESULTS: Cancer data

Clínic Barcelona | Cancer Institute and Blood Disorders

	OVERALL Deaths N=9,140,258	CANCER Deaths N=2,351,989
Age (Range)		
> 50 years	8,607,199 (94.2%)	2,200,465 (93.6%)
≤ 50 years	533,059 (5.8%)	151,524 (6.4%)
Sex		
Male	4,710,369 (51.5%)	1,451,814 (61.7%)
Female	4,429,889 (48.5%)	900,175 (38.3%)
Tumor type		
Lung Cancer	468,525 (19.9%)	
Colon Cancer	244,457 (10.4%)	
Breast Cancer	143,126 (6.1%)	



- **Municipalities:**
  - 87 (10.7%) were in high-radon areas
  - 153 (19.7%) in intermediate
  - 527 (69.5%) in low-radon areas

Ferriol M, ESMO 2024; manuscript in preparation

RESULTS: 20 years Mortality evolution

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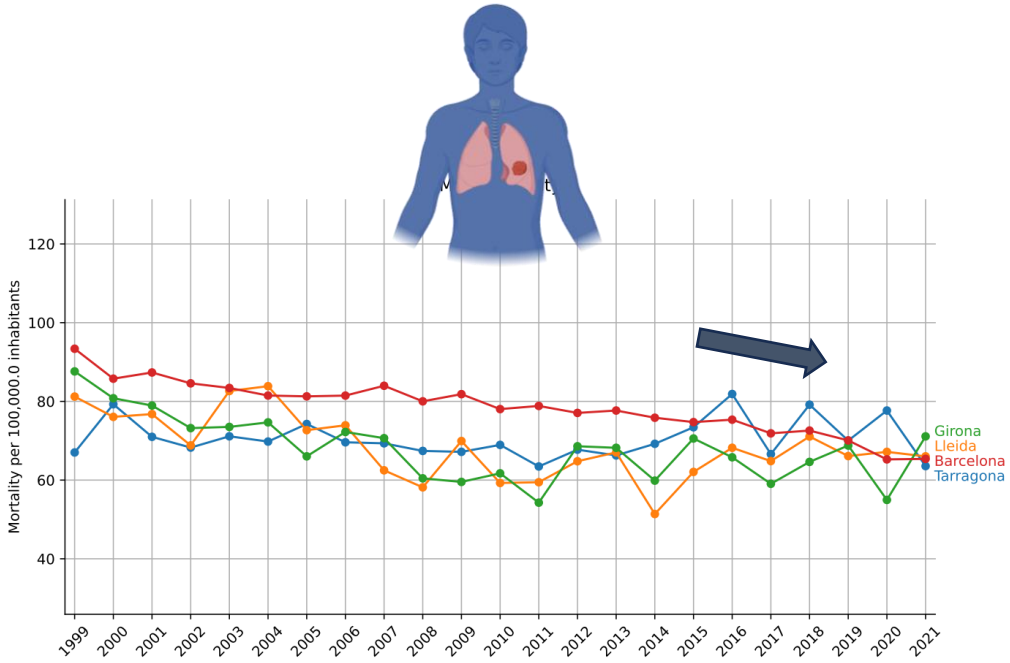
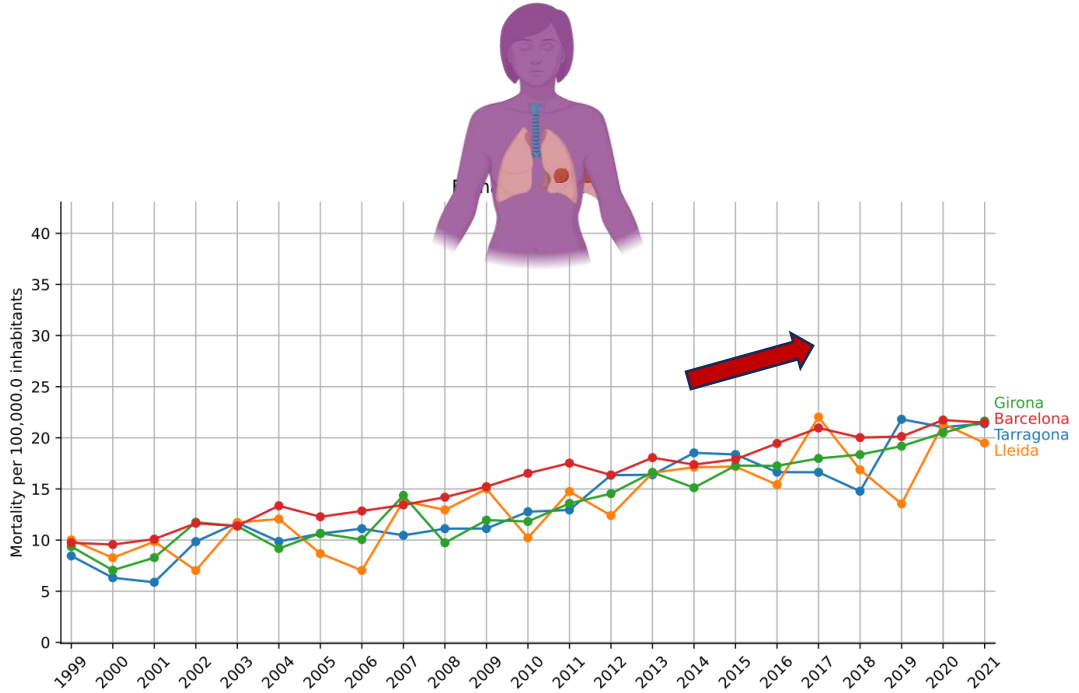
Evolution - dynamics

