

IARC Evaluation of the Carcinogenicity of Outdoor Air Pollution

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Evaluation

- Outdoor air pollution is *carcinogenic to humans* (Group 1)

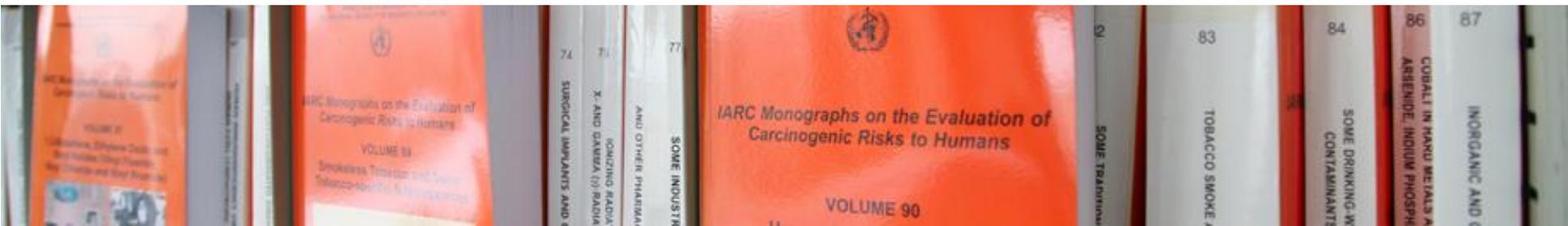
- Particulate matter in outdoor air pollution is *carcinogenic to humans* (Group 1)

Summary: [http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(13\)70487-X/fulltext](http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(13)70487-X/fulltext)

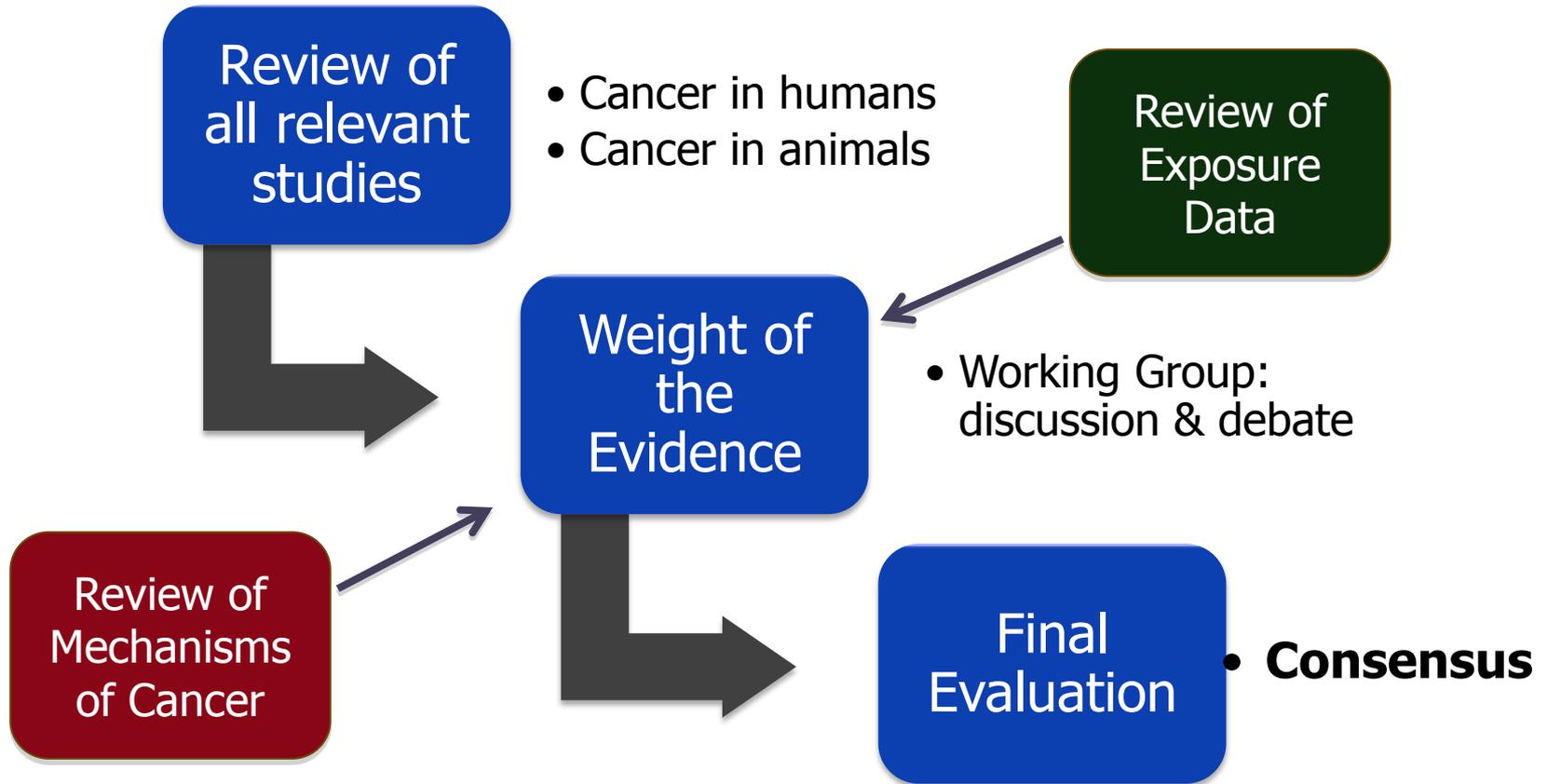
The IARC Monographs

(<http://monographs.iarc.fr/indexfr.php>)

- Evaluate factors capable of causing cancer in humans
 - Environmental & occupational exposures
 - Physical, chemical & biologic agents
 - Lifestyle factors
- “The Encyclopedia of Carcinogens”
- More than 900 agents evaluated since 1971
 - >100 carcinogenic to humans
 - >300 probably or possibly carcinogenic
- National & international health agencies use the Monographs
 - To identify carcinogens
 - To support prevention or regulation



