Burden of disease due to environmental exposure

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Outline

- Attributable risk
  - for the exposed group
  - for the population

- Population attributable risk due to environmental exposure
  - without temporal relationship between exposure and risk
  - with temporal relationship: Forward and backward perspective

Attributable risk

- Much statistical analysis seeks to identify associations between exposures and outcomes.

The relative risk (RR) a major consideration in deriving causal inferences.

How much of the disease that occurs can be attributed to a certain exposure?

i.e., how much disease can be prevented if we have an effective means of eliminating the exposure in question?

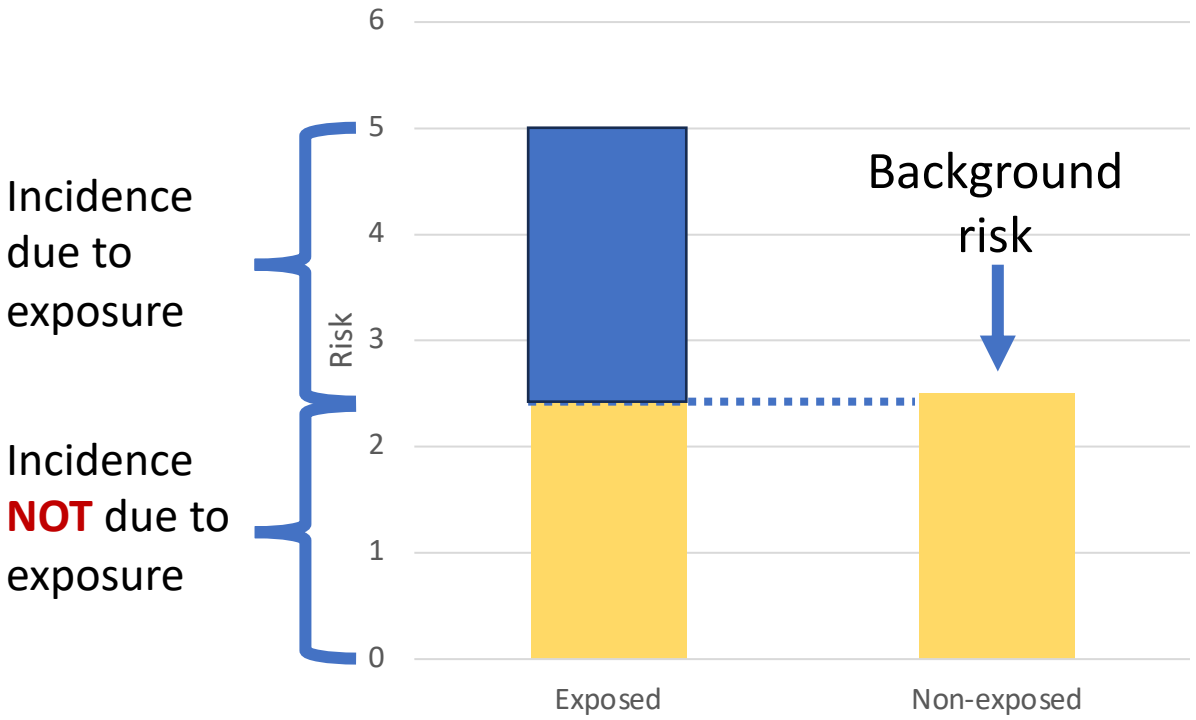
- **Attributable risk:**

The amount amount or proportion of disease incidence (or disease risk) that can be attributed to a specific exposure.

- Attributbale risk for **the exposed group**
- Attributable risk for **the total population** (including both exposed and nonexposed persons).

