

London Fog

How Epidemiology and Pathology Support Evidence of Health Effects

Aims for today

- Share some history of scientific discoveries on air pollution and human health
- Introduce you to some basic epidemiological study methods
- Show how evidence from epidemiology and toxicology can complement each other

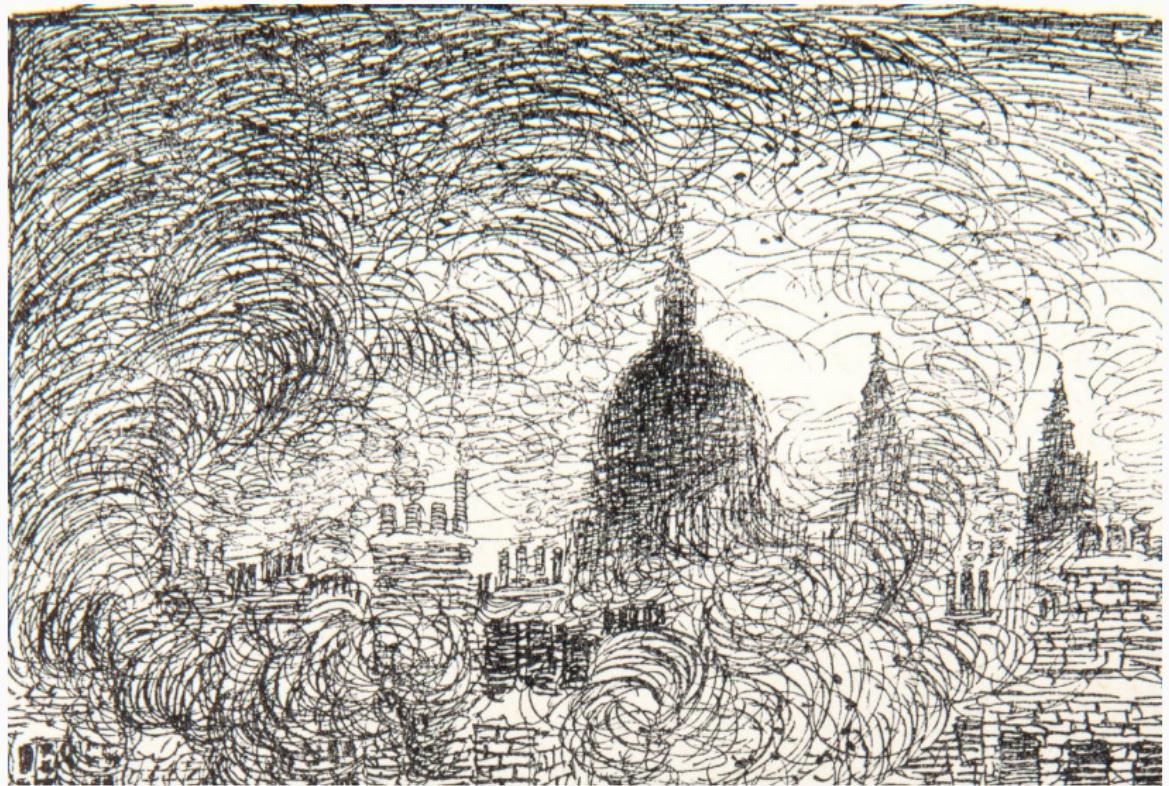
London Fog

London Fog

"Fog everywhere. Fog up the river where it flows among green airs and meadows; fog down the river, where it rolls defiled among the tiers of shipping, and the waterside pollutions of a great (and dirty) city. . . . Chance people on the bridges peeping over the parapets into a nether sky of fog, with fog all round them, as if they were up in a balloon and hanging in the misty clouds."

—Charles Dickens

London Fog



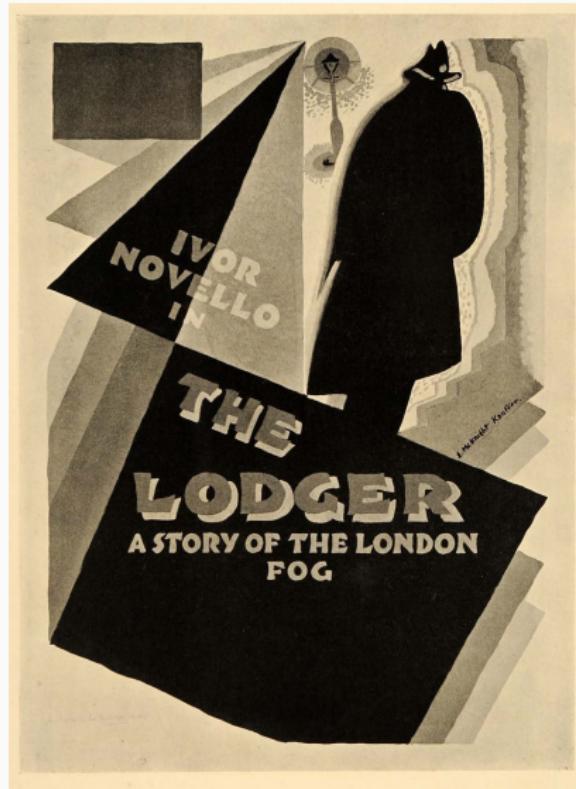
Arthur Rackham illustration for Charles Dickens' *A Christmas Carol*

London Fog



Claude Monet, *Parliament: Sunlight in the Fog*

London Fog



Alfred Hitchcock, poster for *The Lodger*

London Fog



HB1 - 21c

John Barrymore as *Sherlock Holmes*

The case of the fatal fog—Meuse Valley, 1930

Meuse Valley, Belgium



Source: Marc Ryckaert

Meuse Valley fog



Source: Albert Humblet collection

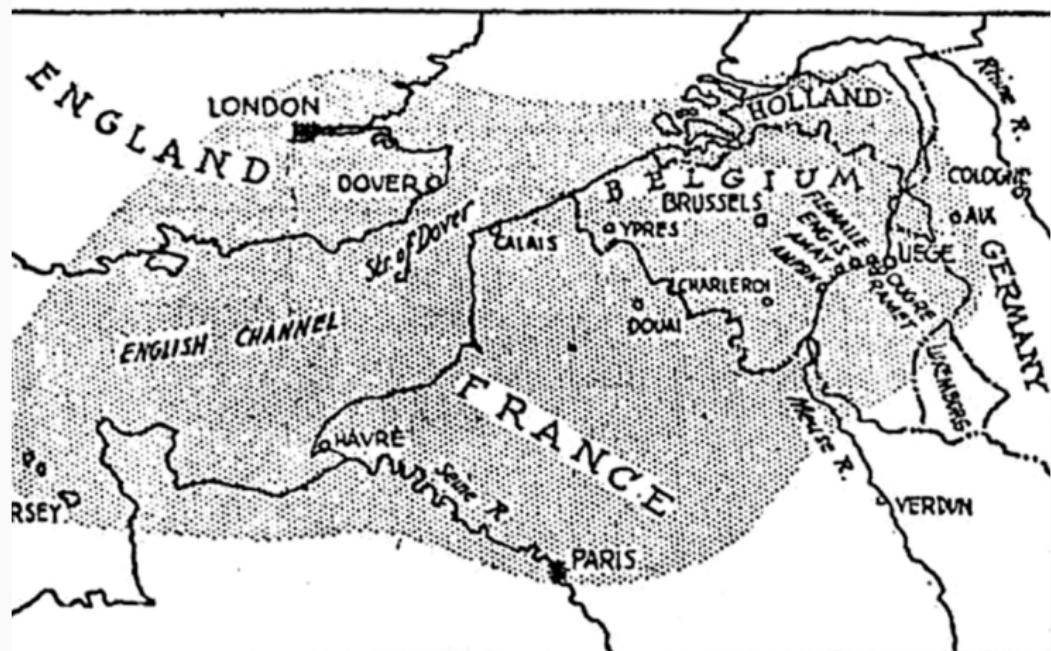
Meuse Valley fog of 1930

- December 1–5, 1930
- More than 60 deaths (10-fold increase from normal)
- Symptoms included: coughing fits, laryngeal irritation, shortness of breath, chest pain, rapid breathing, cyanosis, nausea, vomiting
- Most affected: “people who were elderly, asthmatic, debilitated, or those with cardiac disease”

Source: Nemery et al., 2001. The Meuse Valley fog of 1930: an air pollution disaster. *The Lancet*

Meuse Valley—Killer on the loose

"Poison Fog" Terrorizes Northwestern Europe



Source: *Brussels Times*

Meuse Valley—Initial theories

- War gases
- Toxic sand from the Sahara desert
- Toxic gases from polluted soil

Source: Nemery et al., 2001. The Meuse Valley fog of 1930: an air pollution disaster. *The Lancet*

Meuse Valley—Figuring out what happened

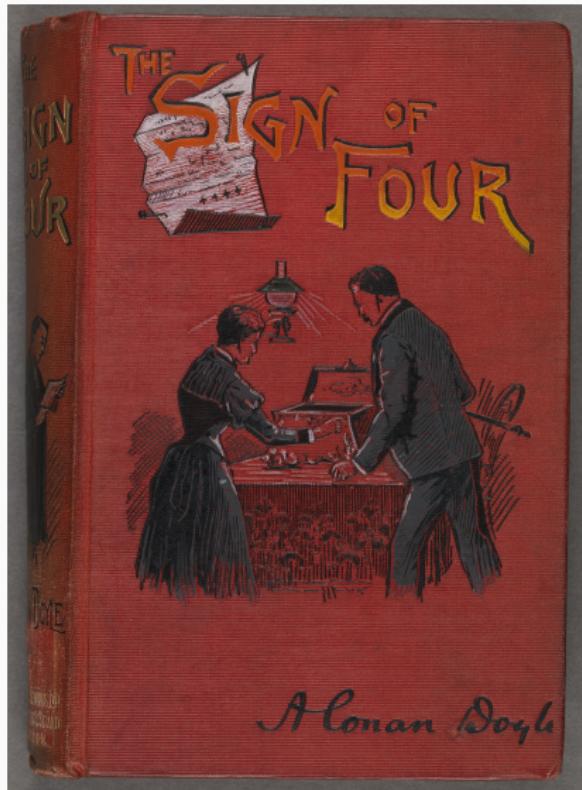
- Report commissioned, presented to Royal Academy of Medicine of Belgium in 1931
- Committee included experts on forensics, toxicology, meteorology, pathological anatomy, and industrial chemistry

Source: Nemery et al., 2001. The Meuse Valley fog of 1930: an air pollution disaster. *The Lancet*

Meuse Valley

"When you have eliminated the impossible, whatever remains, however improbable, must be the truth."