Evaluation in the IARC Monographs



Weight of the Evidence Evaluation

Cancer in humans

- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

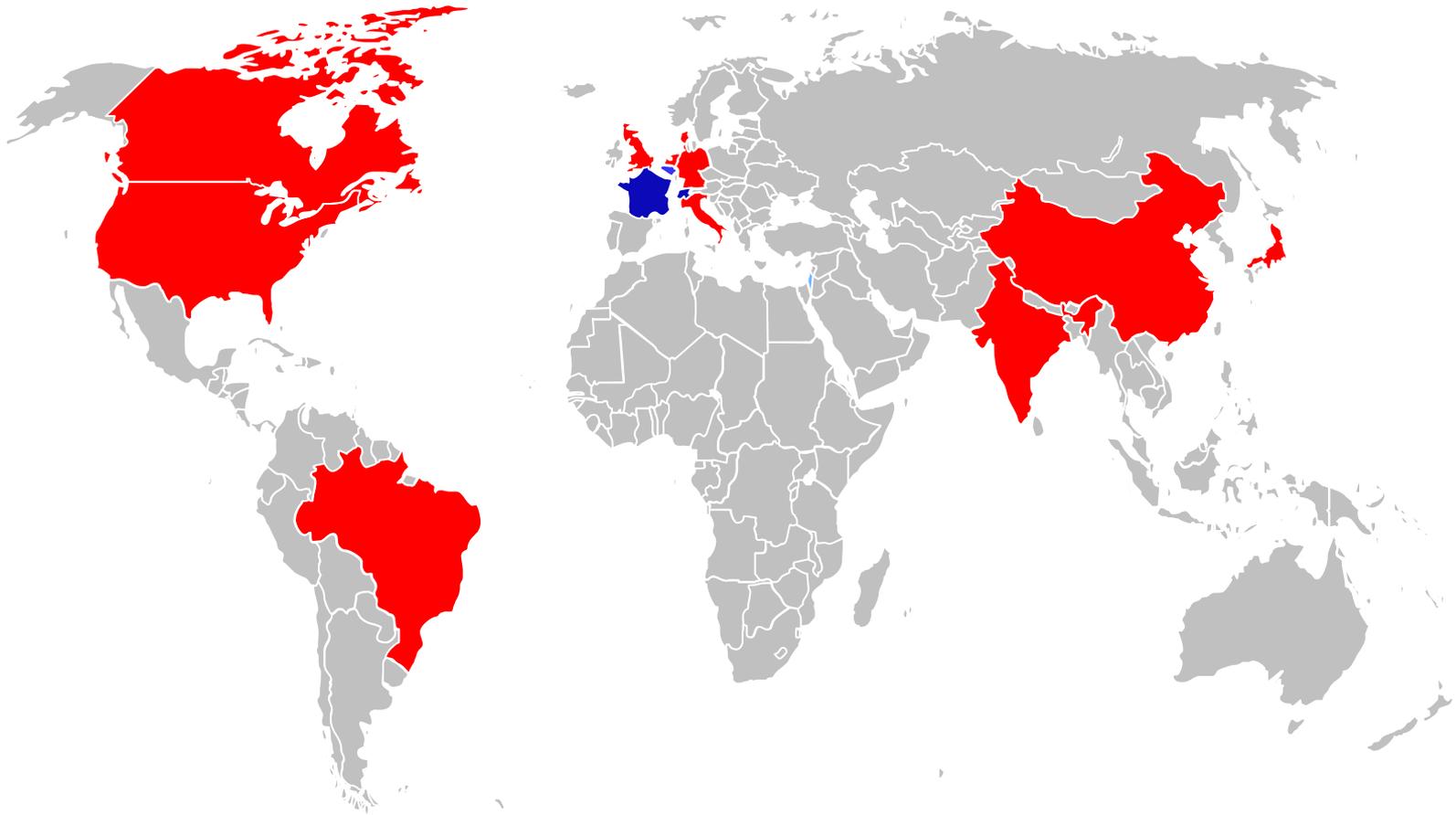
Cancer in animals

- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

Overall Evaluation

1. Carcinogenic to humans
- 2A. Probably carcinogenic
- 2B. Possibly carcinogenic
3. Not classifiable as to carcinogenicity
4. Probably not carcinogenic