Example: Catalonia, Lung Cancer



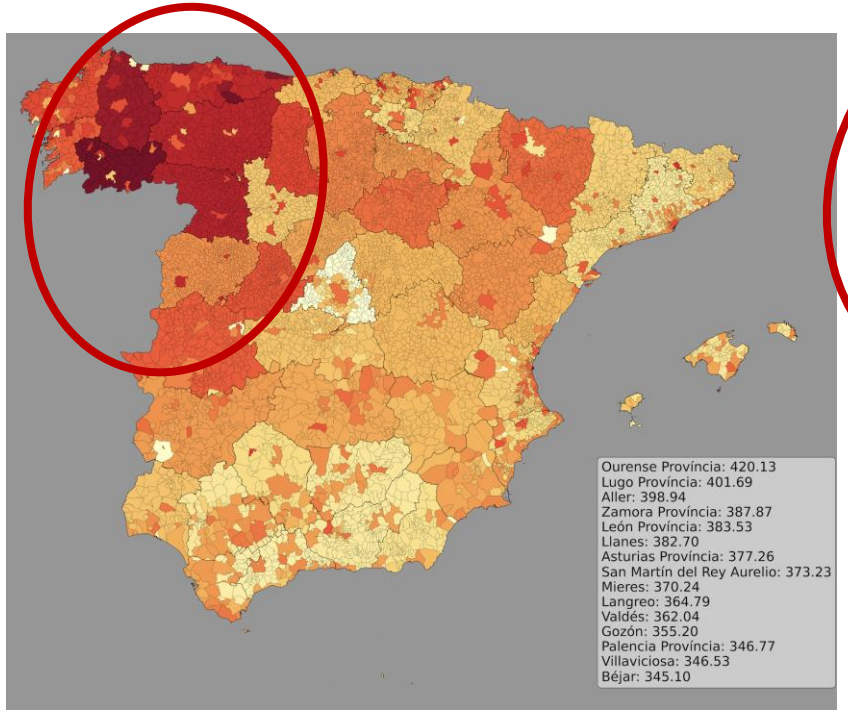


20 years period – lung cancer mortality evolution

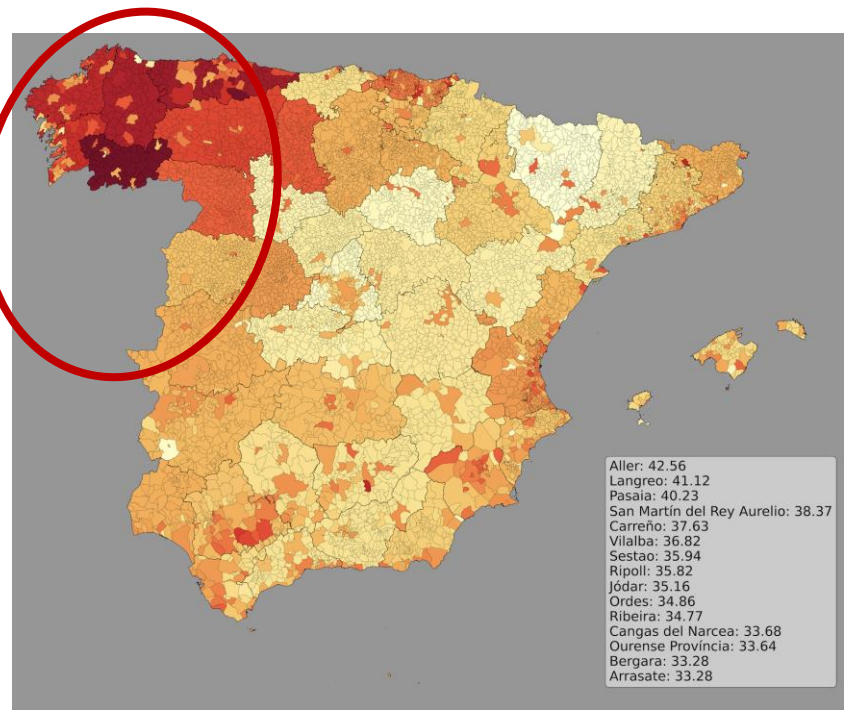
RESULTS: Cancer data (Map)

Clínic Barcelona | Cancer Institute and Blood Disorders

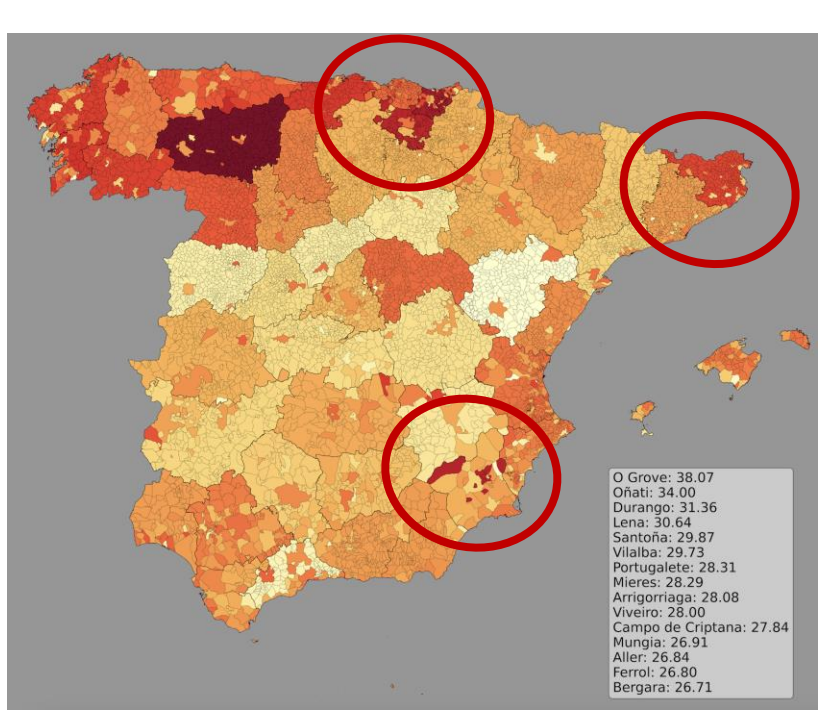
Overall



Male (<50 yrs)



Female (<50 yrs)