—*The Sign of the Four*, Arthur Conan Doyle



Meuse Valley

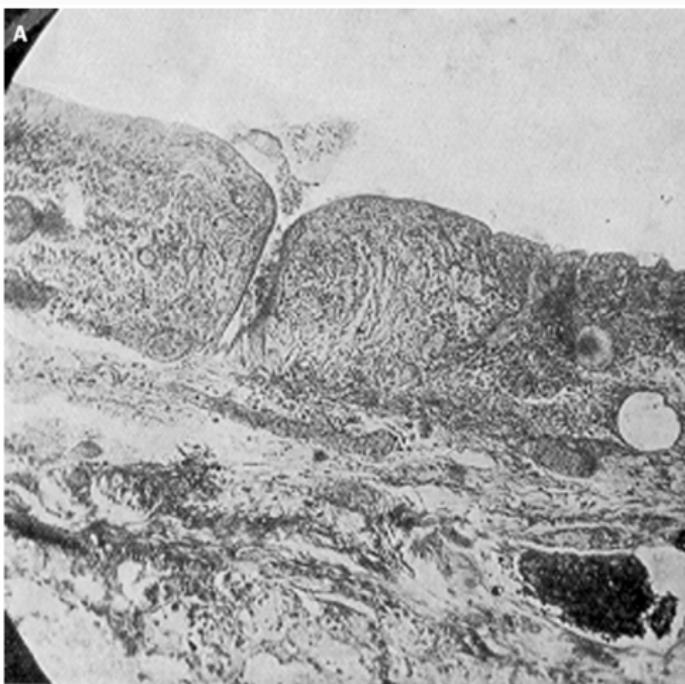
[Investigators] ruled out the low temperature and the density of the fog, since similar weather conditions had prevailed over large parts of Belgium. Respiratory infections were also excluded, mainly on clinical grounds."

—Nemery et al., 2001

Evidence from necropsies

"In all [10] necropsies, there was 'congestion of tracheal mucosa and large bronchi—sometimes with an exudate of mucosa and fibrin—and areas of epithelial loss, capillary dilation of the dermis, and a slight leucocyte exudate'."

—Nemery et al., 2001



Meuse Valley

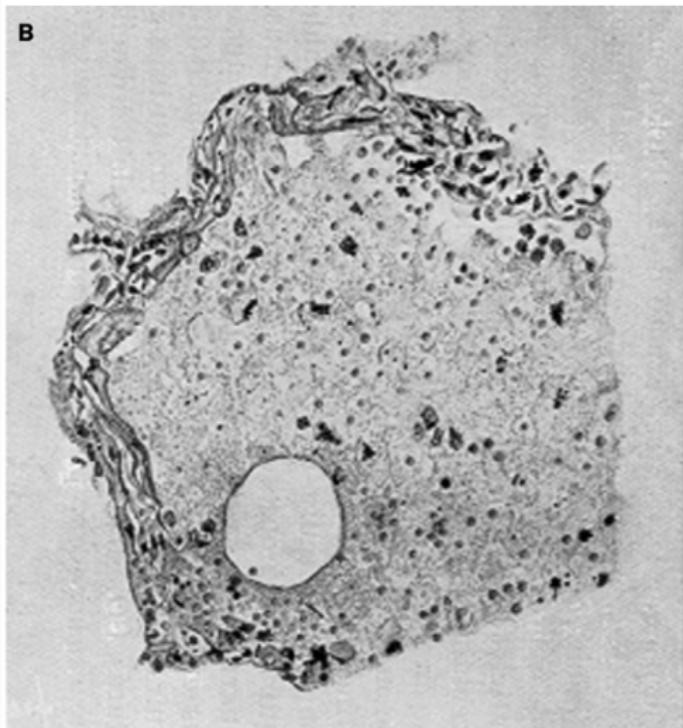
"Lack of oxygen was dismissed as the cause of the victims' suffocation. However, 'the diffuse superficial mucosal congestion that occurred throughout the respiratory tract down to the bronchioles and lung parenchyma . . . could be attributable to fine irritant particles.' "

—Nemery et al. 2001

Evidence from necropsies

"In lung parenchyma, 'there were foci of haemorrhage next to areas of moderate oedema and desquamations of alveolar epithelium.' Pure carbon dust particles of 0.5–1.35 micrometer diameter were seen free within the alveoli or engulfed in polynuclear leucocytes."

—Nemery et al., 2001



Meuse Valley

"The free or phagocytosed particles in alveoli suggested that they had been inhaled a short time before death. However, carbon particles should have been innocuous, unless they had adsorbed irritant acids. The report writers thus postulated that: 'fine soot particles, onto which irritant gases had been adsorbed, had a major role in the noxiousness of the fog.' "

—Nemery et al. 2001

Meuse Valley, geographic evidence

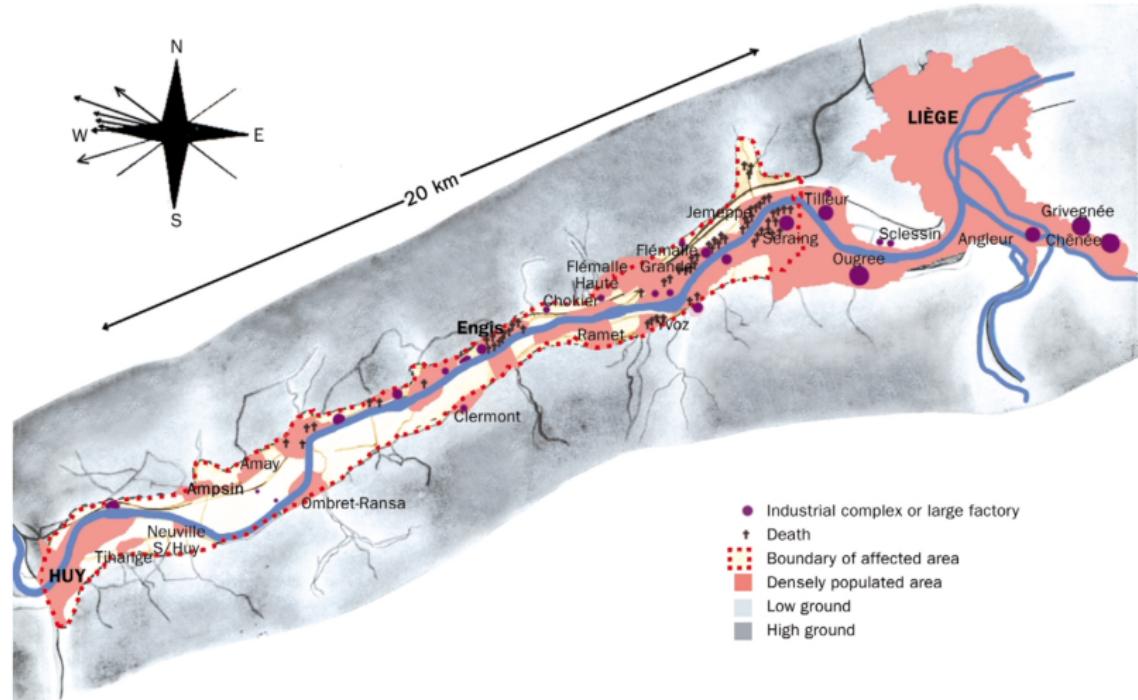


Figure 1: Map of the Meuse Valley between Liège and Huy, indicating the fog-covered area and location of fatalities and factories
Reproduced and modified from figure 1 of Firket and colleagues' report.¹⁰

Meuse Valley

"After a process of successive elimination, the commission concluded 'that the sulphur produced by coal burning has had a deleterious effect, either as sulphurous anhydride or acid, or as sulphuric acid; the production of which was made possible by unusual weather conditions.' "

—Nemery et al. 2001

Meuse Valley legacy

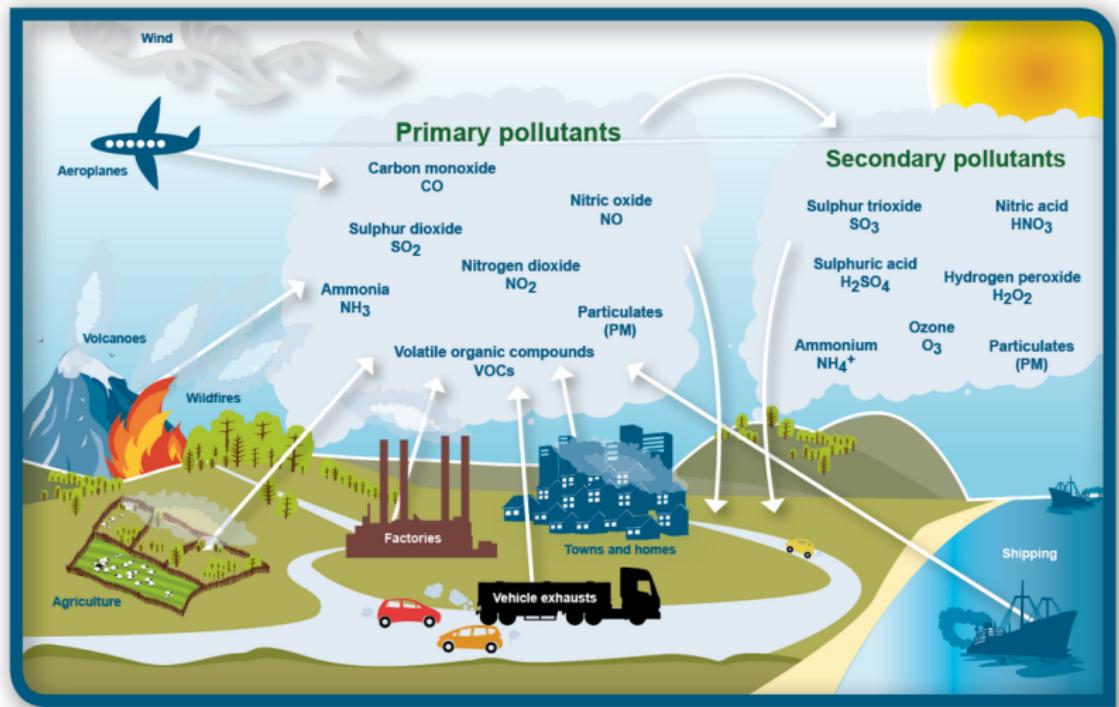
“The Meuse fog disaster provided incontrovertible evidence that air pollution could kill and therefore it attracted considerable attention from the scientific community.”

“A weak aspect of the study was its formal epidemiological methods. . . No graphs were done or statistical tests done.”

—Nemery et al. 2001

Why was the fog so bad?