Vol. 109: 24 invited experts from 11 countries

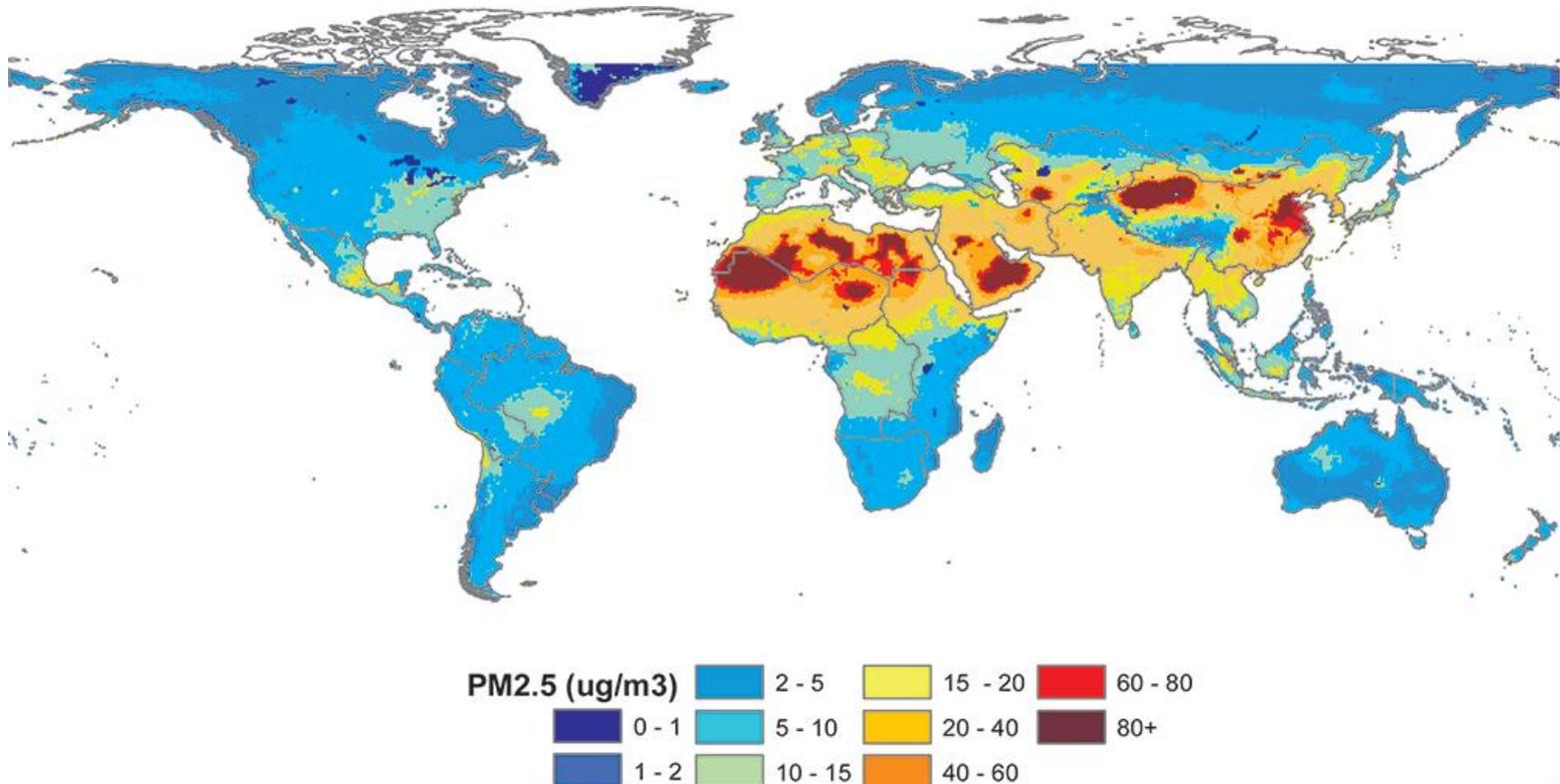


Working Group members



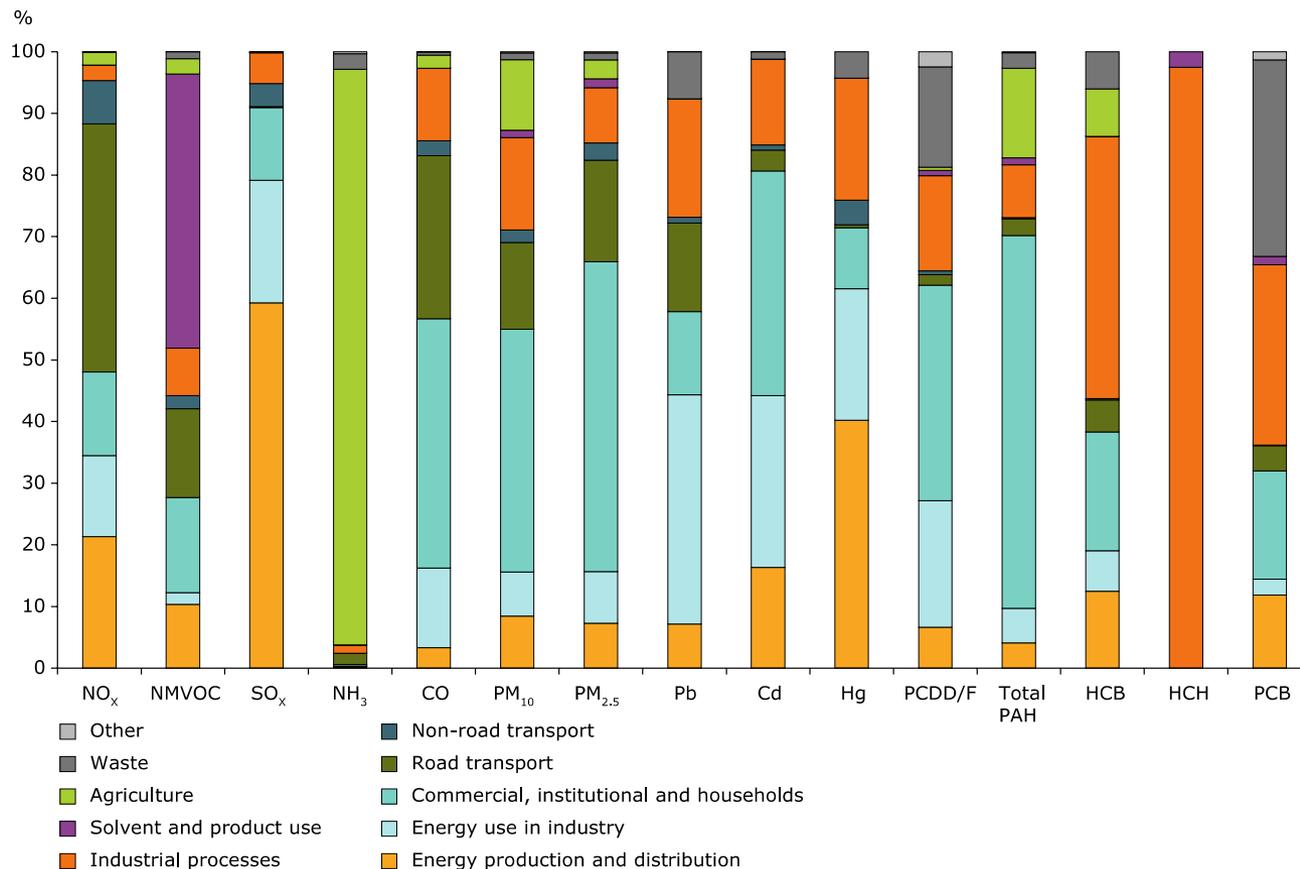
IARC and representatives

Outdoor Air Pollution is Global and Highly Variable



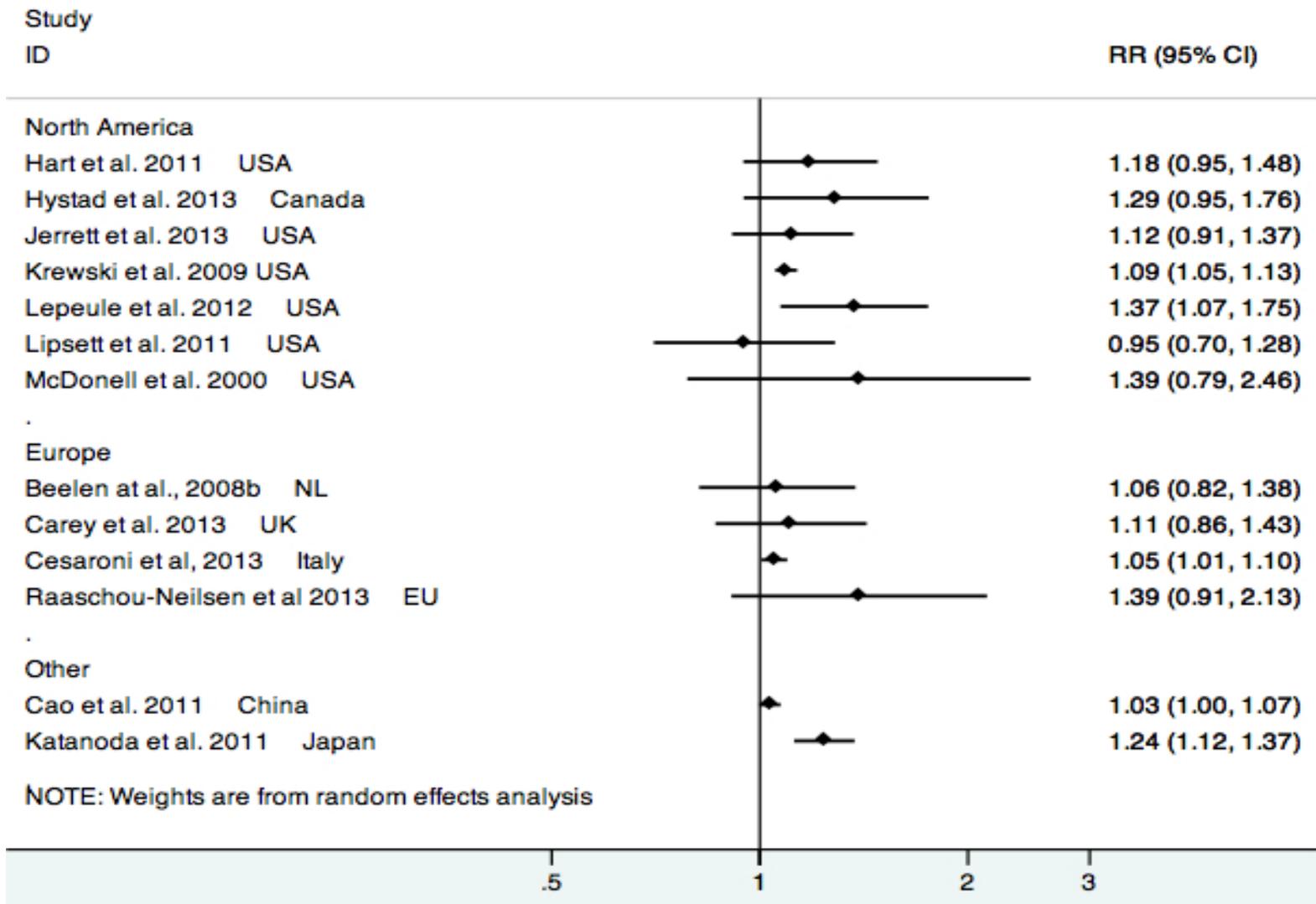
Source: Brauer et al. (2012). Environ Sci Technol 46:652-60