Attributable risk for the exposed group

$$\textbf{\textit{Attributable numbers}} = \begin{pmatrix} Incidence\ in \\ exposed\ group \end{pmatrix} - \begin{pmatrix} Incidence\ in \\ nonexposed\ group \end{pmatrix}$$



$$RR = \frac{Incidence\ in\ exposed\ group}{Incidence\ in\ nonexposed\ group}$$

$$Attributable\ numbers$$
$$= Incidence\ in\ exposed\ group * (1 - \frac{1}{RR})$$

$$\textbf{\textit{Attributable}}\ \textbf{fraction} =$$

$$\frac{\begin{pmatrix} Incidence\ in \\ exposed\ group \end{pmatrix} - \begin{pmatrix} Incidence\ in \\ nonexposed\ group \end{pmatrix}}{\begin{matrix} Incidence\ in \\ exposed\ group \end{matrix}}$$

Attributable risk for the exposed group

Relative risk V.S. Attributable risk

RR measures the strength of the association and the possibility of a causal relationship.

Attributable risk indicates the potential for prevention if the exposure could ve eliminated.

The practicing clinician is mainly interested in the attributbale risk in the exposed group.

Example: the attributbale risk for lung cancer in smokers

Population attributable risk

What will the impact of achieving WHO guideline for PM10 in City A?
What is the impact of heat in City B?

$$\boldsymbol{Attributable\ numbers} = \begin{pmatrix} Incidence\ in \\ total\ population \end{pmatrix} - \begin{pmatrix} Incidence\ in \\ nonexposed\ group \end{pmatrix}$$

$$AN = Incidence\ in\ total\ population - \frac{Incidence\ in\ total\ population\ * Percentage\ of\ the\ total\ population\ exposed}{RR}$$

$$AF = 1 - \frac{Percentage\ of\ the\ total\ population\ exposed}{RR}$$

Population attributable risk

- Population attributable risk is a valuable concept for the public health worker.
- It quantifies the overall adverse effects, including the number of cases, deaths, and disability associated with the risk factor.
- Understanding the burden of a risk factor is crucial for public health planning, resource allocation, and prioritising interventions.

Attributable risk in time series setting

In the setting of **time series analysis for environmental stressors**, the whole population is usually considered as exposed, and the definition of attributable risk can be more generally interpreted as the **population attributable risk**.

$$AF = 1 - \frac{Percentage\ of\ the\ total\ population\ exposed}{RR} \qquad AF = 1 - \frac{1}{RR}$$

$$AF_x = 1 - \exp(-\beta_x)$$
$$AN_x = n \cdot AF_x$$

With n as the total number of cases for a given expoure;

β_x is the risk associated with the exposure, referring to the association with a specific exposure intensity x compared to a reference value x_0