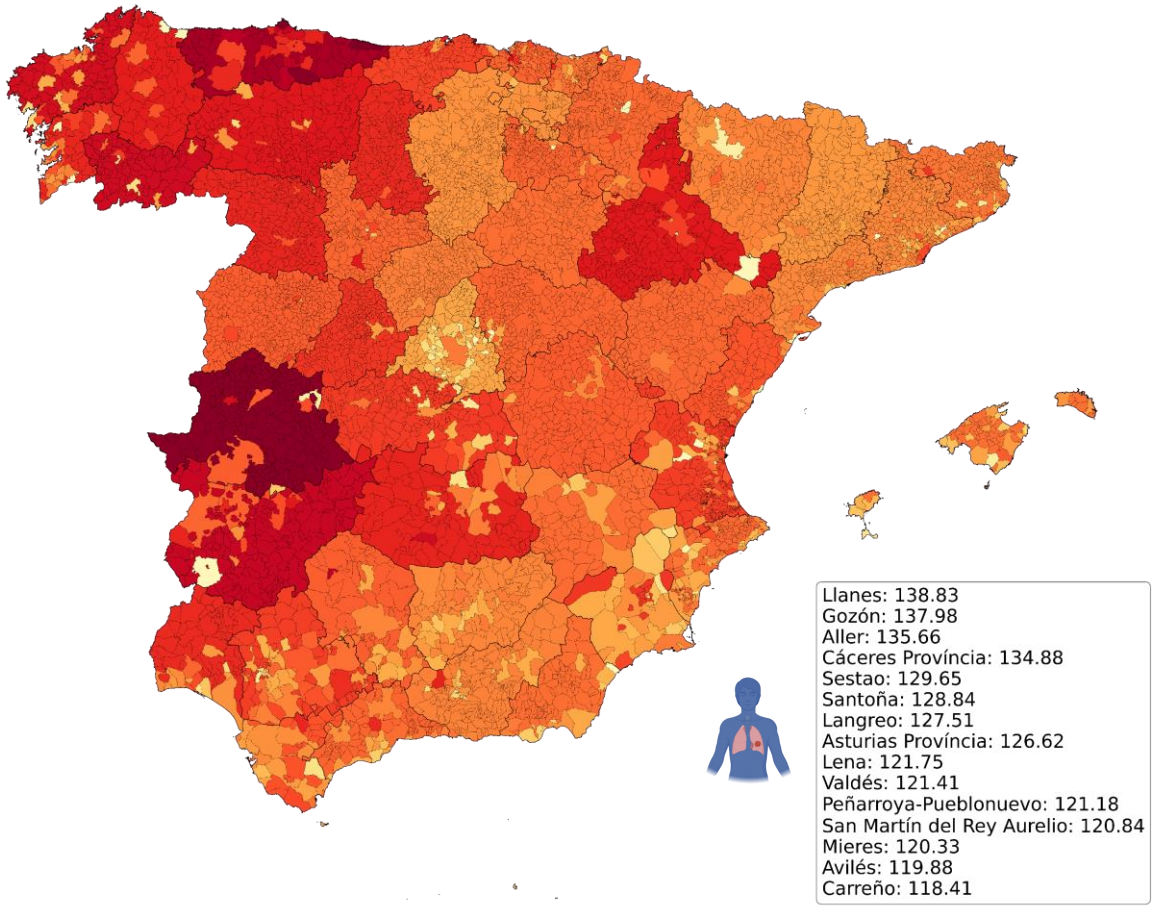
To STUDY – Age and Sex differences

RESULTS: Lung cancer Mortality

Clínic Barcelona | Cancer Institute and Blood Disorders

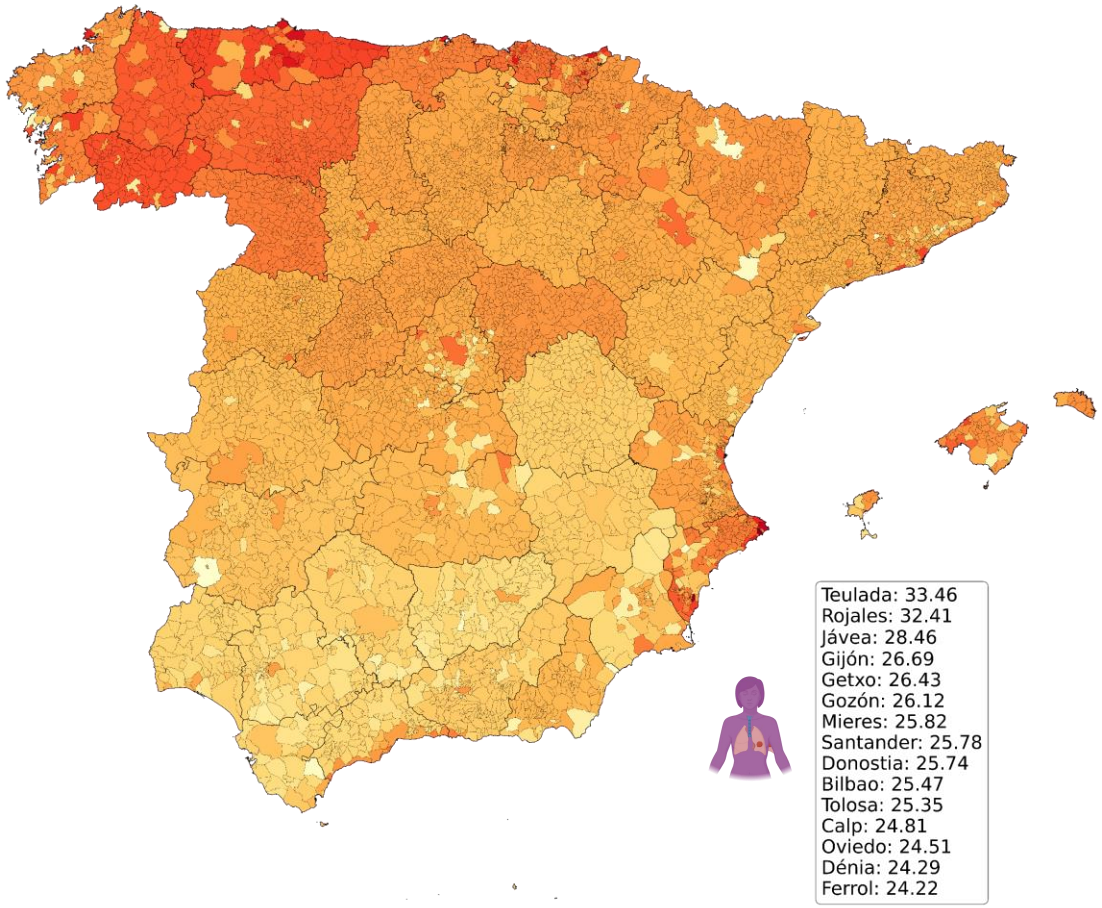
Sex differences

Male



Llanes: 138.83
Gozón: 137.98
Aller: 135.66
Cáceres Província: 134.88
Sestao: 129.65
Santoña: 128.84
Langreo: 127.51
Asturias Província: 126.62
Lena: 121.75
Valdés: 121.41
Peñarroya-Pueblonuevo: 121.18
San Martín del Rey Aurelio: 120.84
Mieres: 120.33
Avilés: 119.88
Carreño: 118.41

Female



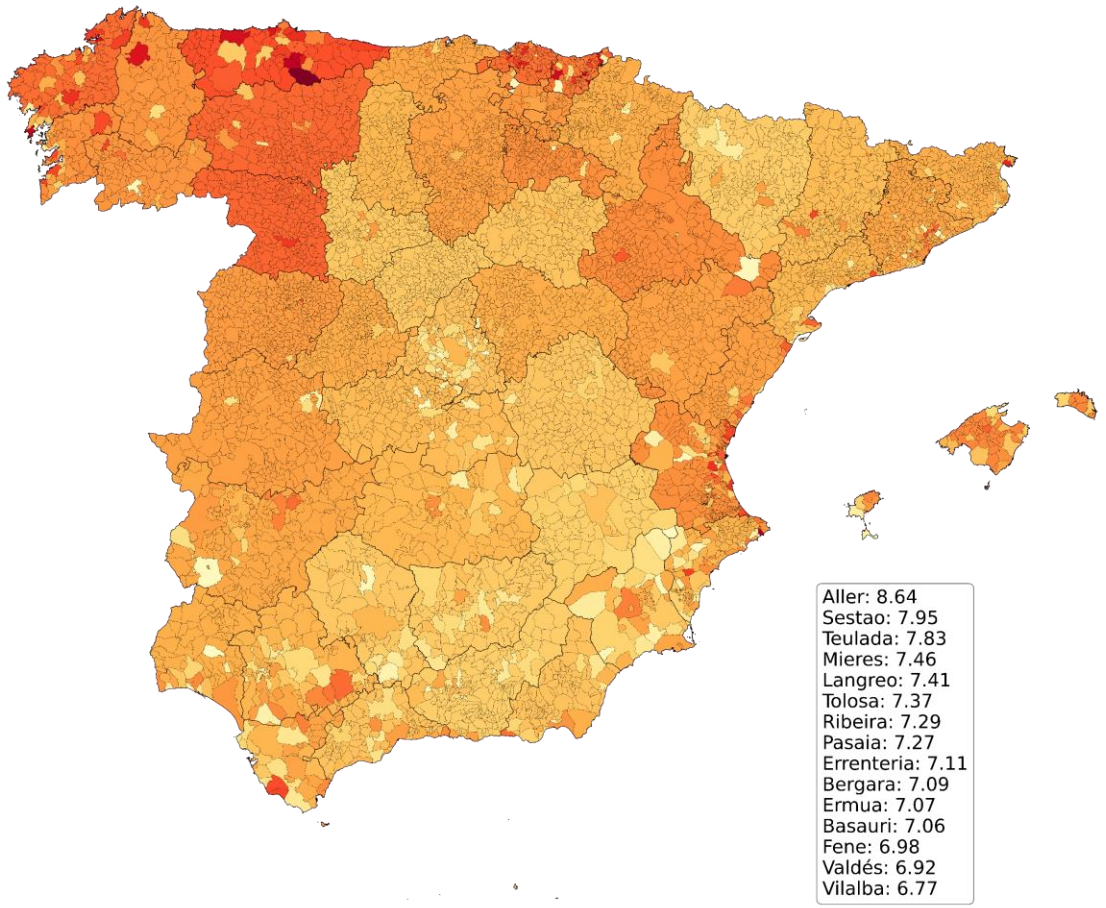
Teulada: 33.46
Rojales: 32.41
Jávea: 28.46
Gijón: 26.69
Getxo: 26.43
Gozón: 26.12
Mieres: 25.82
Santander: 25.78
Donostia: 25.74
Bilbao: 25.47
Tolosa: 25.35
Calp: 24.81
Oviedo: 24.51
Dénia: 24.29
Ferrol: 24.22