Sources of Principal Air Pollutants, Europe

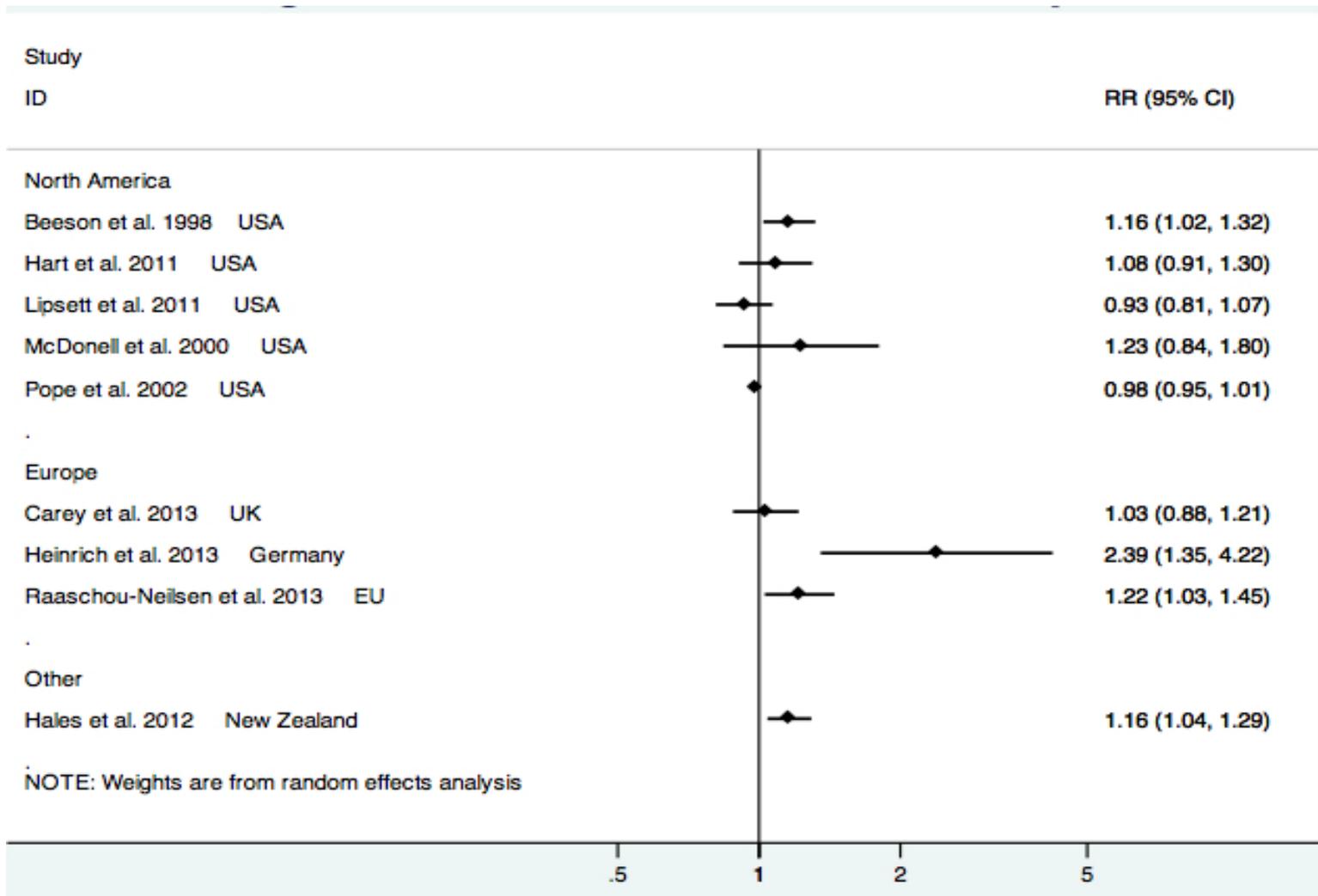


Epidemiologic Studies

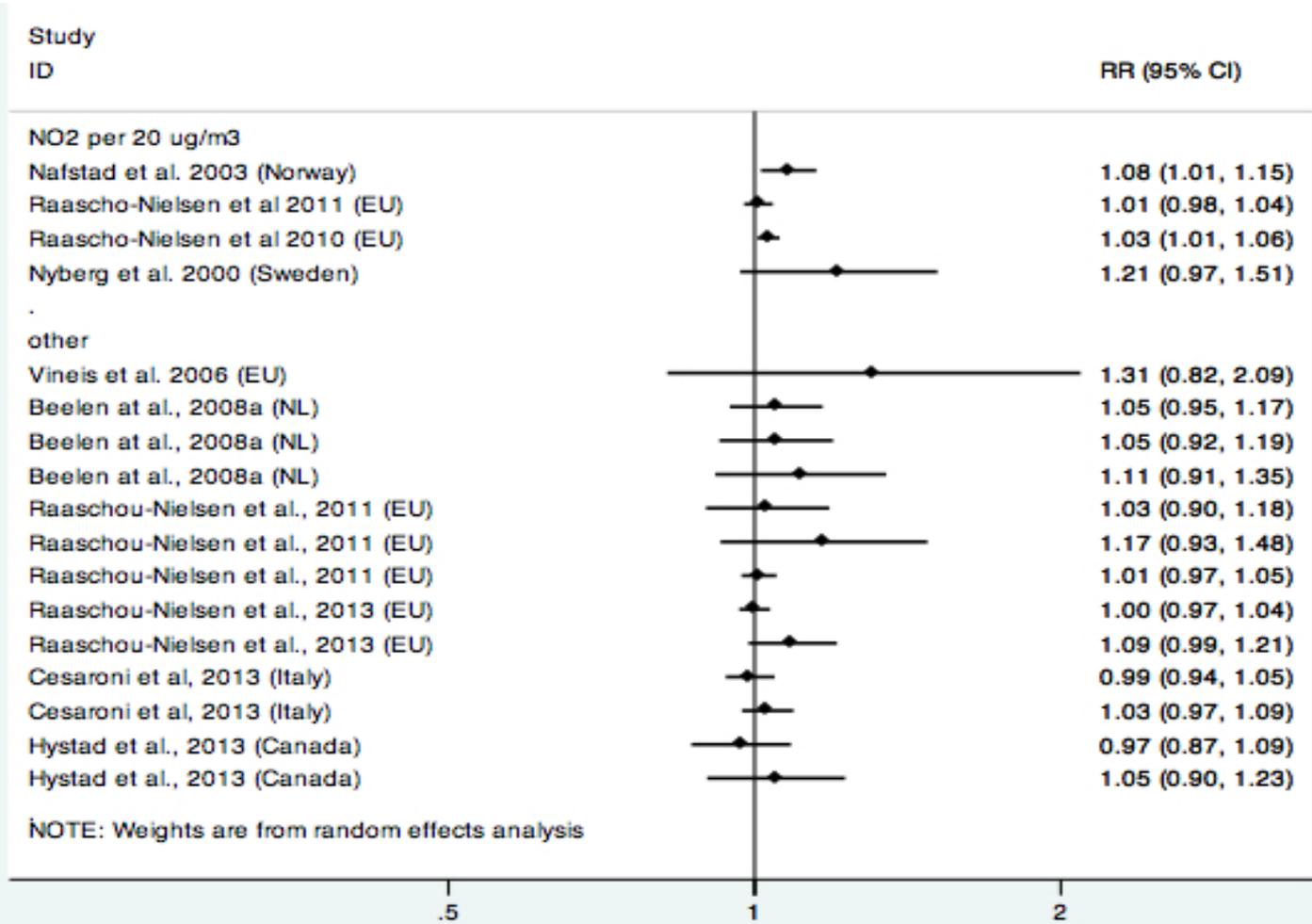
- All available studies of air pollution and cancer were reviewed (100s of studies)
- 14 studies of lung cancer were most informative
 - Cohorts from the the general population in Europe, North America & Asia: millions of people and 1000s of cancer cases observed
 - Quantitative exposure information
 - Control of important confounders (smoking)