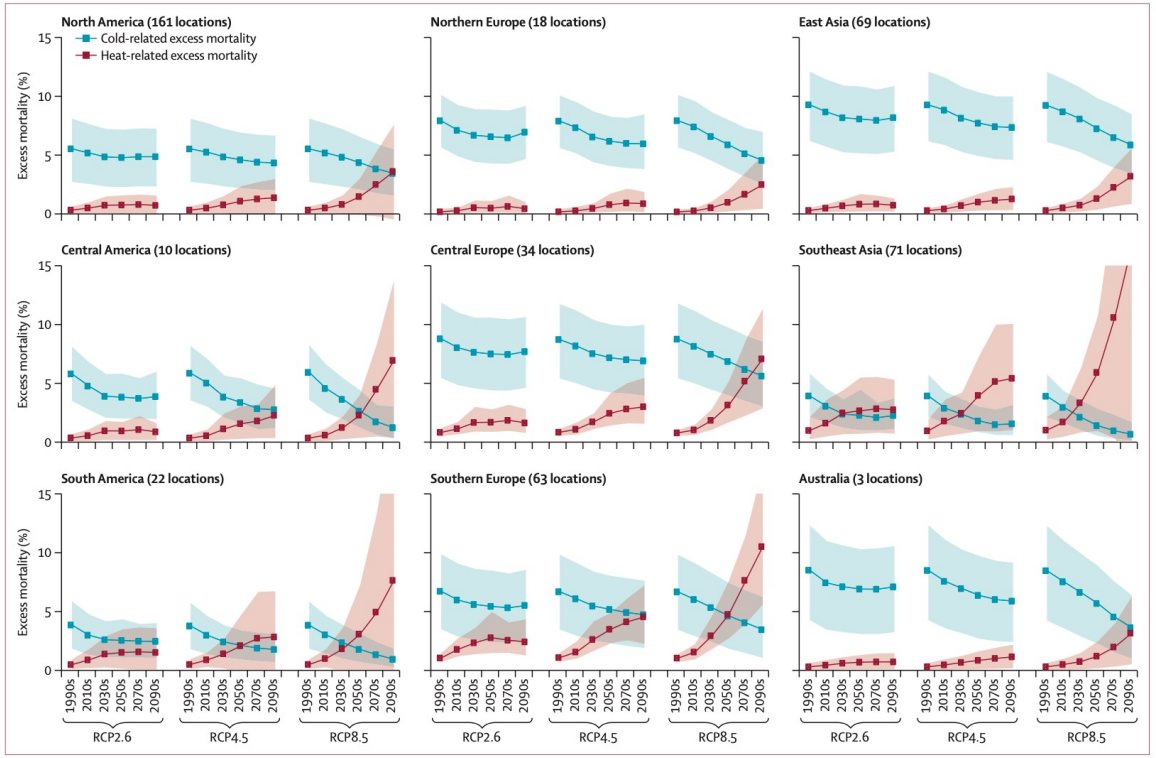
Examples

- “Short-term exposure to ozone above the WHO guideline ($100\mu g/m^3$) was 0.20%, corresponding to 6262 annual excess deaths. ”

-BMJ 2020; 368:m108

- “In total, 7·71% (95% empirical CI 7·43–7·91) of mortality was attributable to non-optimum temperature in the selected countries within the study period, with substantial differences between countries, ranging from 3·37% (3·06 to 3·63) in Thailand to 11·00% (9·29 to 12·47) in China. ”

- Lancet 2015; 386: 369–75



Trends in heat-related and cold-related excess mortality by region

-Lancet Planet Health 2017; 1: e360–67

Concept

$$AF_x = 1 - \exp(-\beta_x)$$
$$AN_x = n \cdot AF_x$$

With n as the total number of cases for a given expoure;
β_x is the risk associated with the exposure, referring to the association with **a specific exposure intensity x compared to a reference value x_0**

The theoretical nature of these effect measures is based on the definition and comparison of factual and counterfactual conditioins.

Factual condition: observations (exposure intensity x).

Counterfactual condition: the exposure level of the same population changes to reference value x_0.