RESULTS: Lung cancer Mortality

Clínic Barcelona | Cancer Institute and Blood Disorders

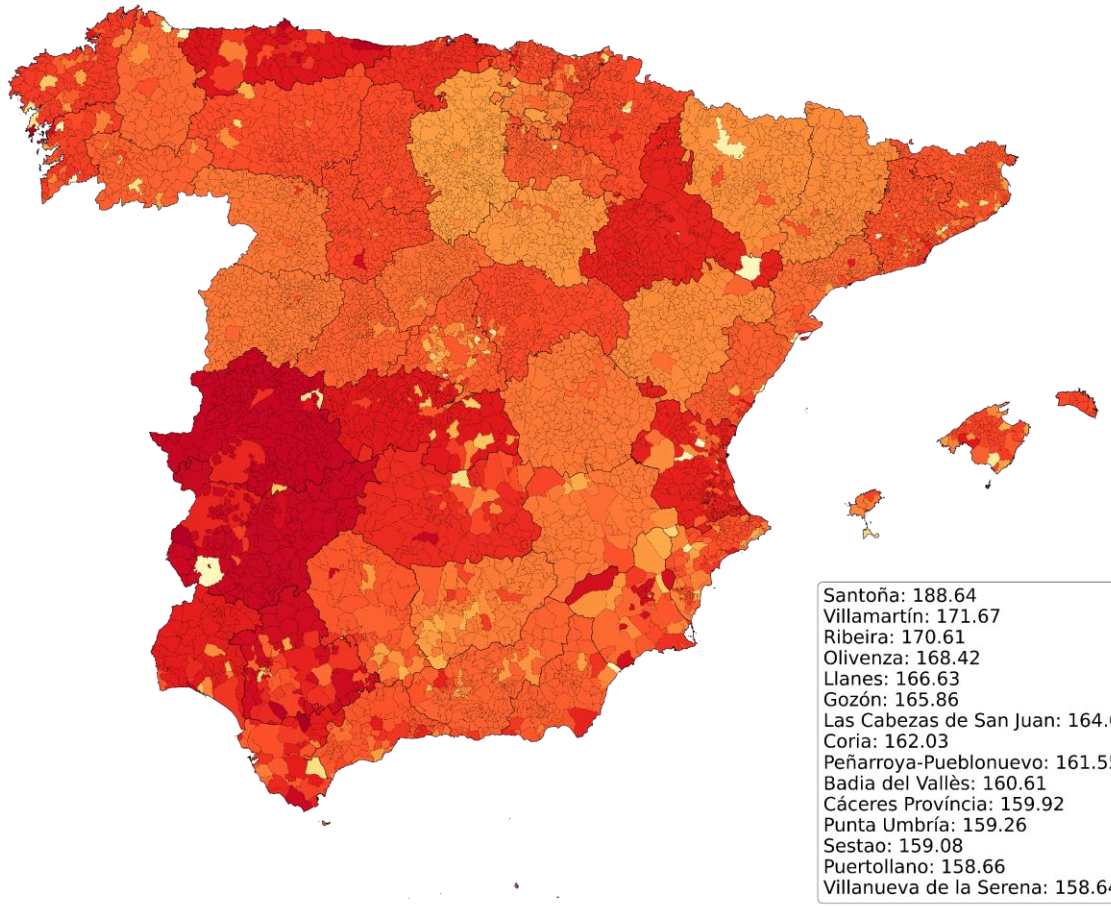
Age differences

Age ≤ 50



Aller: 8.64
Sestao: 7.95
Teulada: 7.83
Mieres: 7.46
Langreo: 7.41
Tolosa: 7.37
Ribeira: 7.29
Pasaia: 7.27
Errenteria: 7.11
Bergara: 7.09
Ermua: 7.07
Basauri: 7.06
Fene: 6.98
Valdés: 6.92
Vilalba: 6.77

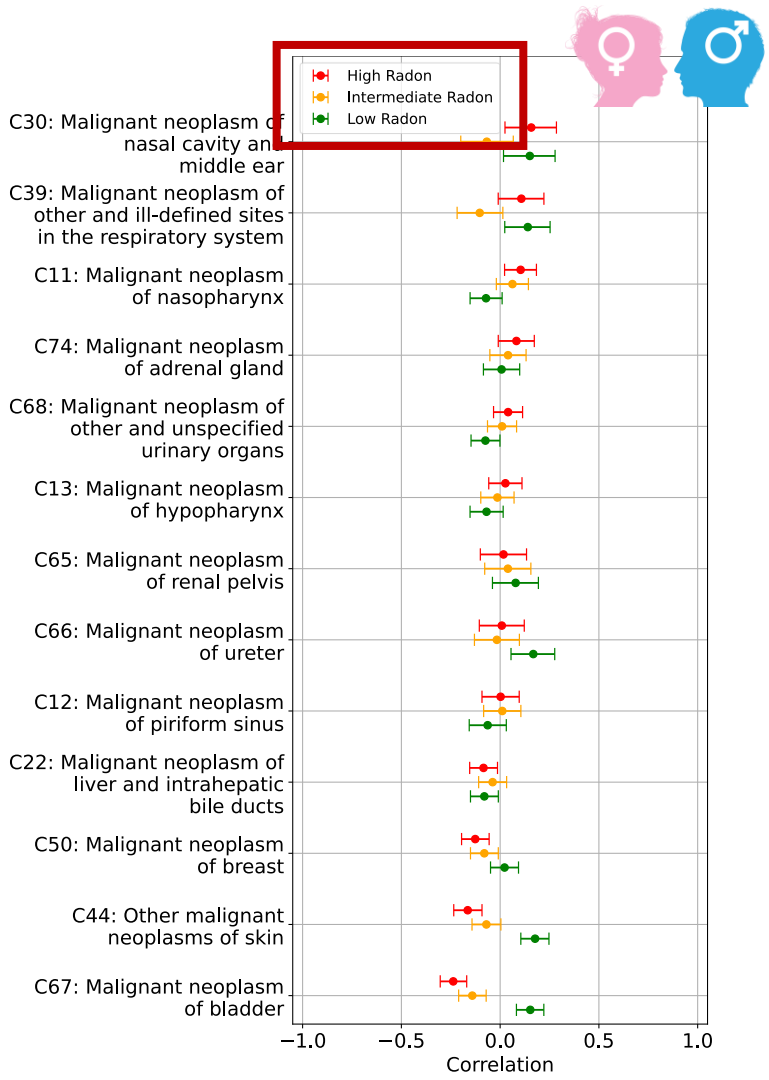
Age > 50

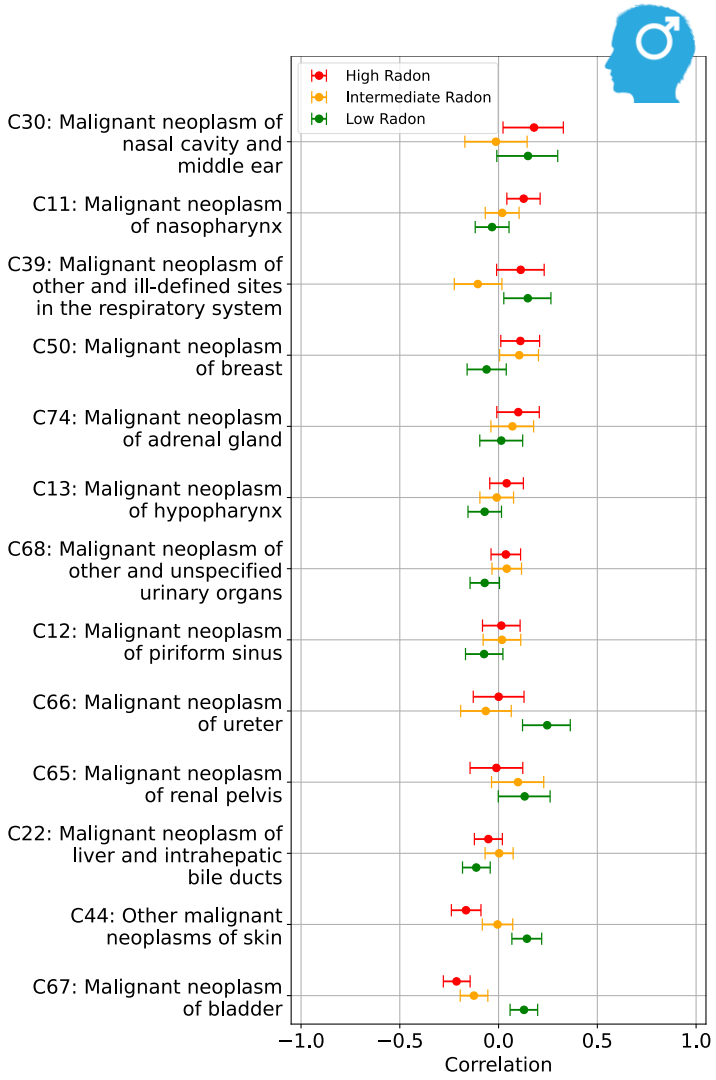


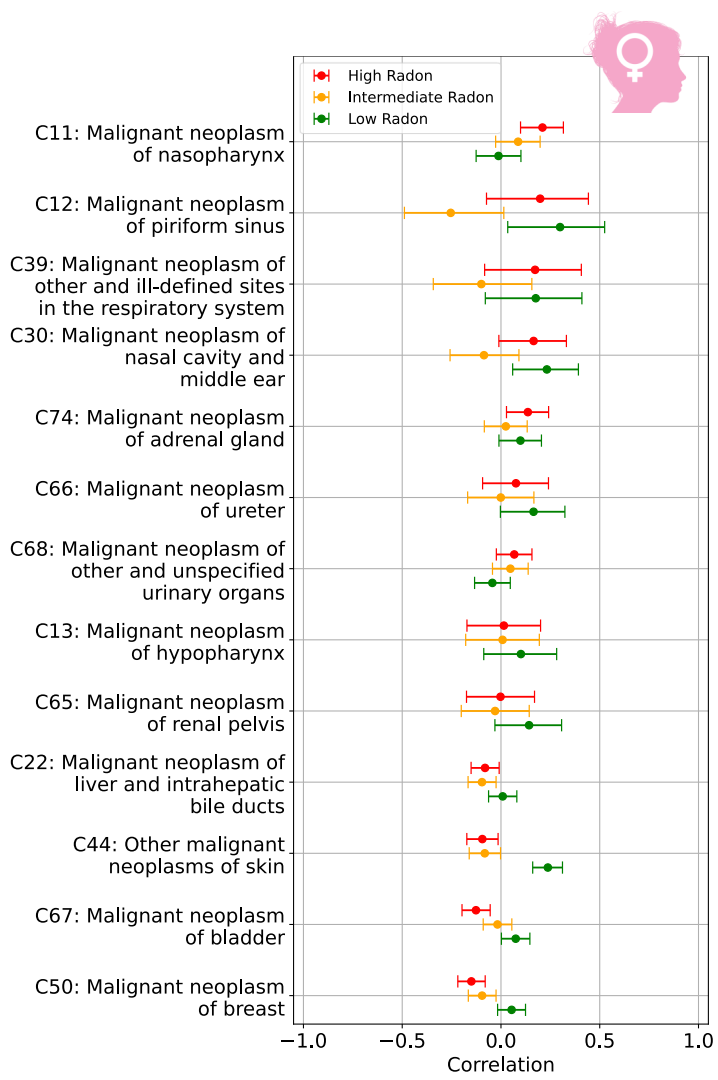
Santoña: 188.64
Villamartín: 171.67
Ribeira: 170.61
Olivenza: 168.42
Llanes: 166.63
Gozón: 165.86
Las Cabezas de San Juan: 164.68
Coria: 162.03
Peñarroya-Pueblonuevo: 161.55
Badia del Vallès: 160.61
Cáceres Província: 159.92
Punta Umbría: 159.26
Sestao: 159.08
Puertollano: 158.66
Villanueva de la Serena: 158.64