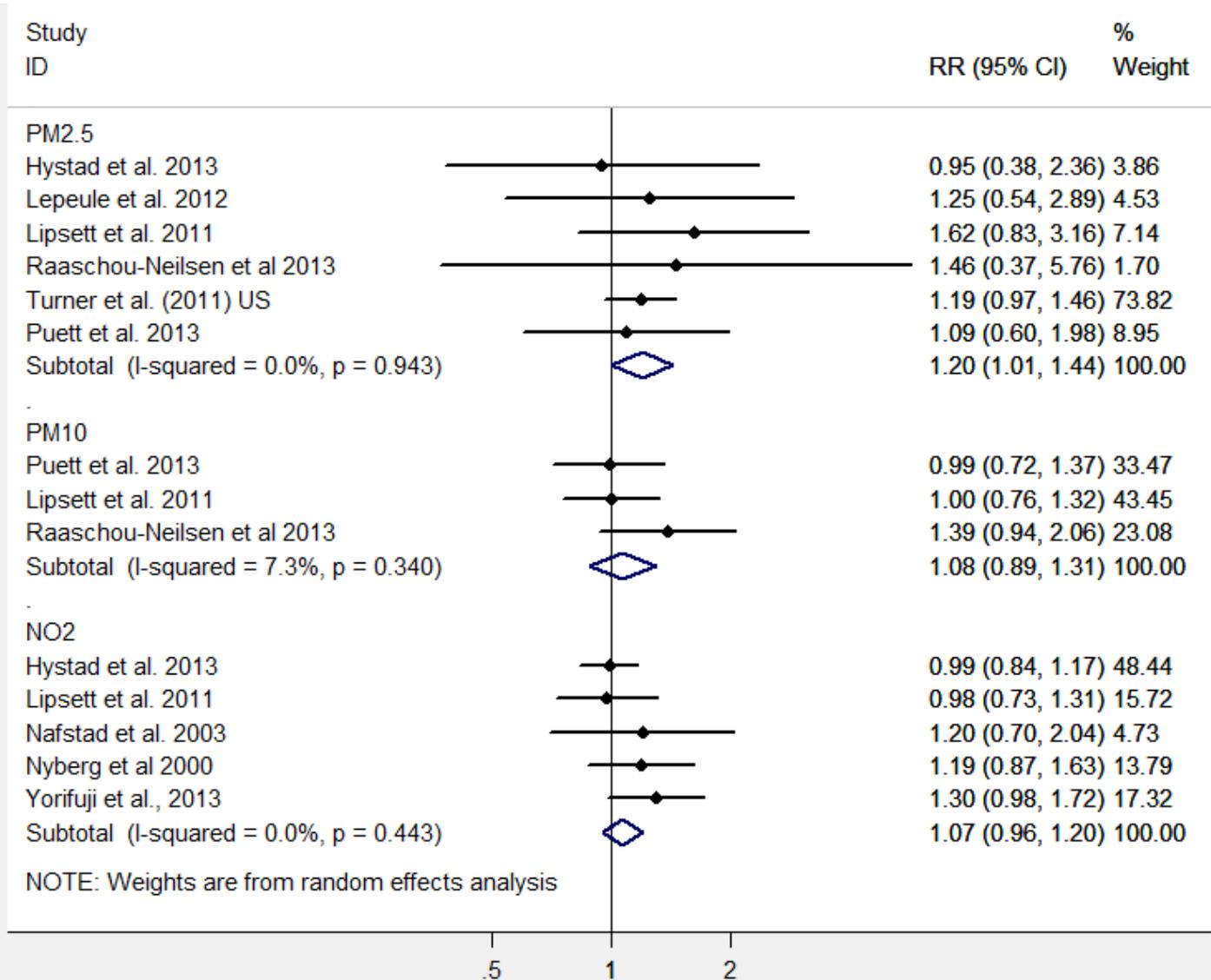
Lung Cancer and PM-2.5 (RR per 10 μ g/m³)



Lung Cancer and PM-10 (RR per 10 μ g/m³)



Lung Cancer and NO₂ or Indicators of Exposure to Traffic



RRs for Lung Cancer and Air Pollution: Non Smokers

Meta-Analysis of Lung Cancer and Particulate Matter

- Statistical analysis combining results from 14 studies in Europe, Asia & North America
- Random effects model
- Meta-RR 1,09 (1,04-1,14) per 10 $\mu\text{g}/\text{m}^{-3}$ $\text{PM}_{2.5}$
- Meta-RR 1,08 (1,00-1,17) per 10 $\mu\text{g}/\text{m}^{-3}$ PM_{10}
- RR not substantially affected by gender, smoking status, or social class

(Hamra et al., in press)

Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE)

Ole Raaschou-Nielsen, Zorana J Andersen, Rob Beelen, Evangelia Samoli, Massimo Stafoggia, Gudrun Weinmayr, Barbara Hoffmann, Paul Fischer,