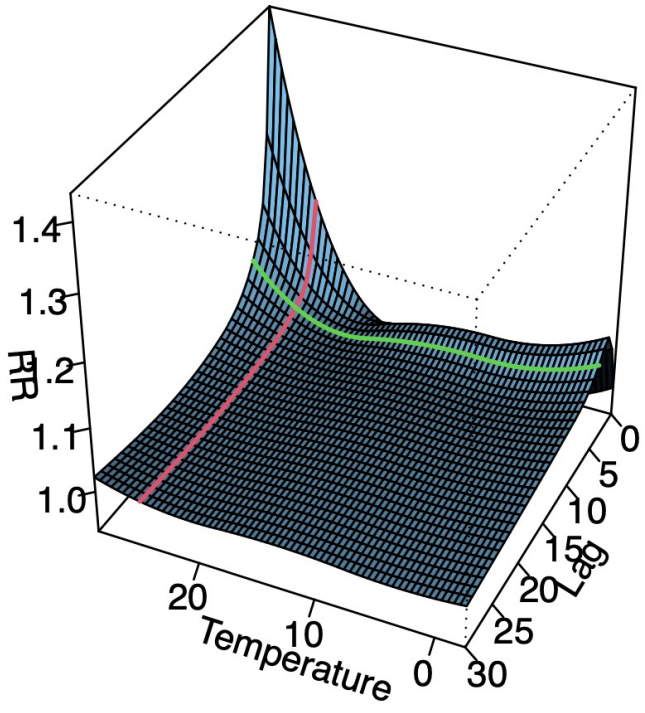
Forward and backward perspectives

$$AF_{x,t} = 1 - \exp(-\beta_{x,t})$$
$$AN_{x,t} = n_t \cdot AF_{x,t}$$

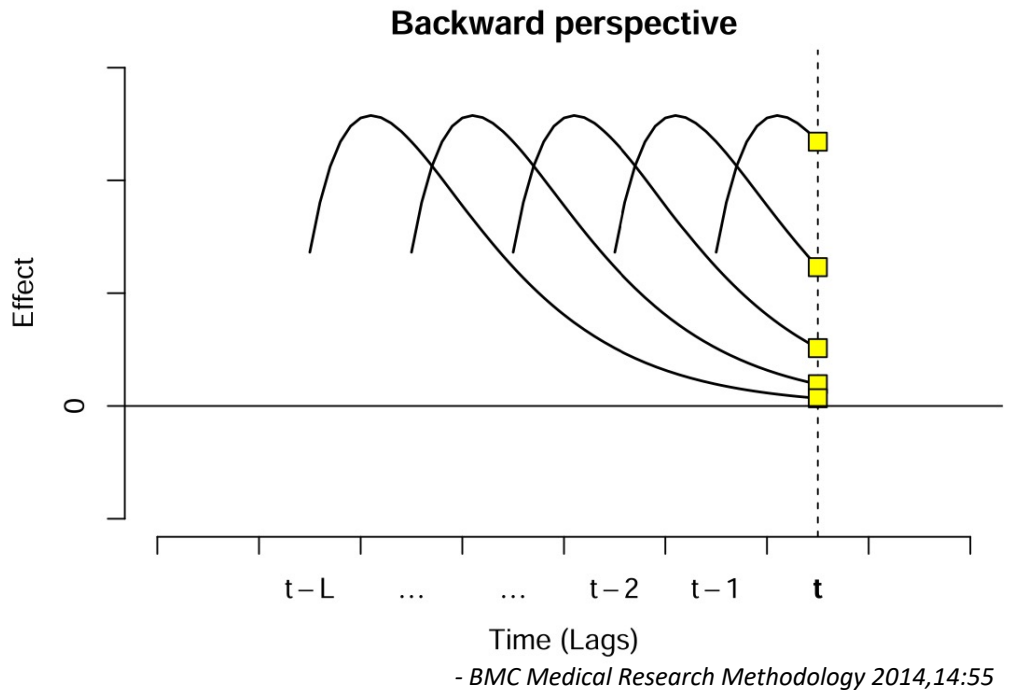
In time series, we can compute the number of outcomes at time t attributable to an environmental stressor using the corresponding risk estimate associated with the exposure level at time t.

This defintion does not consider any temporal relationship between exposure and risk (i.e., delayed effect lasting beyond time t).

Forward or backward approach to account for complex temporal patterns.



Backward perspective



- BMC Medical Research Methodology 2014,14:55

Conceptual model for the interpretation of exposure-lag-response associations from a backward perspective