Air pollution sources



Source:

<https://www.mrgscience.com/ess-topic-63-photochemical-smog.html>

Smog formation—Meuse Valley

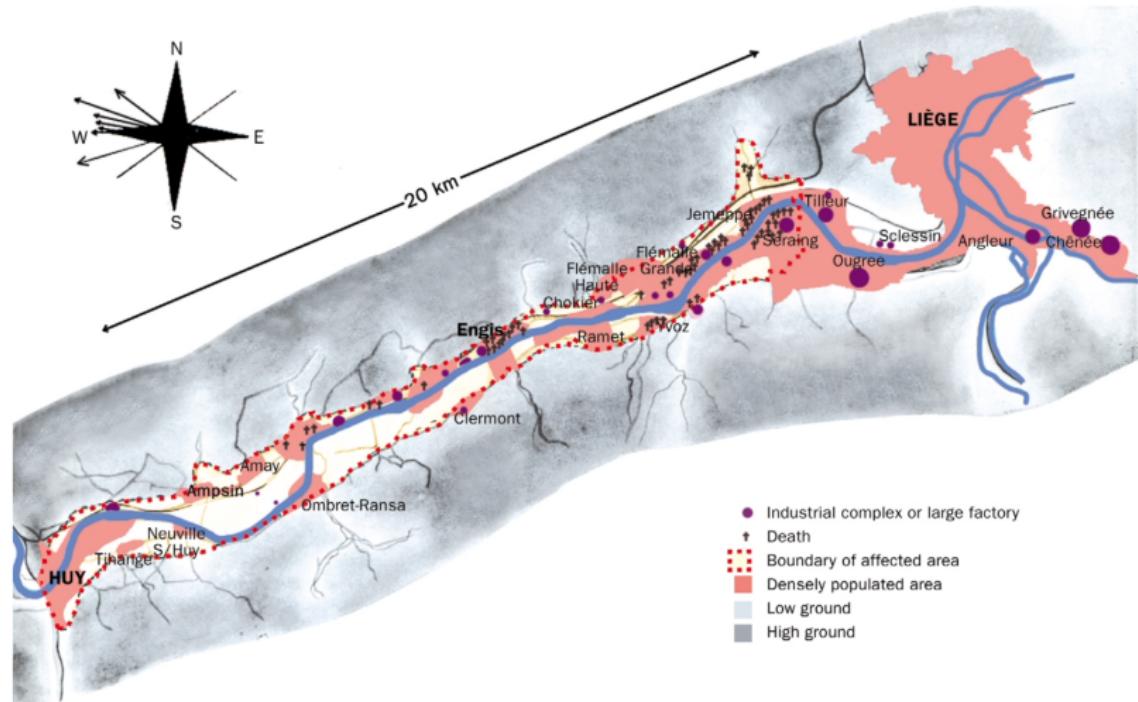
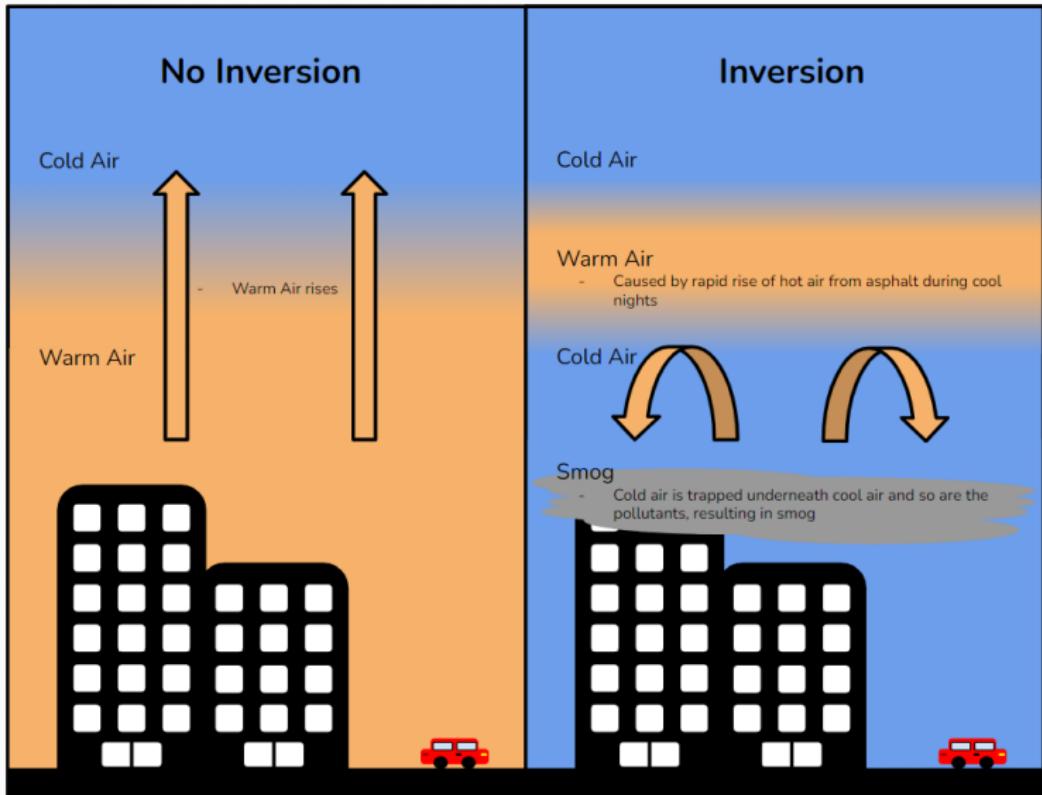


Figure 1: Map of the Meuse Valley between Liège and Huy, indicating the fog-covered area and location of fatalities and factories
Reproduced and modified from figure 1 of Firket and colleagues' report.¹⁰

Temperature inversion



Source: Tyler Chow

Temperature inversion—Lake District, England



Source: Penny Johnson

Temperature inversion—Lochcarron, Scotland



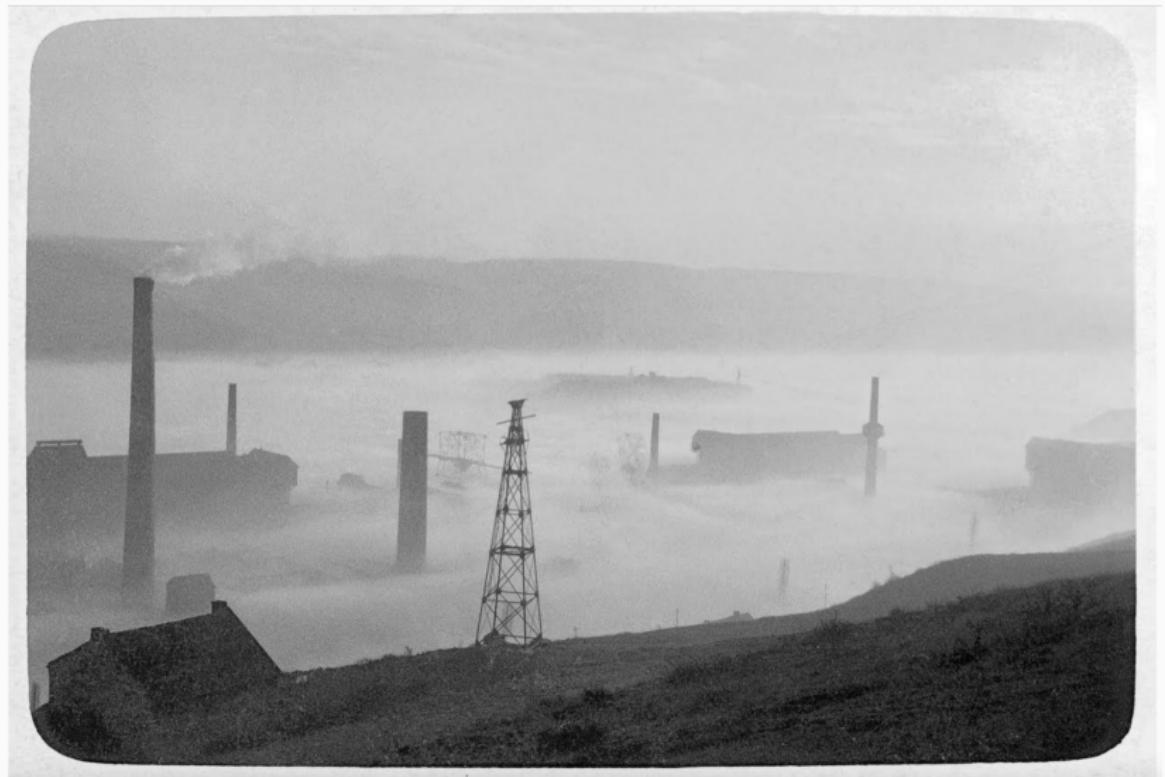
Source: S/V Moonrise

Temperature inversion—Almaty, Kazakhstan



Source: Igors Jefimovs

Smog formation—Meuse Valley



Source: Albert Humblet collection

The return of the sinister smog—London, 1952

Smog formation—London



Source: Historic England Archive

Smog formation—London



Source: Alan Farrow

Great Smog of 1952



Source: Keystone via Getty Images

Great Smog of 1952



Public Domain

The Crown, “Act of God”, Season 1 Episode 4



Source: Netflix

Great Smog of 1952

- December 5–9, 1952
- Visibility below 10 meters (33 feet)
- Birds flew into buildings
- Cars crashed
- People drowned in the Thames River
- Couldn't see across a ward indoors in a hospital

Source: Polivka, 2018. The Great London Smog of 1952. *American Journal of Nursing*

Great Smog of 1952

- Peak sulphur dioxide concentration of 4,000 micrograms per cubic meter
- 4,000 immediate estimated deaths
- Doubling of sickness claims
- Substantial increase in hospitalizations
- Susceptible populations: older adults (65 years and older), young children

Source: Godlee, 1991. Air pollution: I—From pea souper to photochemical smog. *BMJ*

Great Smog of 1952

"The smog event of 1952 was, in terms of human health effects, the most calamitous of the century. It is the sentinel event of the century linking PM exposure to excess mortality and morbidity."

—Hunt et al., 2003

Missing information

"The 1952 smog stimulated extensive expansion of aerosol sampling in London and elsewhere, but actual sampling of the PM comprising the December 1952 aerosol was minimal, and to our knowledge no archival samples are available for analysis using modern techniques."

—Hunt et al., 2003

Missing information

“... by characterizing the form and composition of the PM ... we might obtain otherwise unavailable information relevant to exposures related to the high mortality observed.”

—Hunt et al., 2003

Great Smog of 1952

"We consider it unlikely that London residents were exposed to some new PM source during the smog event; rather, they were subject to an increased dose of the typical exposure aerosol. However, increased levels of diesel PM were probably present in the London aerosol following the final conversion of public transportation from trams to diesel buses in the summer of 1952."

—Hunt et al., 2003

Data, data, data

"Data! data! data!" he cried impatiently. 'I can't make bricks without clay.'"

—The Adventure of the Copper Beeches, Arthur Conan Doyle



Data from the Great Smog of 1952

Research | Article

Toxicologic and Epidemiologic Clues from the Characterization of the 1952 London Smog Fine Particulate Matter in Archival Autopsy Lung Tissues

Andrew Hunt,¹ Jerrold L. Abraham,¹ Bret Judson,¹ and Colin L. Berry²

¹Department of Pathology, State University of New York Upstate Medical University, Syracuse, New York, USA; ²Department of Morbid Anatomy and Histopathology, Queen Mary and Westfield College, Royal London Hospital, London, United Kingdom

"We hypothesized that the archived preserved lung tissues from persons dying at the time of the epidemic would contain inhaled and retained PM representative of the December 1952 PM (the lung record)."