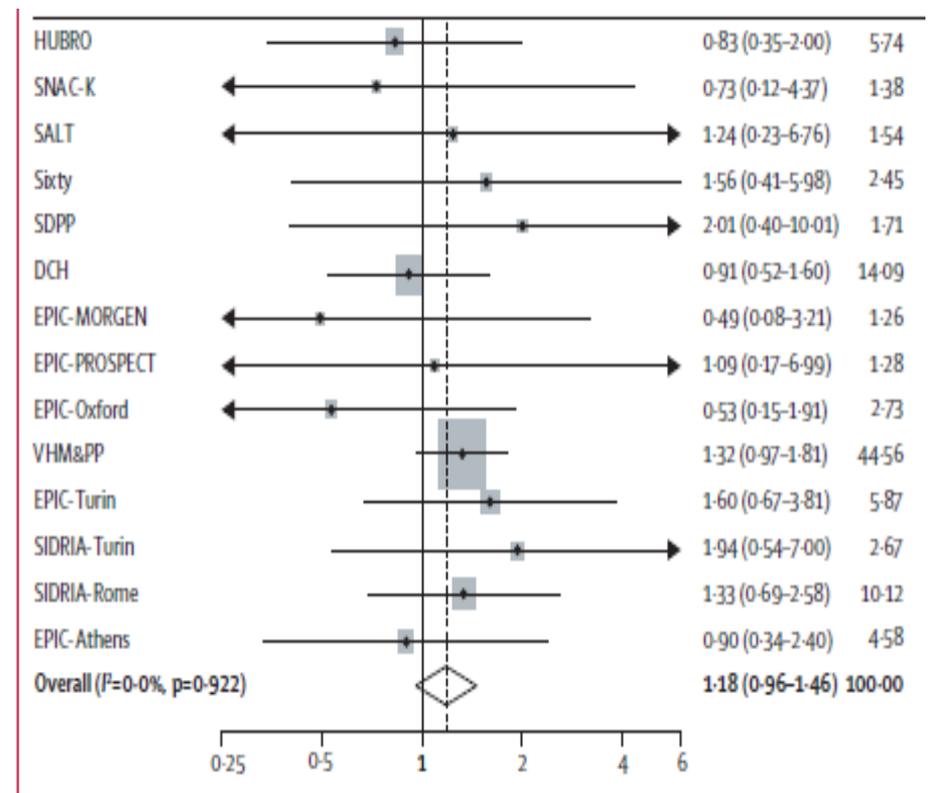
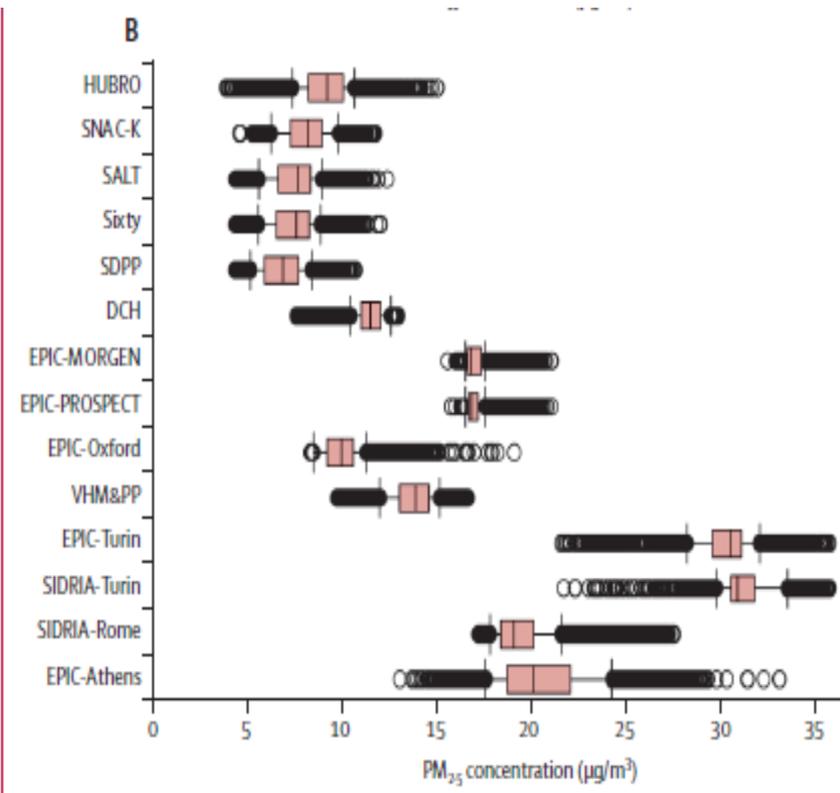


Figure 2: Distribution of particulate matter air pollution at participant addresses in each cohort

Figure 3: Risk for lung cancer according to concentration of particulate matter in each cohort study

Lung cancer risk per 5 µg/m³

Summary – Human Studies

- Lung cancer is positively associated with indicators of air pollution in nearly all studies
- The associations with particulate matter are the most consistent
- Risk increases about 10% per $10 \mu\text{g}/\text{m}^{-3}$ of PM
- Associations are not explained by smoking or other confounders
- Limited evidence of an association with bladder cancer
- Inadequate data for other cancers (breast, leukemia, childhood cancer)

Evaluation: Cancer in humans

- There is *sufficient evidence* in humans for the carcinogenicity of **outdoor air pollution**. Outdoor air pollution causes *cancer of the lung*. A positive association has been observed for cancer of the urinary bladder.
- There is *sufficient evidence* in humans for the carcinogenicity of **particulate matter in outdoor air pollution**. Particulate matter in outdoor air pollution causes *cancer of the lung*.

Cancer in experimental animals

There is *sufficient evidence* in experimental animals for the carcinogenicity of:

- **Organic solvent-extracted material from particles collected from outdoor air pollution**
- **Particulate matter in outdoor air pollution**
 - Solvent-extracted materials collected from outdoor air
 - Diesel engine exhaust
- **Outdoor air pollution**
 - Promotion of tumours in animals exposed to polluted outdoor air
 - Updating and confirming previous IARC evaluations, including: diesel engine exhaust, coal combustion, wood combustion

Other relevant data

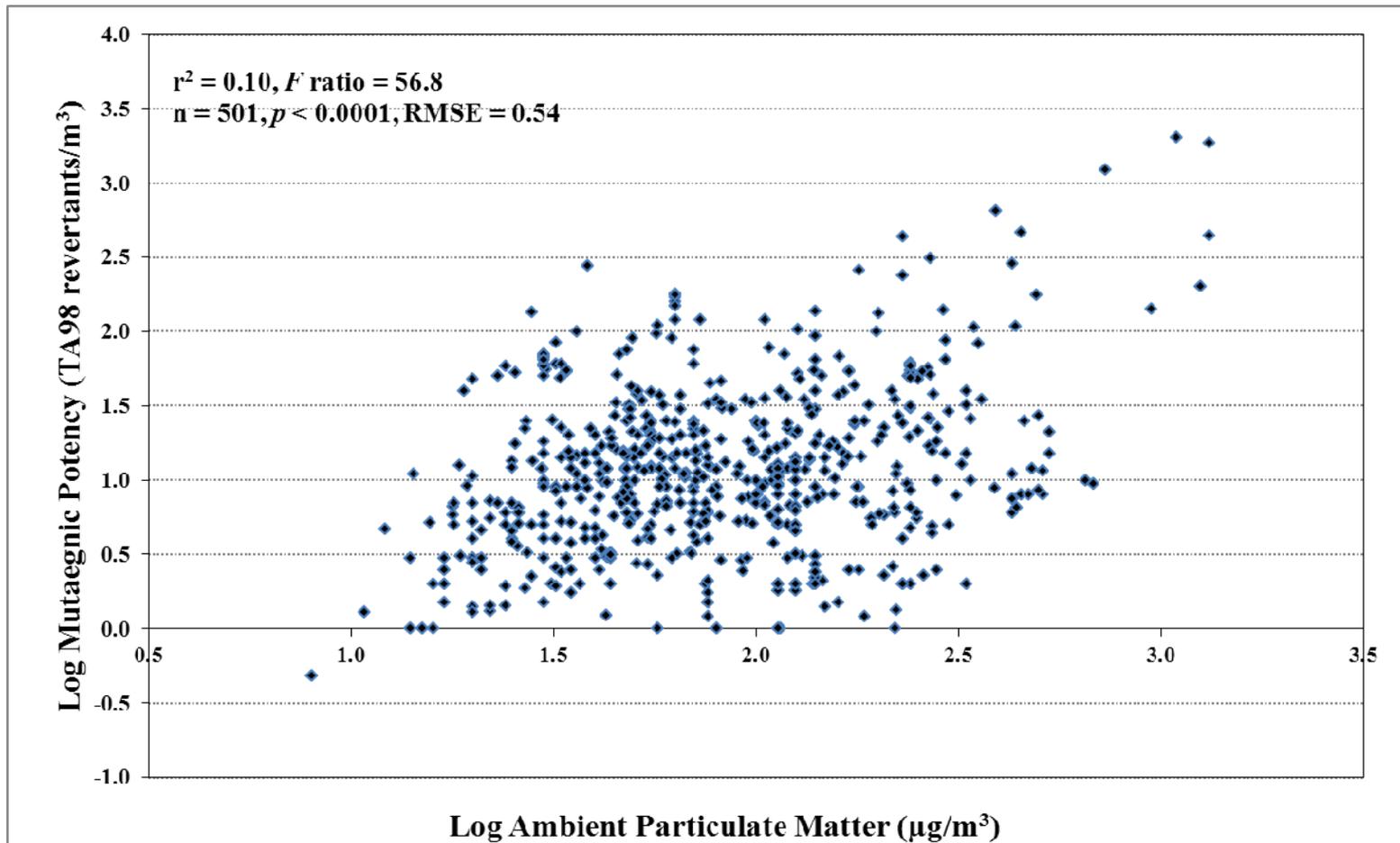
- Review of 100s of studies of mechanisms of cancer in exposed humans, animals and experimental systems.
- **Strong mechanistic support:** Exposures to outdoor air pollution, or particulate matter in polluted outdoor air, are associated with increases in genetic damage that have been shown to be predictive of cancer in humans.