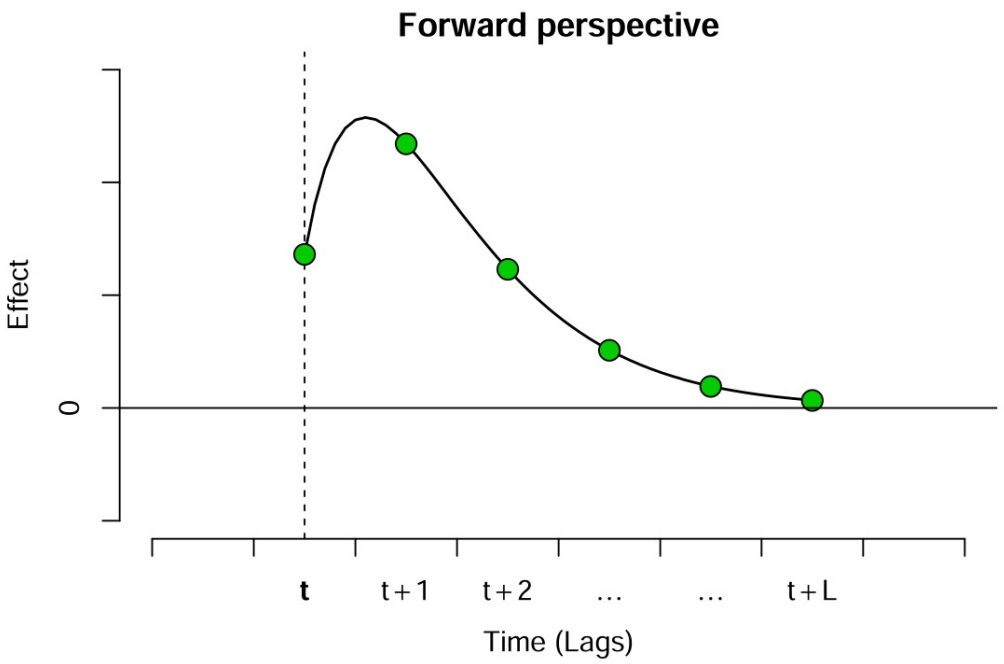
$$b{-}AF_{x,t} = 1 - \exp(-\sum_{l=l_0}^{L} \beta_{x_{t-l},l})$$

$$b{-}AN_{x,t} = b{-}AF_{x,t} \cdot n_t$$

Looking from current risks to past exposures, $\beta_{x,l}$ are the contributions from the exposure $x_{t-l_0}, \dots, x_{t-L}$ experienced at $t - l_0, \dots t - L$.

It requires an extended version of the counterfactual condition accounting for the additional lag dimension, where the counterfactual condition is defiend as the constant exposure x_0 in the period $t - l_0, \dots t - L$.

Forward perspective



- BMC Medical Research Methodology 2014,14:55

Conceptual model for the interpretation of exposure-lag-response associations from a forward perspective

$$f\text{-}AF_{x,t} = 1 - \exp(-\sum_{l=l_0}^{L} \beta_{x_t,l})$$

$$f\text{-}AN_{x,t} = f\text{-}AF_{x,t} \cdot \sum_{l=l_0}^{L} \frac{n_{t+l}}{L-l_0+1}$$

Looking from current exposure to future risks, $\beta_{x,l}$ are the contributions from the exposure x_t occuring at time t to the risk at times $t + l_0, \ldots t + L$.

The total number of cases at given exposure x is computing, by averaging the totwl counts experienceed in the next $l_0, \ldots, L$ times, thus only approximating lag structure of risks

Backward V.S. forward perspective

	Backward perspective	Forward perspective
Strengths	Provides more consistent estimators from lag-reponse association	- The counterfactual condition is simpler - Suit better for separating the risks in components attributable to different range - The overall cumulative risk for a given exposure is available, a step often needed in multi-site studies.
Limitation	Extended conterfactural condition	approximate the lag structure of risks. (may underestimate the AN)

Extensions

- The calculation can be extended to separate the attributable components related to specific exposures or exposure ranges (e.g., mild and extreme cold and hot).

- The calculation for each observation can be added together to obtain total AF and AN.

- Monte Carlo simulations can be used to compute 95% empirical confidence intervals (95%eCI).

- *Assume the parameters from the function for the exposure follows (multivariate) normal distribution with point estimate beta and variance derived from the regression model.*
- *Take random samples from the distribution above*
- *Derive attributable risks for each sample, which empirically reconstruct the distribution of attributable risk*
- *The related 2.5th and 97.5th percentiles of such distribution → 95%eCI*

References

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- Kyle Steenladn and Ben Armstrong. An overview of methods for calculating the burden of disease due to specific risk factors. Epidemiology. 2006;17:512-519.
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Hands-on exercise

- **Data:**

Daily time series data on mean PM_{10}, mean temperature, and all-cause mortality from 2002 to 2006 in London

- Mortality risk attributable to PM_{10}
- Mortality risk attributbale to non-optimum temperature
  - backward and forward perspective
  - Separating attributable components