—Hunt et al., 2003

Data from the Great Smog of 1952

In interstitial-macrophages,
"inorganic particles of various
compositions were found interspersed
in the carbonaceous matrix"

—Hunt et al., 2003

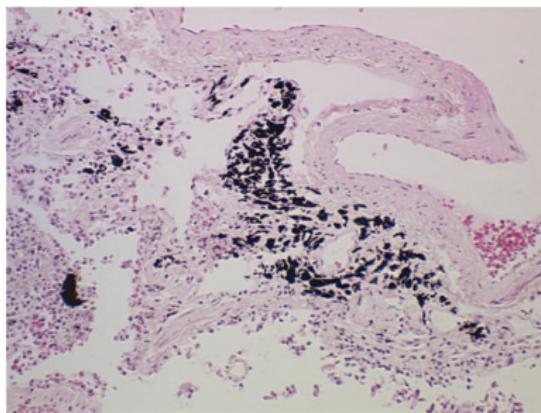


Figure 4. Light micrograph (H&E stain) showing interstitial macrophages from case 1 with opaque PM. Magnification approximately 100x.

Data from the Great Smog of 1952

In interstitial-macrophages, they found "a heavy PM loading and inorganic particle content consistent with the airspace- and lymph node–macrophage compartments"

—Hunt et al., 2003

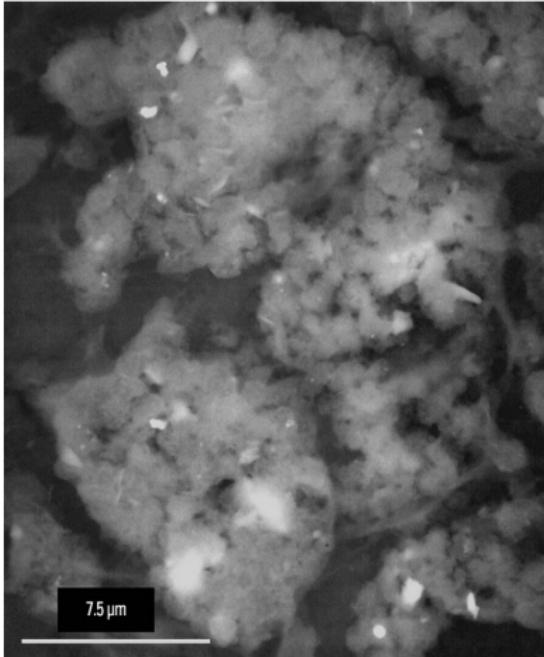


Figure 6. BE micrograph detail of Figure 5 of interstitial macrophages containing numerous inorganic (bright) particles.

Data from the Great Smog of 1952

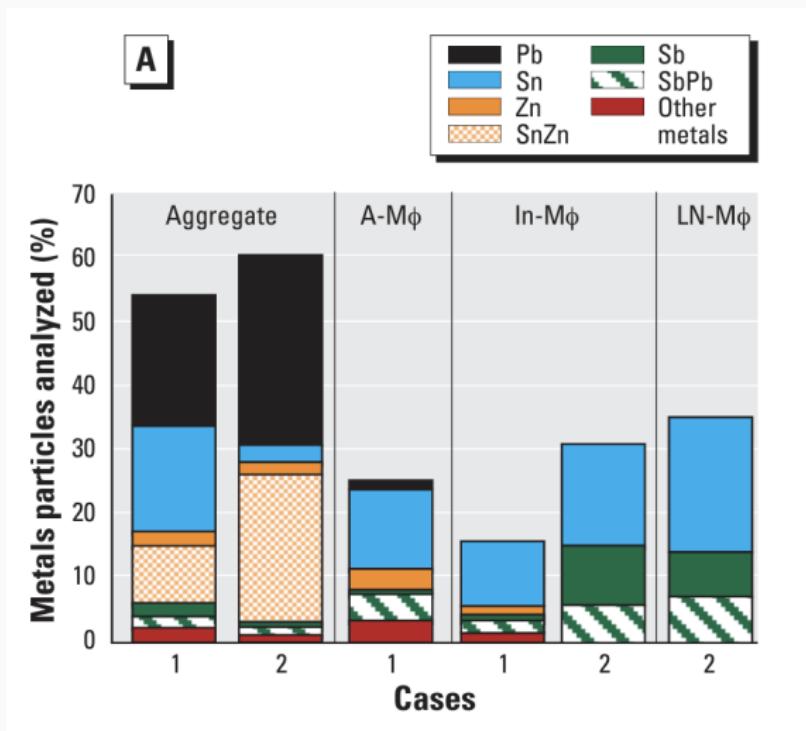
In situ lung compartment approach targeted four lung compartments:

- Airways
- Airspace macrophages
- Interstitial macrophages
- Lymph node macrophages

"This compartmentalization allowed inhaled PM to be separated on retention time, with lung residence time increasing [from top to bottom]."

Source: Hunt et al., 2003

Data from the Great Smog of 1952



Source: Hunt et al., 2003

Data from the Great Smog of 1952

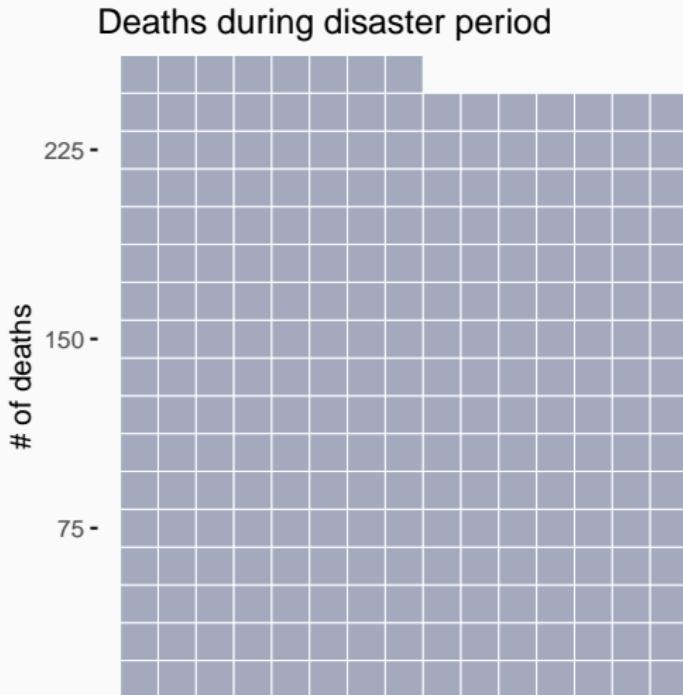
"Certain heavy metal-bearing particle types that are abundant in the most recent retention compartment (e.g., Pb, ZnSn in the airway aggregates) are almost totally absent from the longer-term storage compartments."

"We suggest that such changes in PM content are a response to variations in metal solubility. If soluble components of PM affect physiologic processes, metal solubility may be a factor in PM-mediated mortality and morbidity."

—Hunt et al., 2003

Ideal vs. observed information

Mortality information from a disaster



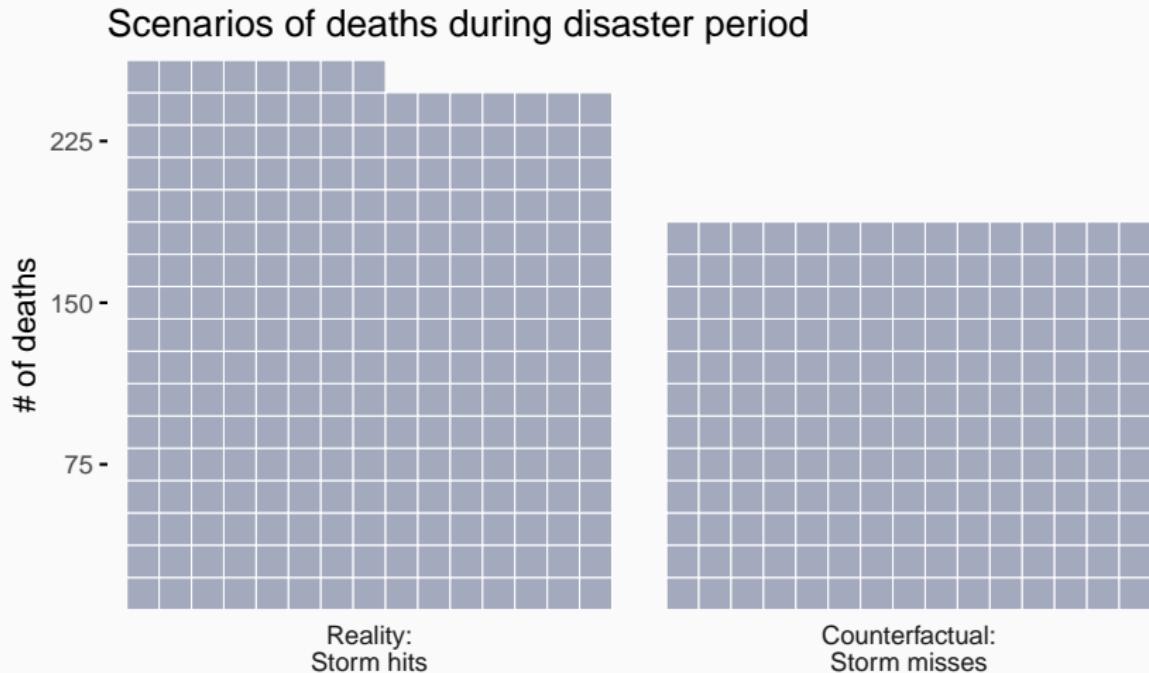
Each square represents a death during the disaster period in a disaster-affected community.