Other relevant data

Key findings:

- Atmospheric mutagenic potency is quantitatively related to levels of atmospheric particulate matter
- Cytogenetic damage, DNA damage and mutations in animals, birds and plants exposed to outdoor air pollution.
- Altered expression of genes involved in DNA damage and repair, cell cycle control, inflammation, and oxidative stress response in people occupationally or environmentally exposed to outdoor air pollution
- Increased frequencies of chromosome aberrations and micronuclei in exposed outdoor workers

Mutagenic potency of PM extracts and atmospheric PM concentration in 26 countries



Cytogenetic effects in humans exposed to polluted outdoor air

Table 1. Cytogenetic effects in humans associated with exposure to polluted outdoor air in China

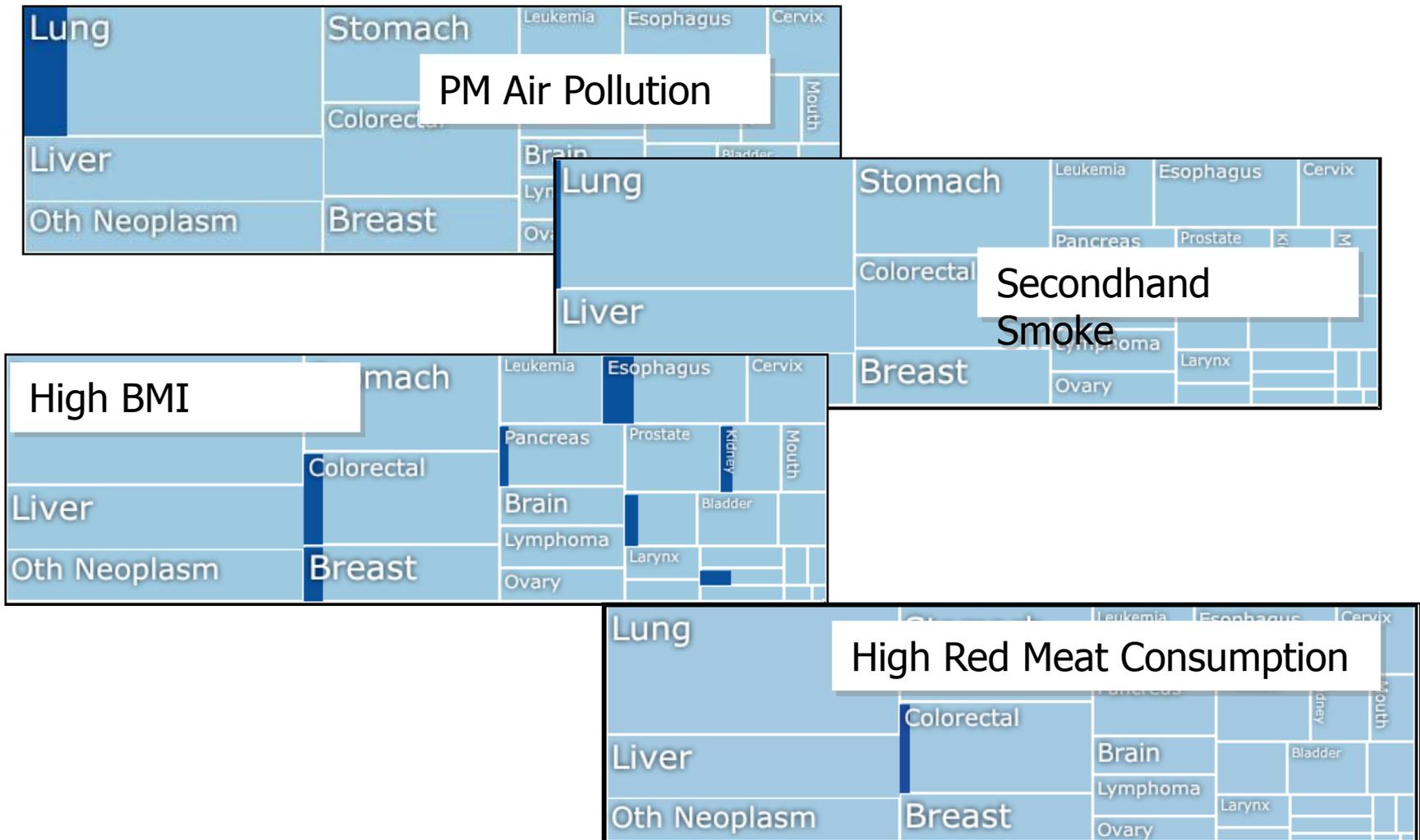
Reference	Endpoint	Control subjects	Results	Exposed subjects	Results	P
Chen <i>et al.</i> 1999 ^[27]	CA ^a	Indoor police officers in Hebi, Henan (<i>n</i> = 30)	0.40%	Traffic policemen exposed to outdoor air pollution from coal combustion and automobile exhaust in Hebi, Henan (<i>n</i> = 45)	0.98%	<0.01
Cui <i>et al.</i> 1991 ^[28]	CA ^a	Chorionic villi in pregnant women in Dalian, Liaoning (<i>n</i> = 827)	0.11%	Chorionic villi in pregnant women in Shenyang, Liaoning (<i>n</i> = 811)	1.66%	<0.01
				Chorionic villi in pregnant women in Zhengzhou (<i>n</i> = 1,060)	0.52%	<0.01
Zhao <i>et al.</i> 1998 ^[29]	MN ^b	Household register police officers in Lanzhou, Gansu (<i>n</i> = 34)	3.22±1.31	Traffic policemen exposed to outdoor air pollution from automobile exhaust in Lanzhou, Gansu (<i>n</i> = 67)	5.72±2.57	<0.05
	SCE ^c	Household register police officers in Lanzhou, Gansu (<i>n</i> = 34)	3.73±1.51	Traffic policemen exposed to outdoor air pollution from automobile exhaust in Lanzhou, Gansu (<i>n</i> = 67)	8.81±1.83	<0.05
Bai <i>et al.</i> 2005 ^[30]	MN ^d	Indoor police officers in Tangshan, Hebei (<i>n</i> = 49)	1.97±0.21	Traffic policemen exposed to outdoor air pollution from automobile exhaust at crossroads in Tangshan, Hebei (<i>n</i> = 65)	4.27±0.68	<0.05
	SCE ^c	Indoor police officers in Tangshan, Hebei (<i>n</i> = 49)	2.69±0.35	Traffic policemen exposed to outdoor air pollution from automobile exhaust at crossroads in Tangshan, Hebei (<i>n</i> = 65)	4.32±0.58	<0.05
Peng <i>et al.</i> 1995 ^[31]	MN ^b	Botanical garden officers, Shanghai (<i>n</i> = 36)	0.69±0.06	Bus drivers or bus ticket officers on route through DaPu tunnel in Shanghai (<i>n</i> = 40)	1.28±1.02	<0.01
	SCE ^c	Botanical garden officers, Shanghai (<i>n</i> = 36)	4.50±0.99	Bus drivers or bus ticket officers on route through DaPu tunnel in Shanghai (<i>n</i> = 40)	5.94±1.23	<0.01
Ishikawa <i>et al.</i> 2006 ^[32]	MN ^d	Female residents in rural areas in Shenyang, Liaoning (<i>n</i> = 63)	1.02	Female residents in urban and industrial areas in Shenyang, Liaoning (<i>n</i> = 66)	1.56	<0.05