RESULTS: Correlation [all ages]

Clínic Barcelona | Cancer Institute and Blood Disorders





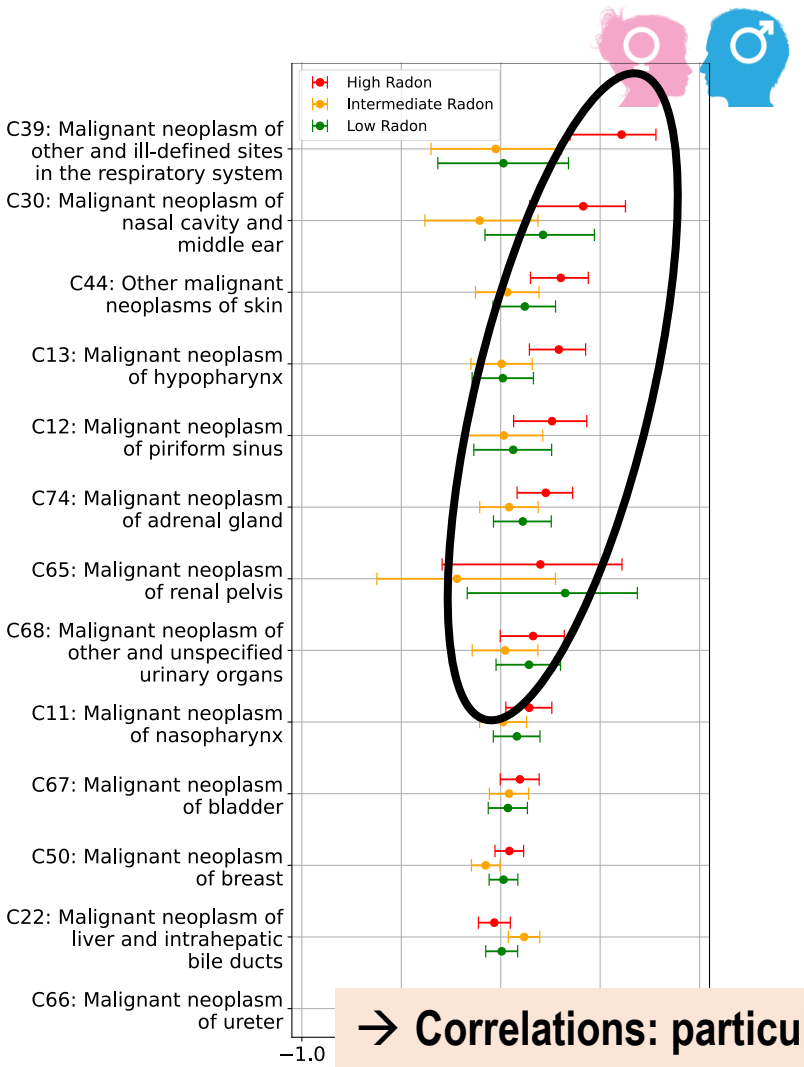


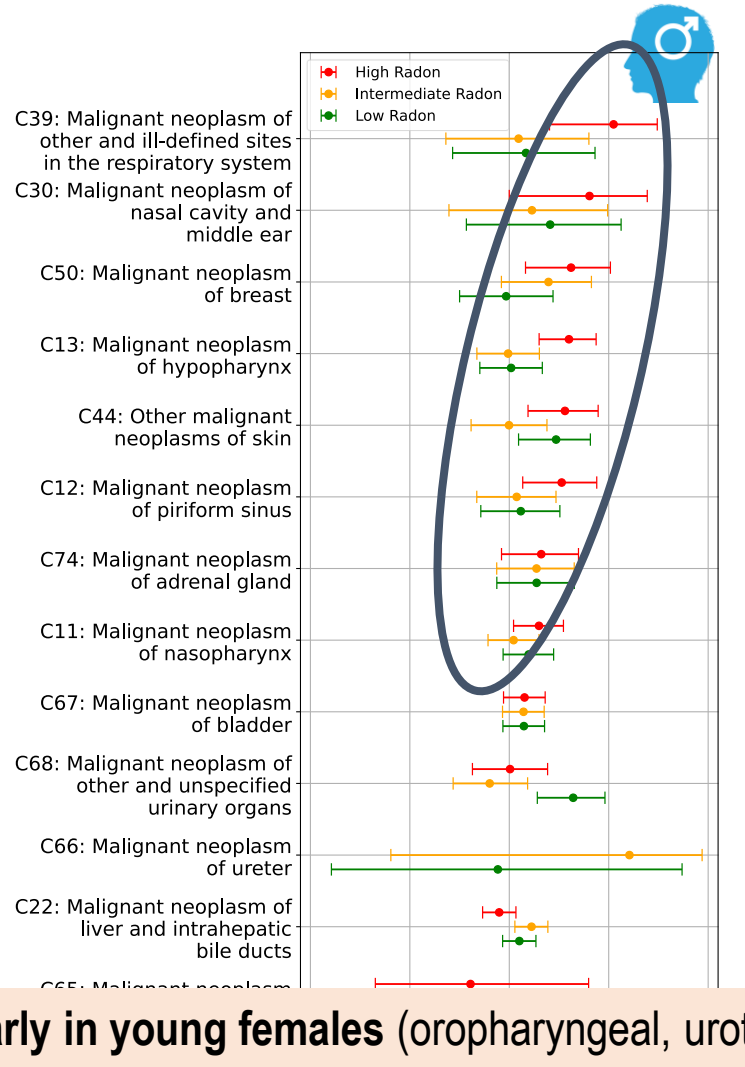
No correlation between cancer mortality & estimated radon risk areas