A disaster's mortality impact



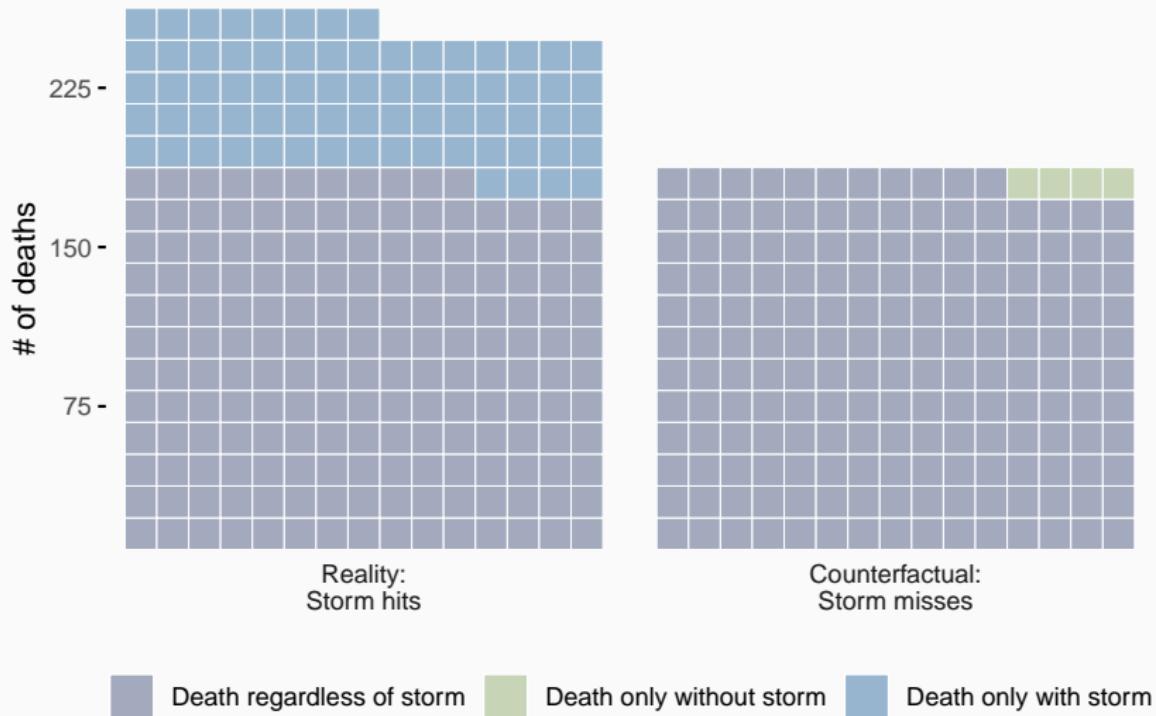
Source: AccuWeather

Ideal information



Ideal information

Scenarios of deaths during disaster period



Figuring out what you don't know from what you do

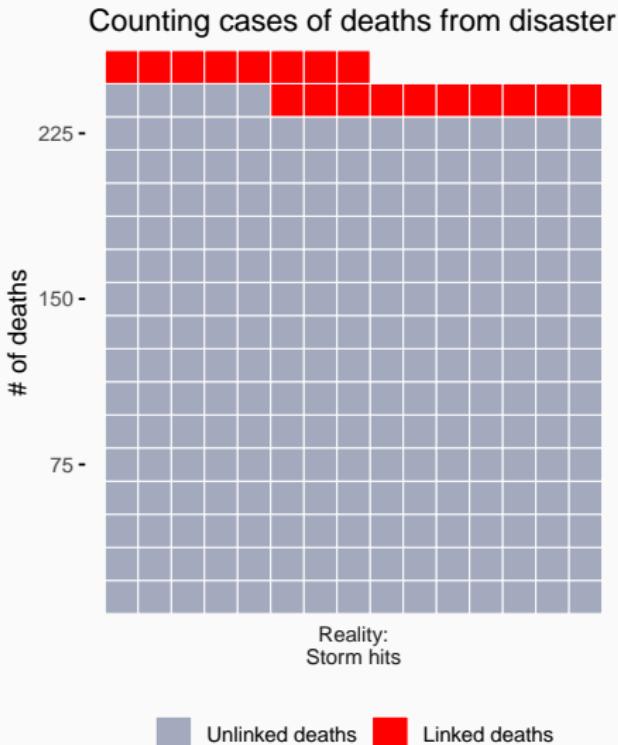
"All the business of war, and indeed all the business of life, is to endeavor to find out what you don't know by what you do; that's what I called 'guess what was at the other side of the hill'."

—Attributed to the Duke of Wellington

1. **Counting cases** of disaster-attributable mortality
2. **Estimating excess** community-wide mortality during the disaster period compared to the counterfactual that the disaster didn't happen

Counting cases

Counting cases



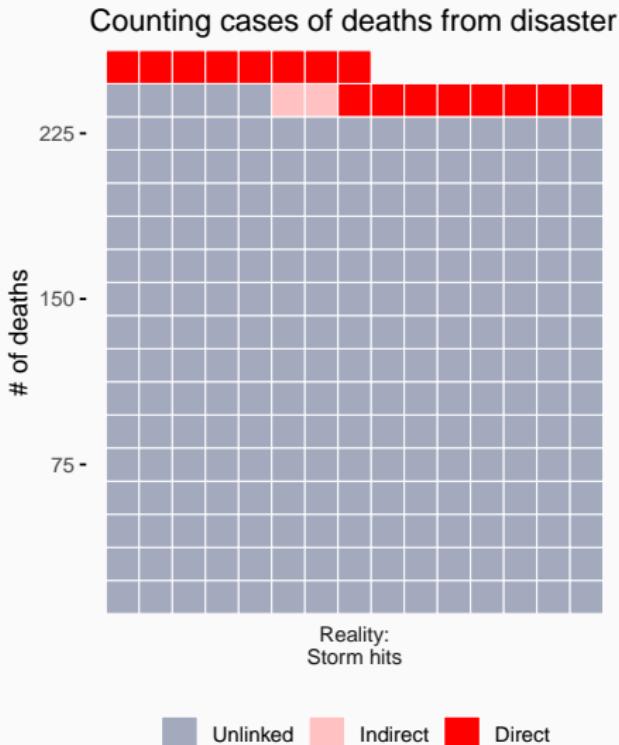
Investigate each death, case-by-case. Use information from the death certificate and other sources to determine if that specific death can be linked to the disaster.

Direct and indirect deaths

- **Direct deaths:** “Caused by environmental forces of the hurricane and direct consequences of these forces.”
- **Indirect deaths:** “Caused by unsafe or unhealthy conditions because of loss or disruption of usual services, personal loss, or lifestyle disruption.”

Source: Issa et al., 2018, “Deaths Related to Hurricane Irma — Florida, Georgia, and North Carolina, September 4–October 10, 2017”, Morbidity and Mortality Weekly Report

Direct and indirect deaths



Investigations of each case can help determine if the death was directly or indirectly attributable to the disaster.

Hurricane Katrina, 2005

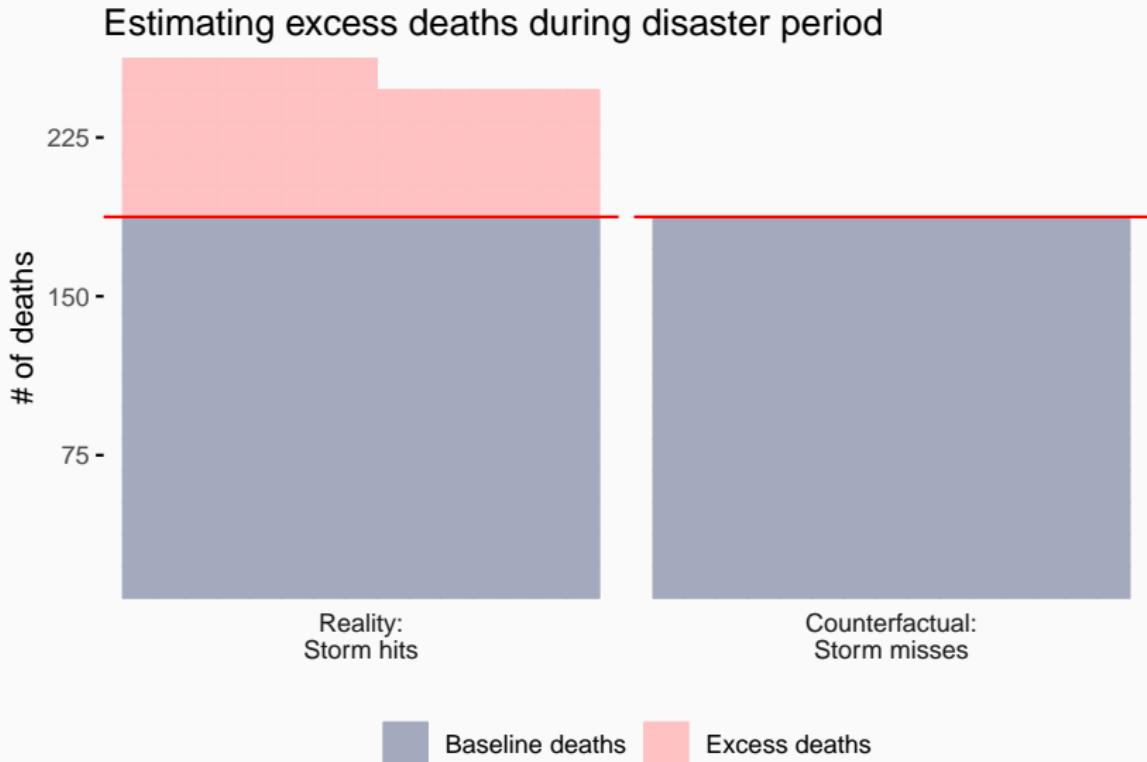
TABLE. Number of deaths directly, indirectly, or possibly related to Hurricane Katrina, by cause of death — selected counties,* Florida and Alabama, August–October 2005

Cause of death	Florida				Alabama				
	Direct	Indirect	Possible	Total	(%)	Indirect	Possible	Total	(%)
Drowning	3			3	(21)	1		1	(4)
Car collision		3†		3	(21)	1		1	(4)
Hit by falling tree limb	2	2		4	(29)				
Carbon monoxide poisoning		2		2	(14)				
Fall from ladder		1		1	(7)				
ASCVD§				6		3		9	(38)
Chronic alcoholism				1				1	(4)
Sepsis				1				1	(4)
Seizure				1				1	(4)
Other CNS¶ disease				1				1	(4)
Traumatic brain injury				1		1		2	(8)
Homicide (gunshot wound)						3		3	(13)
Suicide						1	1	2	(8)
Asphyxia						1		1	(4)
Undetermined			1	1	(7)		1	1	(4)
Total	5	8	1	14		15	9	24	

Source: US CDC, 2006, "Mortality Associated with Hurricane Katrina — Florida and Alabama, August–October 2005", *Morbidity and Mortality Weekly Report*

Estimating excess mortality

Estimating excess mortality



Covid-19

Mortality rates have soared in urban areas worldwide, with overall excess deaths often much higher than reported Covid-19 counts

Number of deaths per week from all causes, 2020 vs recent years:



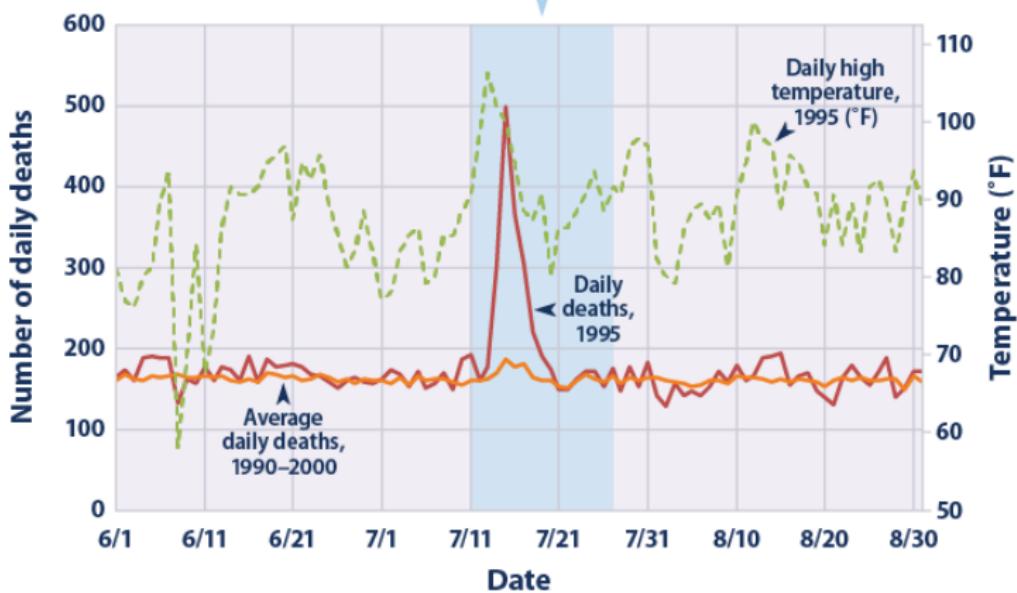
Source: Financial Times

1995 Chicago heat wave

Examining Heat-Related Deaths During the 1995 Chicago Heat Wave

Cook County, July 11–27, 1995:

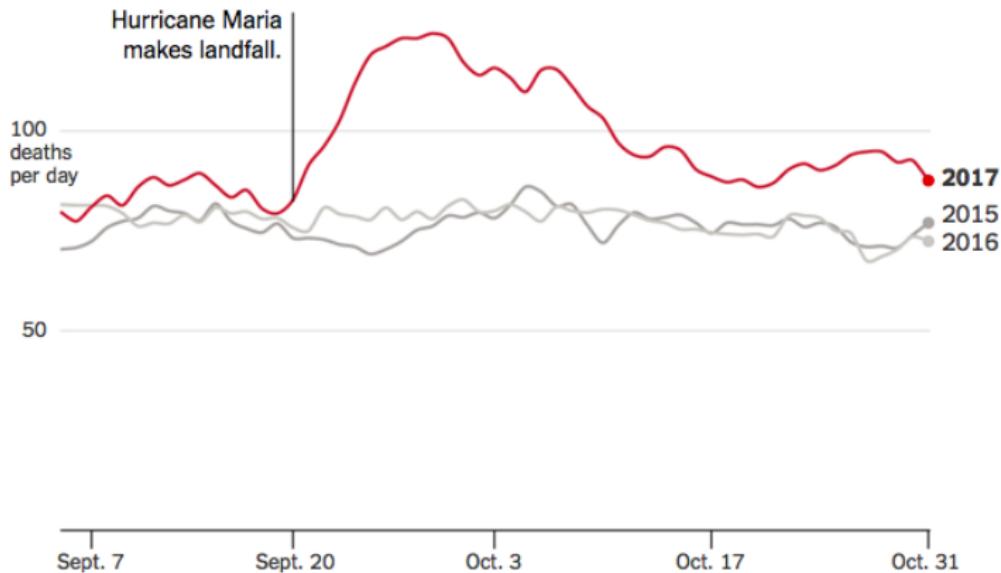
Excess deaths compared with this time period during an average year: about 700
Deaths classified as "heat-related" on death certificates (not shown here): 465



Source: US EPA, "Climate Change Indicators in the United States: Heat-Related Deaths"

Hurricane Maria, 2017

Average Daily Deaths in September and October



Source: New York Times

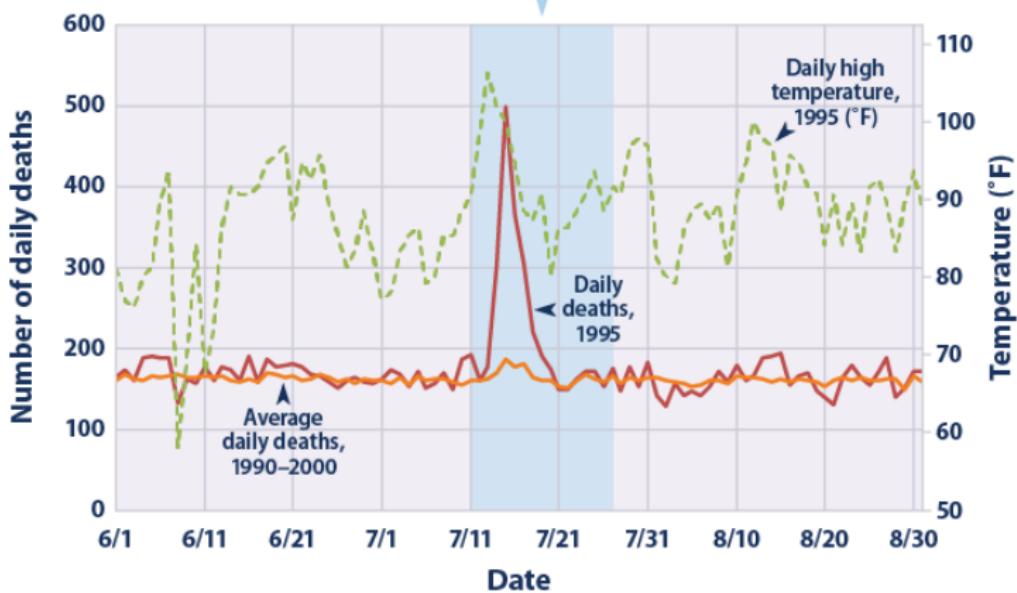
Comparing measurements from the two methods

1995 Chicago heatwave

Examining Heat-Related Deaths During the 1995 Chicago Heat Wave

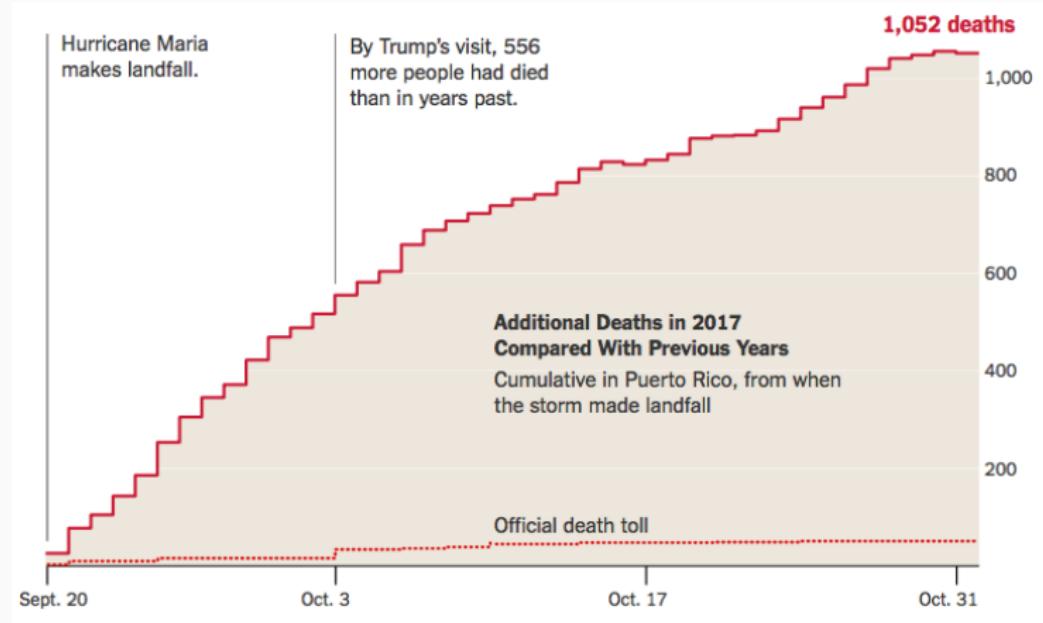
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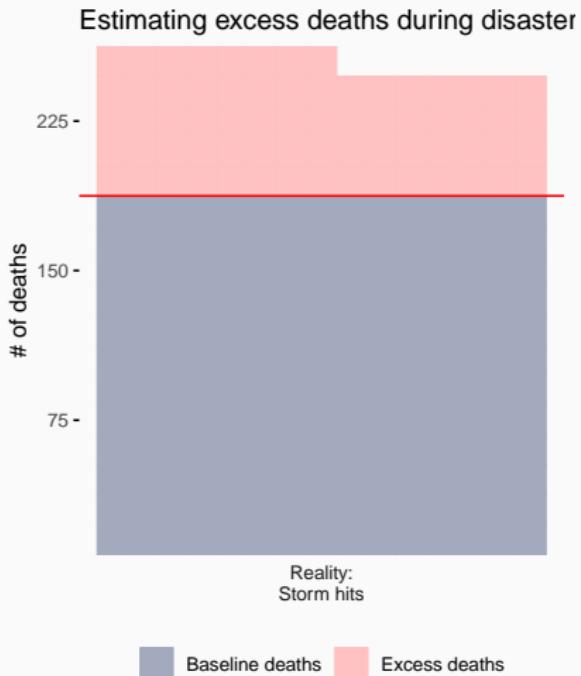
Hurricane Maria, 2017



Source: New York Times

Complementary approaches

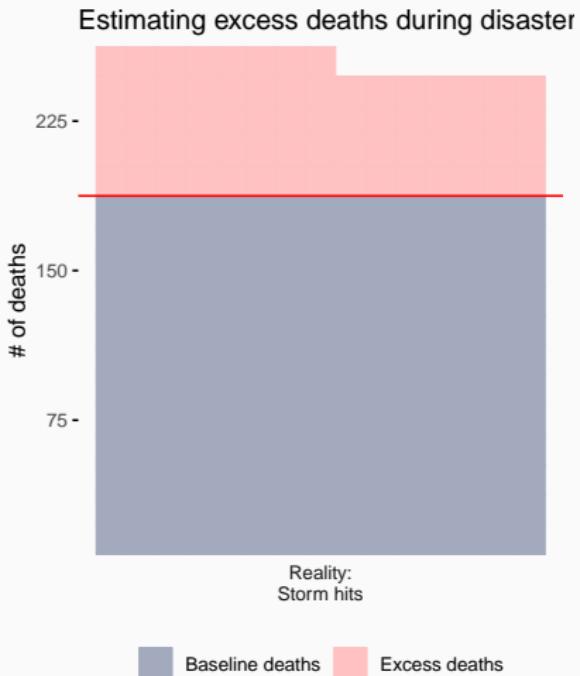
Estimating excess—methodological objective



Strength:

Minimize *error* in estimating number of **excess deaths**.

Estimating excess—methodological objective



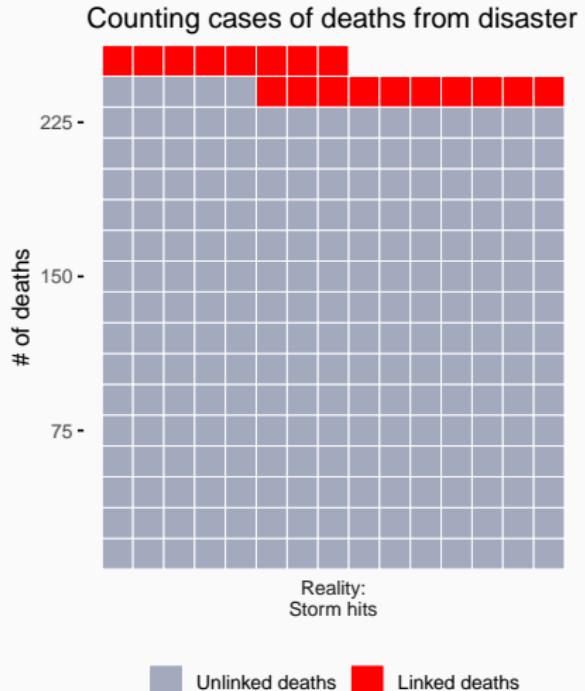
Strength:

Minimize *error* in estimating number of **excess deaths**.