CA, chromosomal aberration; MN, micronucleus; SCE, sister chromatid exchange. ^aThe results are expressed as the percentage of cells with CA, with 100 metaphases examined for each subject. ^bThe results are expressed as the number of MNs per 1,000 cells. ^cThe results are expressed as the number of SCEs per cell. ^dThe results are expressed as the number of MN-containing cells per 1,000 binucleated cells.

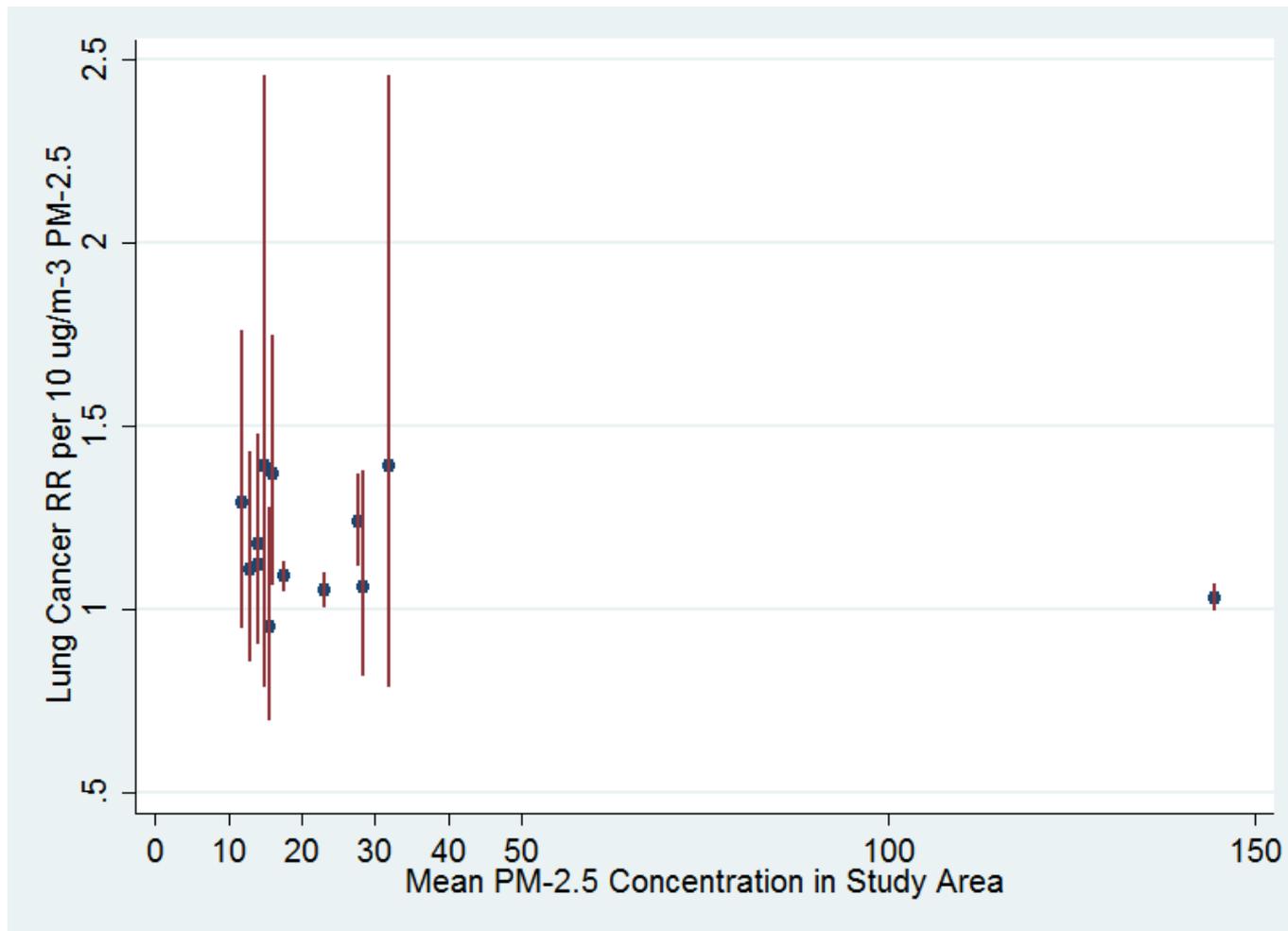
Importance of the Evaluation

- The evaluation of outdoor air pollution concerns the complex mixture of pollutants from all sources
- The evaluation of particulate matter includes all sizes and sources of particles, primary and secondary
- The monographs do not formally quantify risk, but studies indicate risks comparable to passive smoking at levels of air pollution existing in Europe
- Independent data indicate 223 000 lung cancer deaths worldwide (15% of all lung cancer) are related to air pollution

Attributable Cancer Deaths in Comparison



Ranges of Lung Cancer RR and Exposure Concentration for Studies of PM-2.5



Conclusions

- Millions of people are exposed to air pollution at high levels, but the dimensions of the problem are not yet fully known
- Nevertheless, classifying air pollution as a carcinogen is an important step forward
- Effective measures for reducing air pollution are available; most require collective response
- The IARC evaluation of air pollution is a call to take action