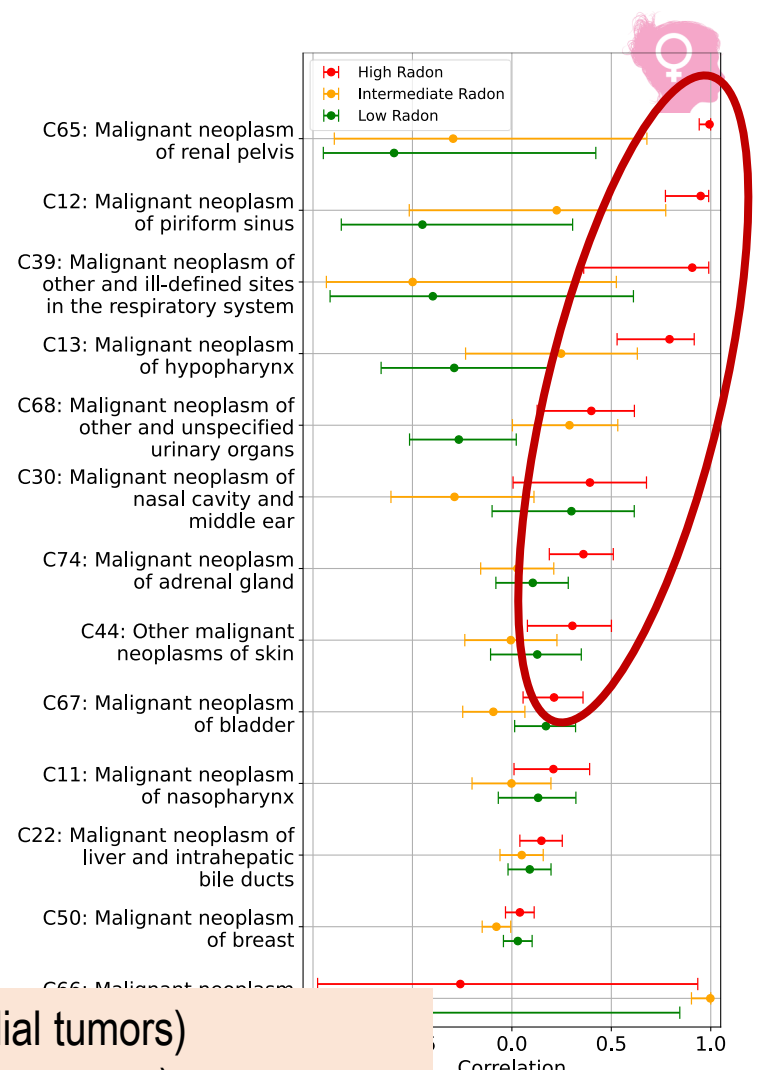
Ferriol M, ESMO 2024; manuscript in preparation

RESULTS: Correlation [young pop]

Clínic Barcelona | Cancer Institute and Blood Disorders







→ **Correlations: particularly in young females** (oropharyngeal, urothelial tumors)

→ **Also, in lung cancer in young females, +++** (↓ cumulative smoking exposure)

Ferriol M, ESMO 2024; manuscript in preparation

Results: Other Cancers Age-Standardized Mortality

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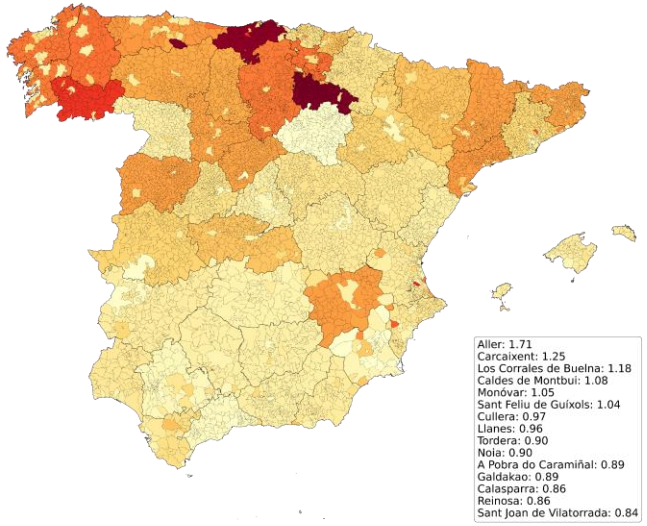
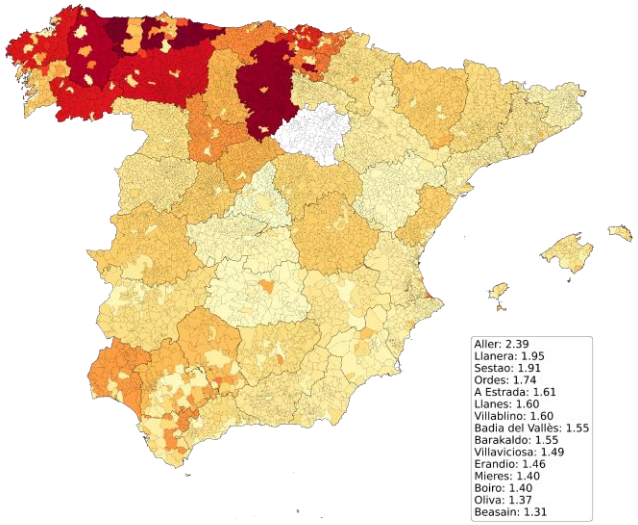
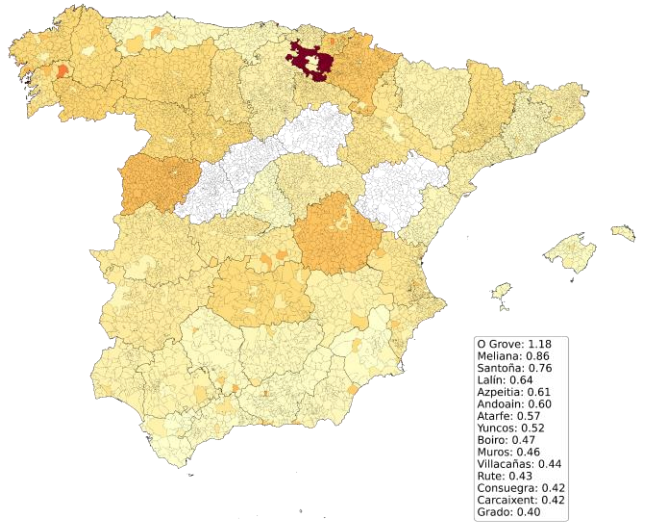
Pyriform Sinus