Compromise:

- Excess deaths are estimated with some uncertainty (variance) because number of baseline deaths is estimated with some uncertainty.
- Individual deaths aren't identified as linked or unlinked.

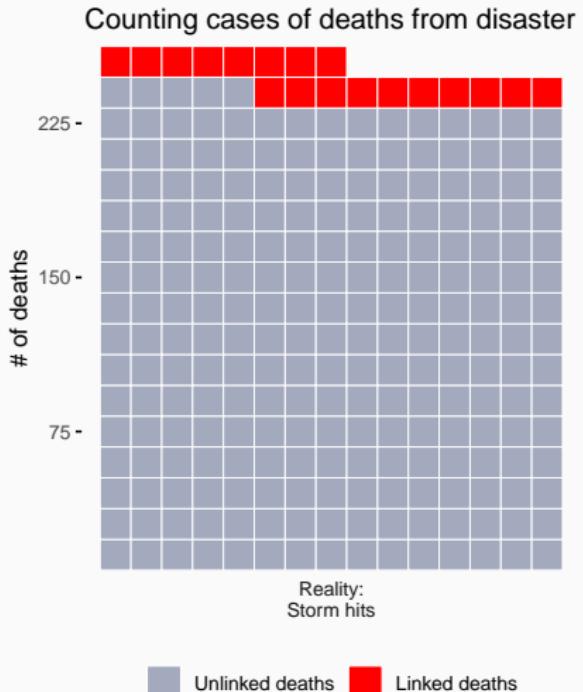
Counting cases—methodological objective



Strength:

Maximize *sensitivity*—the probability that if a death is classified as "**linked**", it really would not have happened without the disaster.

Counting cases—methodological objective



Strength:

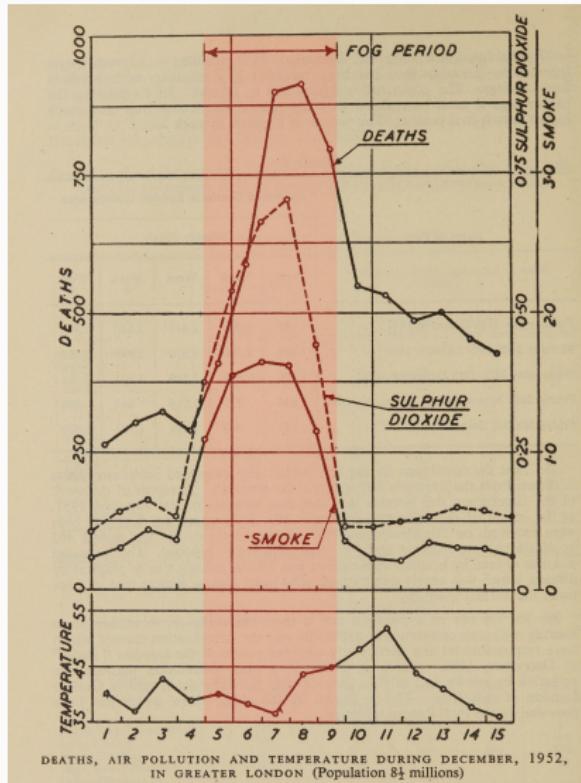
Maximize *sensitivity*—the probability that if a death is classified as "linked", it really would not have happened without the disaster.

Compromise:

- Maximizing *sensitivity* may decrease *specificity*—the probability that if a death is classified as "unlinked", it really would still have happened without the disaster.

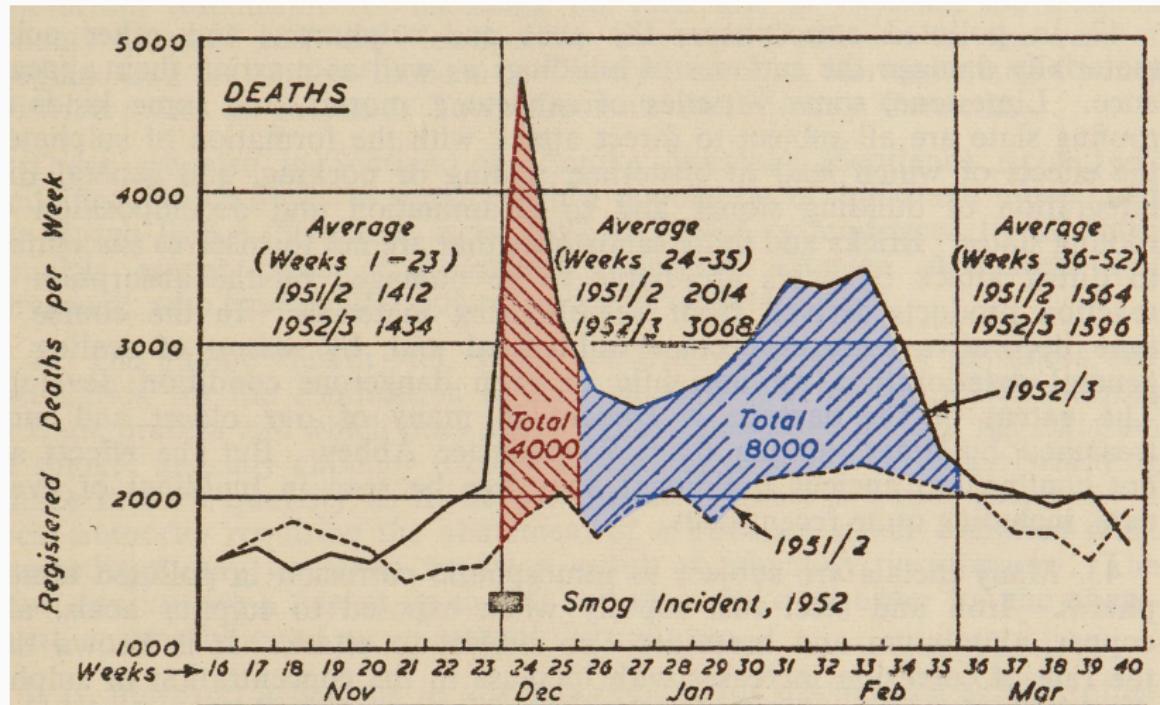
Epidemiology of the Great Smog of 1952

Great Smog of 1952



Source: UK Commission on Air Pollution

Great Smog of 1952



Source E.T. Watkins

Great Smog of 1952—Reassessment

Reassessment of the Lethal London Fog of 1952: Novel Indicators of Acute and Chronic Consequences of Acute Exposure to Air Pollution

Michelle L. Bell¹ and Devra Lee Davis²

¹Johns Hopkins University, Baltimore, Maryland, USA; ²Carnegie Mellon University, Pittsburgh, Pennsylvania, USA

"The official report on the London episode . . . noted morbidity and mortality remained elevated from December 1952 until March 1953 in the region of Greater London. However, the report attributed these increased rates to an influenza epidemic, while recognizing some deaths may have been due to lingering effects of the fog."

—Bell and Davis, 2001

Great Smog of 1952—Reassessment

Control for potential influence of:

- Temperature
- Relative humidity
- Season
- Autocorrelation of weekly mortality
- Influenza epidemic

Great Smog of 1952—Reassessment

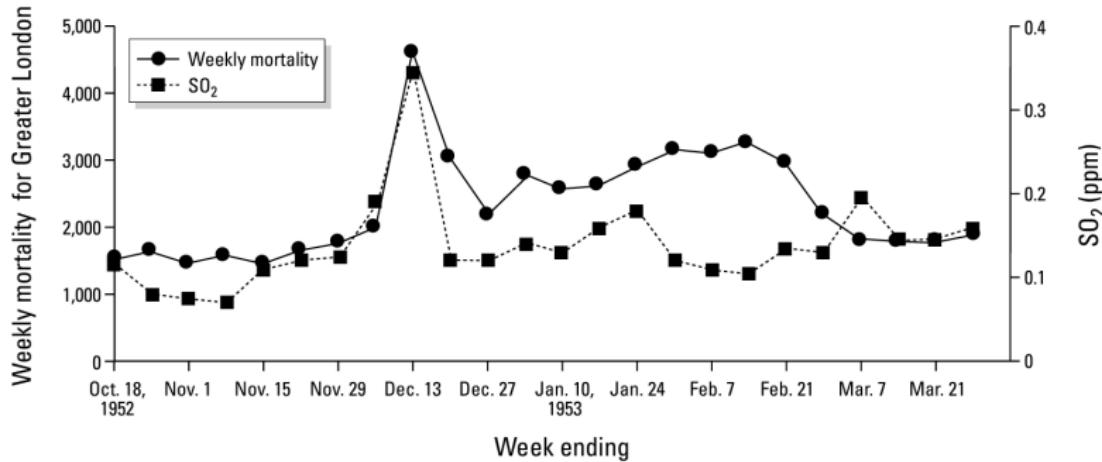


Figure 1. Approximate weekly mortality and SO₂ concentrations for Greater London, 1952–1953.

Great Smog of 1952—Reassessment

Table 2. Relative risk for daily mortality and the previous day's pollution levels.

	Greater London	London Administrative County
SO ₂ (0.10-ppm increase)	1.19 (1.12–1.27)	1.24 (1.14–1.35)
Adjusted for maximum temperature	1.27 (1.17–1.38)	1.34 (1.20–1.51)
TSM (100- $\mu\text{g}/\text{m}^3$ increase)	1.08 (1.05–1.10)	1.10 (1.06–1.13)
Adjusted for maximum temperature	1.08 (1.06–1.10)	1.09 (1.07–1.12)

Epidemiology and Toxicology

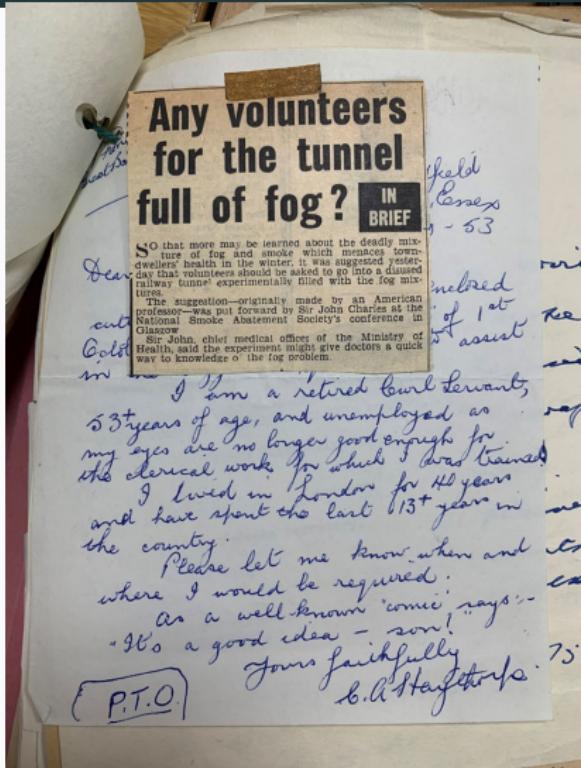
Epidemiology and Toxicology

Types of studies:

- Controlled animal studies with controlled exposure
- Controlled animal studies with real-world air pollution
- Autopsies of humans exposed to real-world air pollution
- Chamber studies of humans with controlled exposure
- Epidemiological studies of real-world populations exposed to real-world air pollution

Controlled human studies

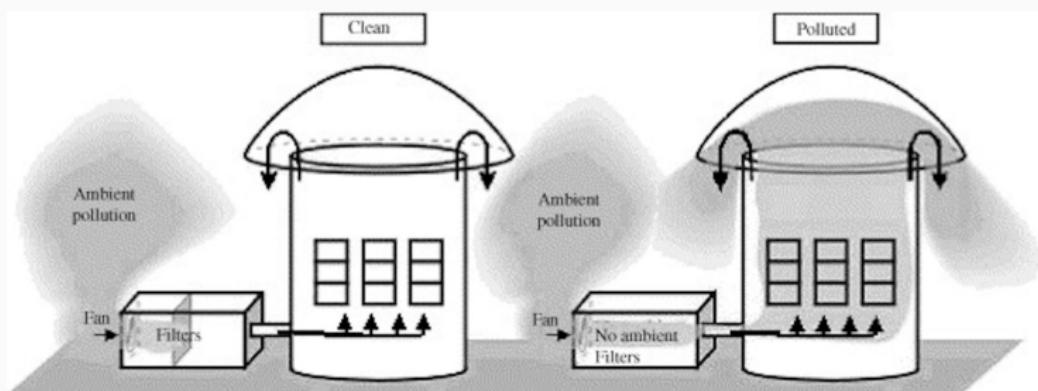
"I hope that I may have the privilege of being included among the volunteers to undergo such treatment ... if the fog has to kill us, it would be better to do it under controlled conditions so that there may be of some benefit to the rest of the world."



Source: UK National Archives (letter from October 2, 1953)

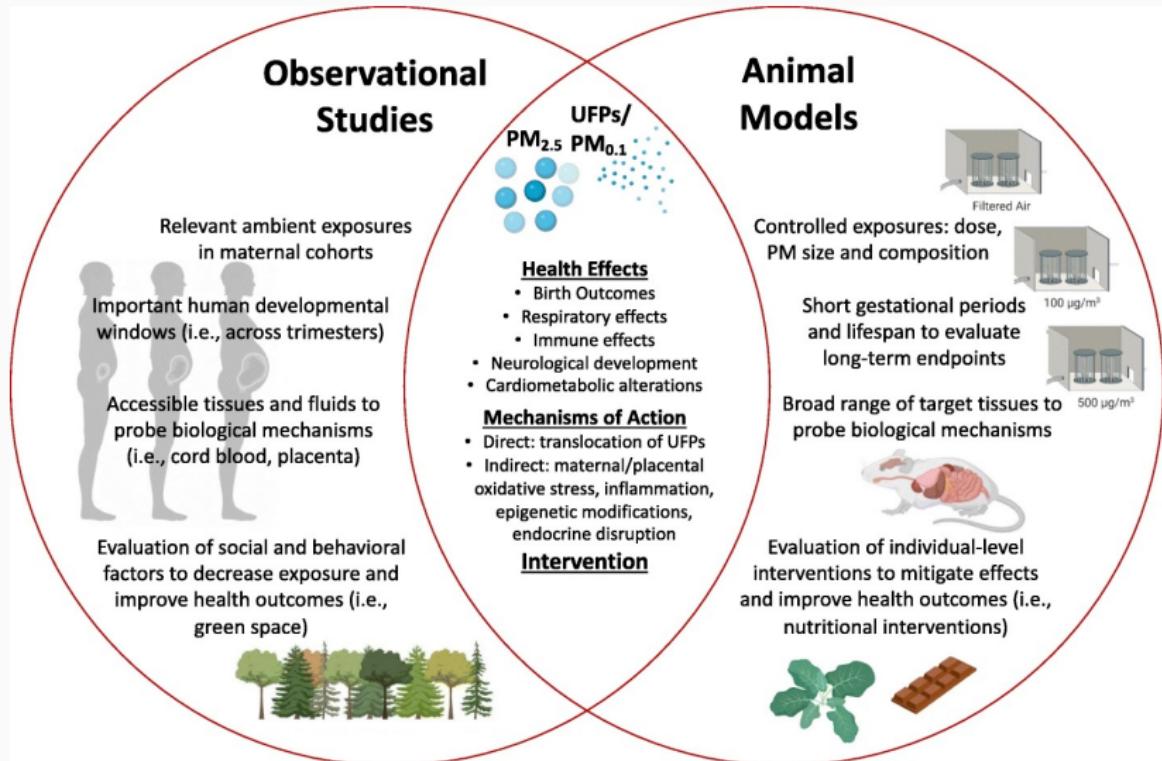
Animal studies of real-life exposures

"The experiments were carried out in downtown São Paulo, in the School of Medicine's garden, which is situated at a crossroad with high traffic density."



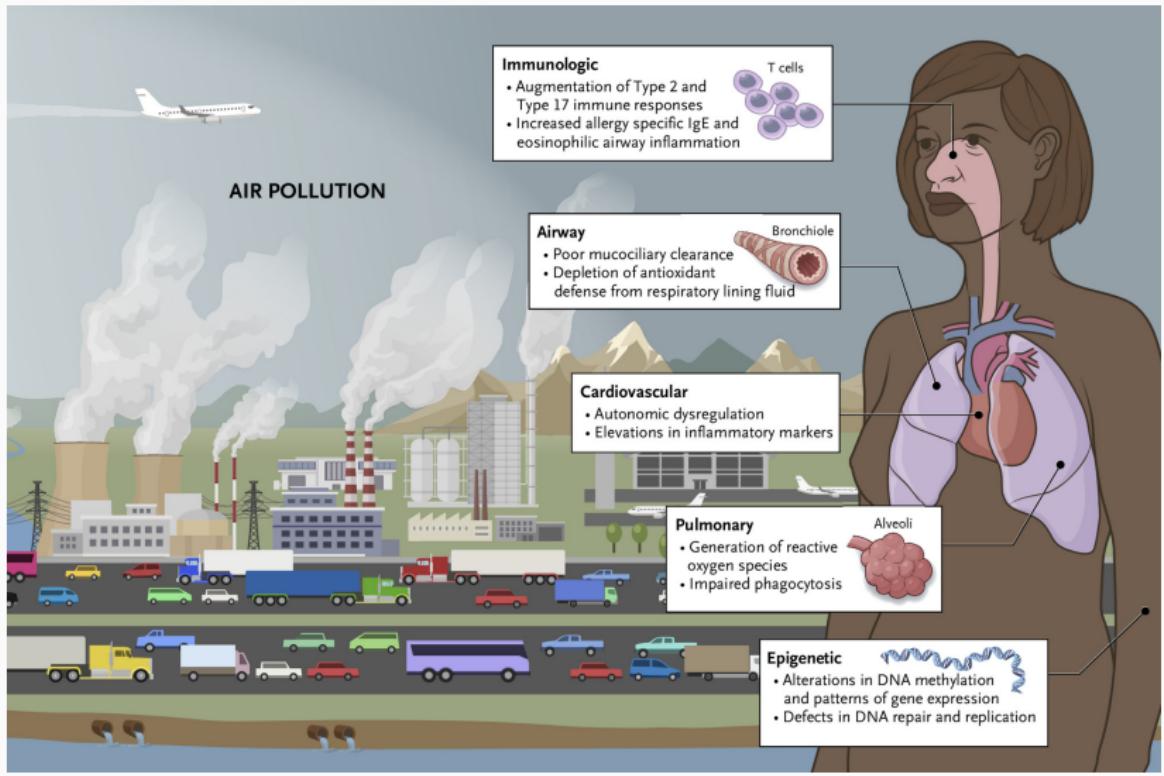
Source: Pires-Neto et al., 2006. Effects of São Paulo air pollution on the upper airways of mice. *Environmental Research*

Evidence from Observational Studies vs Animal Models



Source: Johnson et al., 2021. *Environmental Health and Preventive Medicine*

Toxicology-driven results



Epidemiology-driven results

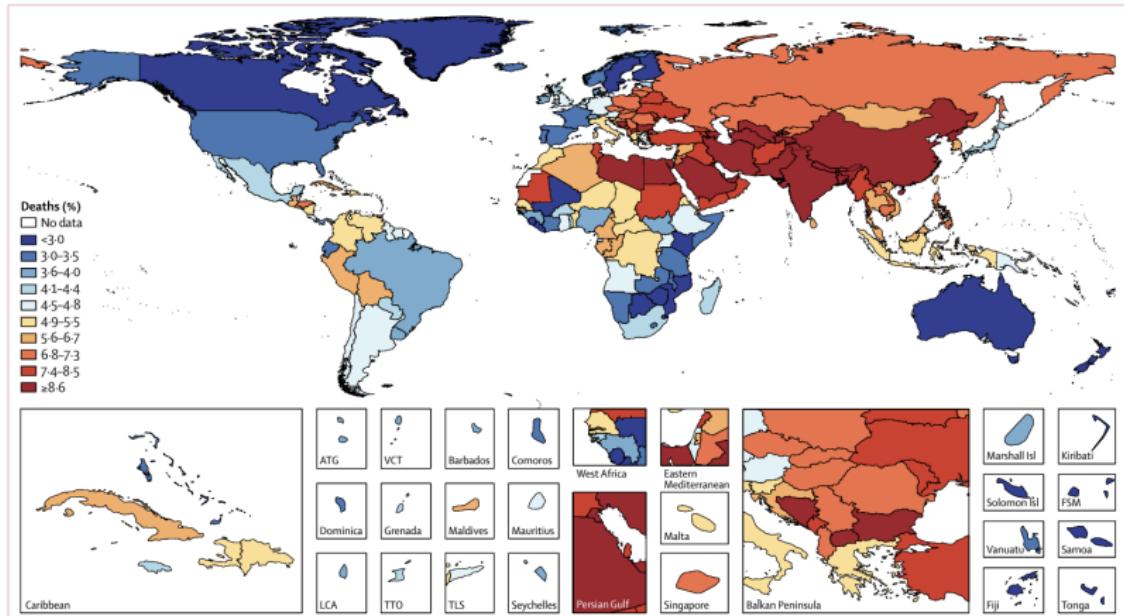


Figure 5: Deaths attributable to ambient particulate matter pollution in 2015

ATG=Antigua and Barbuda. FSM=Federated States of Micronesia. Isl=Island. LCA=Saint Lucia. TLS=Timor-Leste. TTO=Trinidad and Tobago. VCT=Saint Vincent and the Grenadines.

Source: Cohen et al., 2017. *The Lancet*