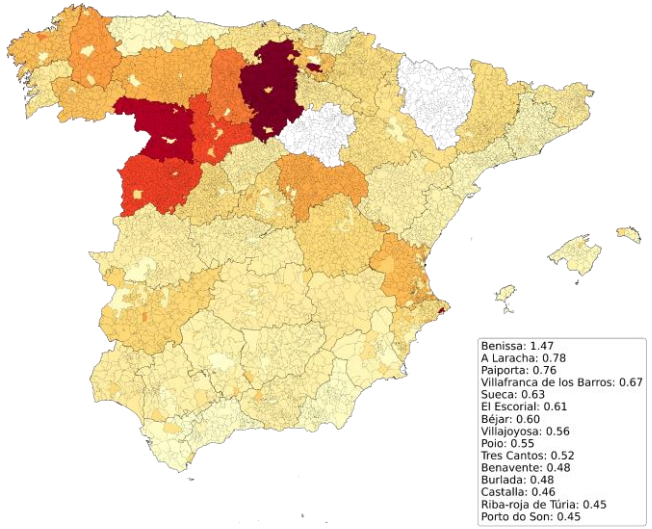
Hypopharynx



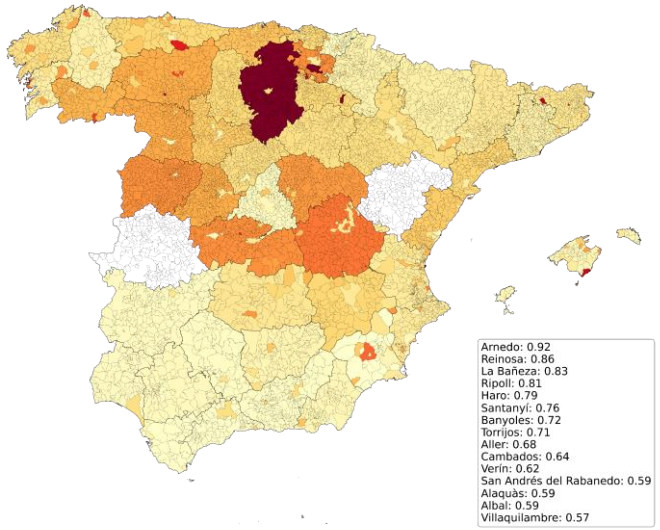
Nasal fossa



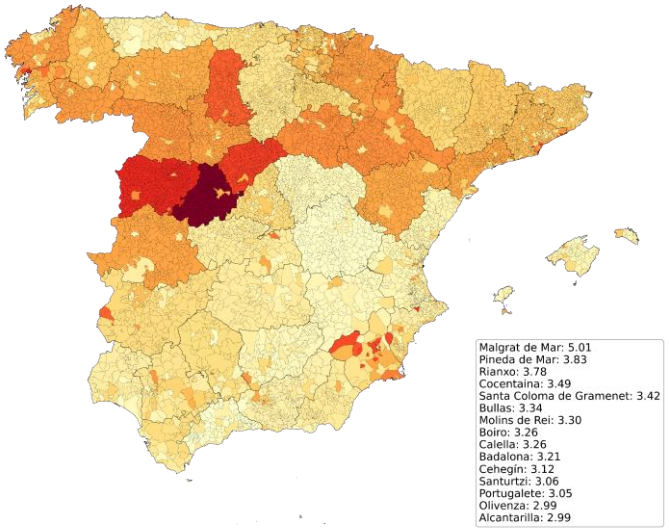
Other Intrathoracic Organs



Renal Pelvis



Other Urinary Organs



Results: Lung cancer Age-Standardized Mortality

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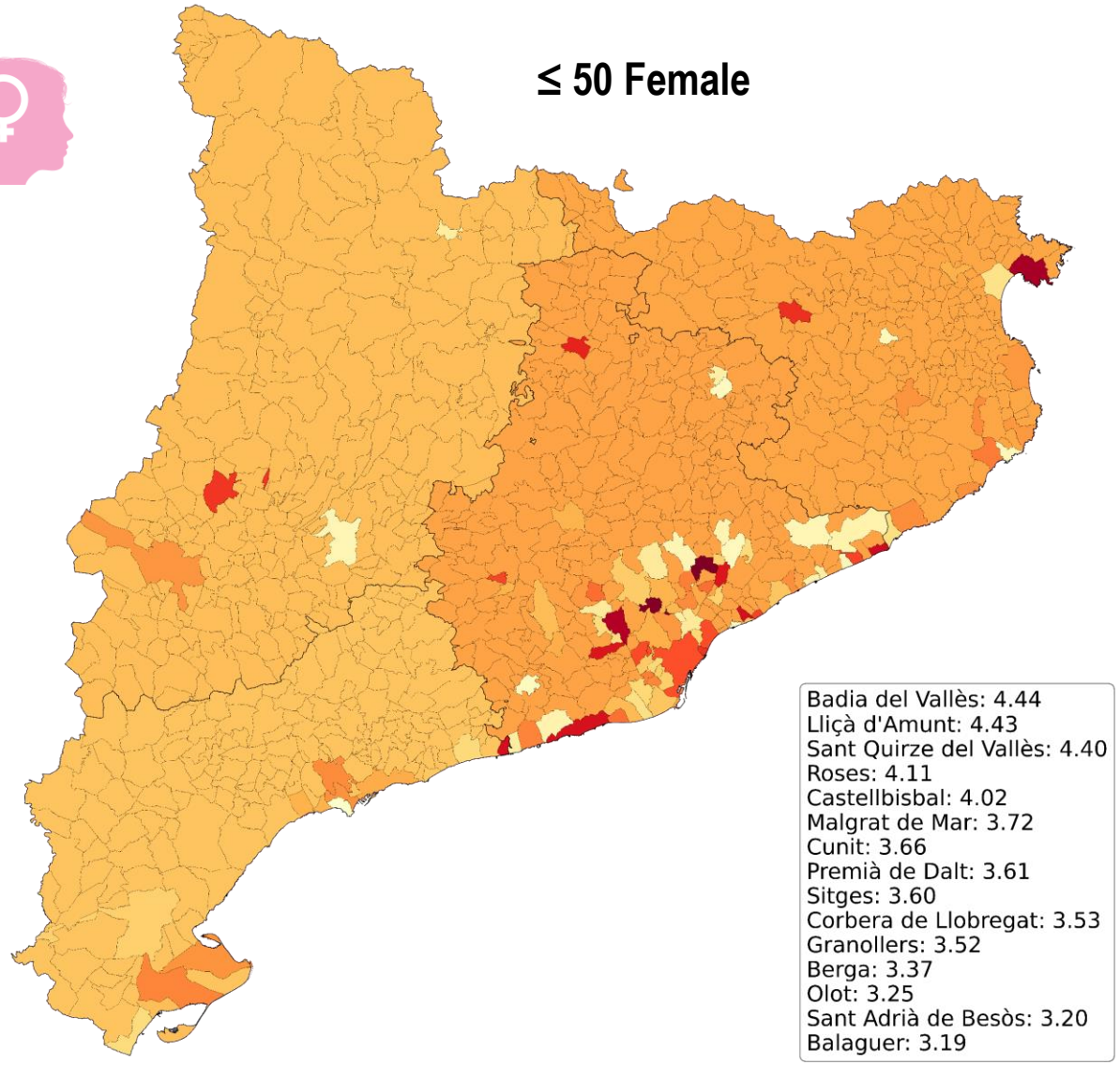
Granularity level

≤ 50 Female



Badia del Vallès: 4.44
Lliçà d'Amunt: 4.43
Sant Quirze del Vallès: 4.40
Roses: 4.11
Castellbisbal: 4.02
Malgrat de Mar: 3.72
Cunit: 3.66
Premià de Dalt: 3.61
Sitges: 3.60
Corbera de Llobregat: 3.53
Granollers: 3.52
Berga: 3.37
Olot: 3.25
Sant Adrià de Besòs: 3.20
Balaguer: 3.19

TO EXPLORE WHAT IS HAPPENING IN THIS AREAS?

HOTSPOT AREAS FOR PRIORITIZING PREVENTION STRATEGIES

Take-home Messages

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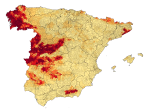
This ecological study showed correlations between age-standardized death rates for certain solid tumors and Radon areas in Spain, notably in **oropharyngeal & urothelial tumors in young females**

Also, a correlation was found between Rn areas and **thoracic malignancies in young females**, a population typically associated with lower cumulative smoking exposure.



This data can provide useful information to **establish priorities** in cancer prevention strategies (radon & other risk factors)

Further **prospective studies** are currently ongoing to explore the role of radon in patients with cancer, particularly for young pop *(BIORADON, MIRROR, EXPOSOME)*

Radon: Impact on patients with lung cancer?

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Grupo de Medioambiente y Cáncer

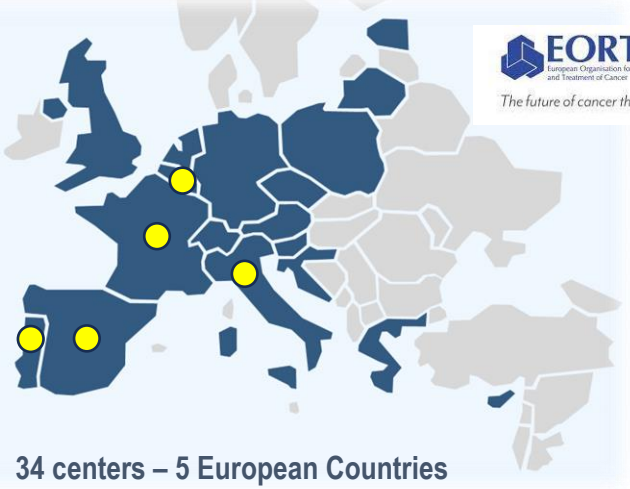
MIRROR

N= 670 patients

14 centers - Spain

BIORADON

N= 975 patients



34 centers – 5 European Countries

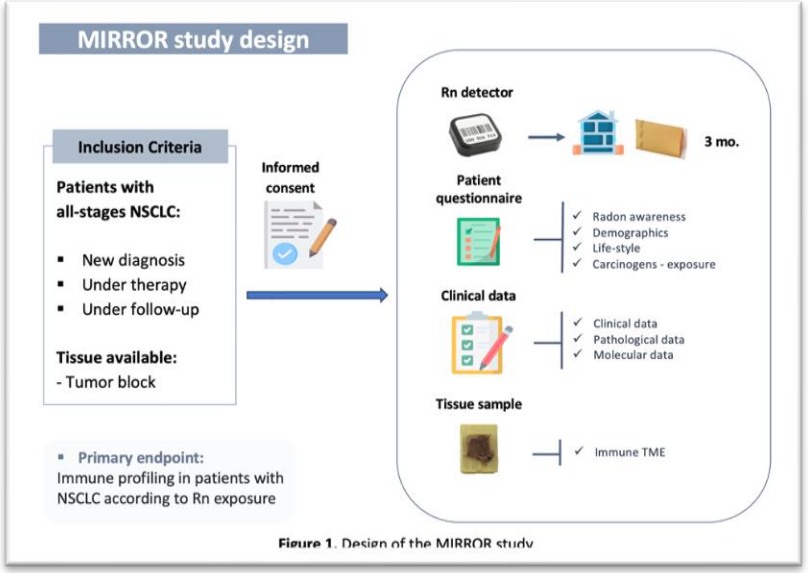
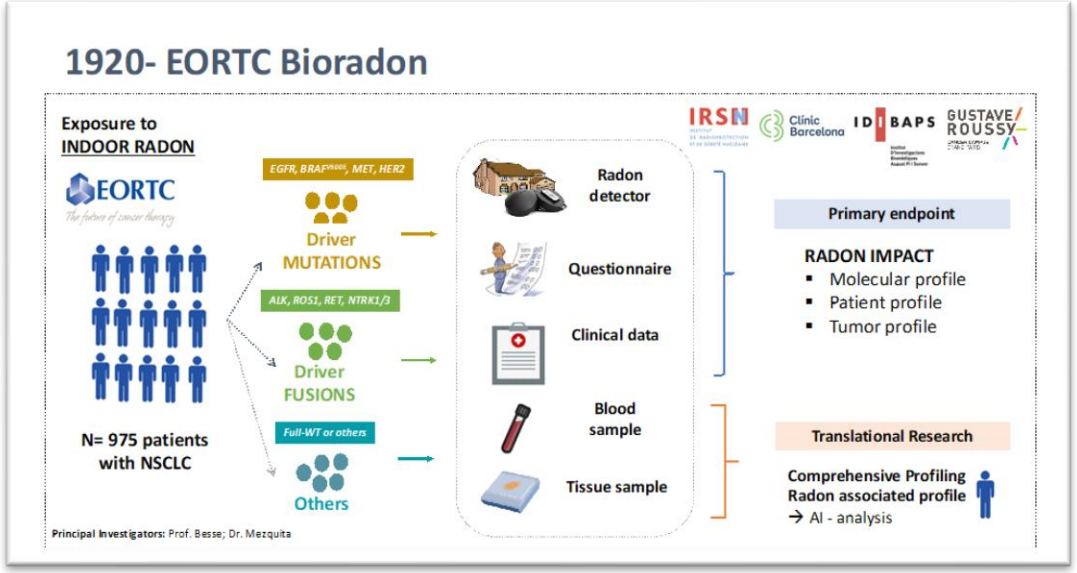
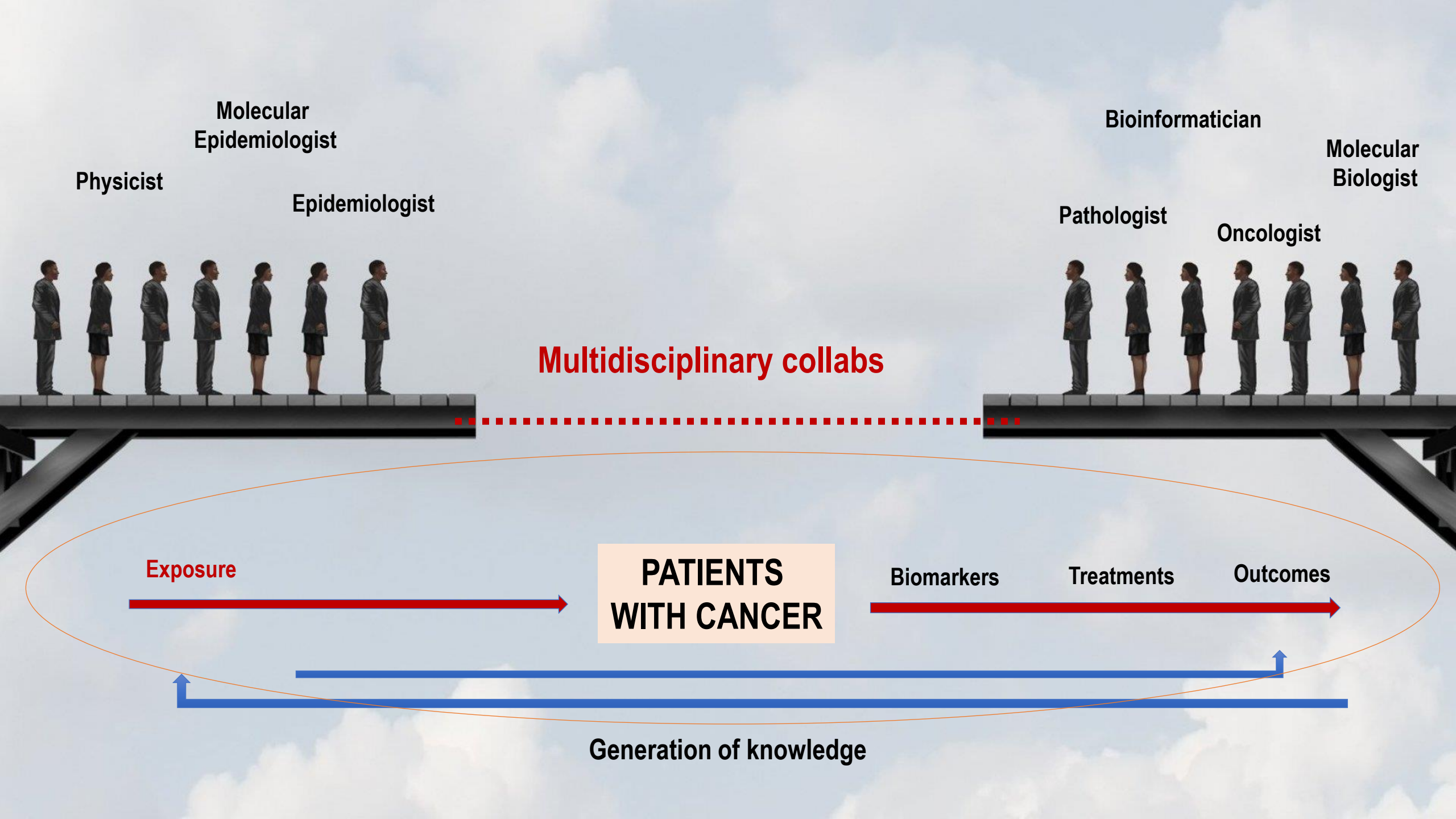


Figure 1. Design of the MIRROR study



Mezquita L, ESMO 2023; García de Herreros M, ESMO 2024, Bernabeu M, SEOM 2024


Molecular Epidemiologist
Physicist
Epidemiologist
Bioinformatician
Molecular Biologist
Pathologist
Oncologist
Multidisciplinary collabs
Exposure
PATIENTS WITH CANCER
Biomarkers
Treatments
Outcomes
Generation of knowledge

Grupo de Medioambiente y Cáncer

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- Miquel Ferriol
- Julieth Mena
- David Delgado
- Laura Alcolea
- Ainara Arcocha
- Giancarlo Castellano
- Cristina Teixidó
- Dr. Juan Carlos Laguna
- Dr. Teresa Gorria
- Dr. Javier Muñoz
- Dr. Carme Crous
- Dr. Alejandro Navarro

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- Prof. Aleix Prat
- Medical Oncology Department
- Thoracic Tumors Group
- Thoracic Tumors Committee
- Molecular Tumor Board (MTB)
- Lab Translational Genomics

RADONORM – BIORADON Group

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- EORTC Bioradon team
- Dr. Maria Gomolka, BfS
- Dr. Sylvie Chevillard, CEA
- Dr. Anna Campalans, CEA
- Dr. Dominique Laurier, IRSN
- All Partners Task 4.5
- Bioradon - European Radon researchers in Spain, Portugal, France, Belgium & Italy

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- Dr. Hugo Arasanz
- Dr. Luis León
- Dr. Patricia Cruz
- Dr. Ruth Álvarez
- Dr. Gustavo Rubio
- Dr. Belen Rubio
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- Dr. Verónica Serrano

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Thank you!

All the PATIENTS, RESEARCHERS & CENTERS participating in this Global Radon – Academic Research

Are you interested on working on this project?

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RadoNorm Managing risks from radon and NORM · EORTC The future of cancer therapy · Gustave Roussy Cancer Campus Grand Paris · IRSN Institut de radioprotection et de sûreté nucléaire · Bundesamt für Strahlenschutz · cea · LUMC Leids Universitair Medisch Centrum · HUN REN · UPC · ISGlobal Barcelona Institute for Global Health · insst Instituto Nacional de Seguridad y Salud en el Trabajo · SEOM Sociedad Española de Oncología Médica · ICAPEM