Ann Ist Super Sanità 2025 | Vol. 61, No. 1: 68-81
DOI: 10.4415/ANN_25_01_09

ORIGINAL ARTICLES AND REVIEWS

Relative excess measures of effect and their use in health impact assessment

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Abstract

Introduction. In health impact assessment, relative excess measures of effect are used in combination with exposure and outcome data to estimate the health impacts under an alternative exposure scenario. The aim of this study is to propose: a classification of relative excess measures of effect functional for health impact assessment; a standard and general framework for calculating health impacts; different approaches when using data at different spatial resolutions.

Methods and results. A classification of the relative excess measures of effect was presented, introducing a new measure. A standard framework for calculating attributable and preventable cases based on the nature of the exposure and the imagined change in exposure was described. The marginal and conditional approaches to calculate health impacts using data at different spatial resolutions were illustrated.

Conclusions. The proposed methods and frameworks are designed to be applicable to a range of different situations. As health impact assessment continues to evolve, the insights and tools provided in this paper could help guide effective and equitable assessments, ultimately contributing to better public health decisions and outcomes.

Key words

- health impact assessment
- risk assessment
- effect measure
- epidemiology
- environment

INTRODUCTION

Health impact assessment (HIA) is a method for evaluating how a proposed policy, programme, or initiative might affect the health of a community. Recommendations are made to decision-makers and stakeholders to maximize the beneficial and minimize the harmful health effects of the proposal. The method combines quantitative, qualitative, and participatory approaches, making it applicable to a wide range of economic sectors. To proactively promote health and prevent illness or injury, it helps decision-makers to choose between alternatives and improvements [1-8].

A common approach in health impact assessment is to use exposure-response functions from previous studies. Typically, health impact assessment, also known as epidemiological risk assessment (ERA), uses relative excess measures of effect in combination with exposure and outcome data to estimate the health impacts under an alternative exposure scenario. The exposure-response functions used for the assessment are mainly taken from meta-analyses to ensure the reliability of the estimates [2, 3, 9-24]. Most studies and technical documents focus on assessing the health impacts of harmful exposures (typically air pollution), while less attention has been paid to the health impacts of beneficial exposures (e.g., green spaces) [2-4, 7, 8, 13-24]. Different approaches and equations have been used, depending on the research question, the quality of the available data, and the working group [1-24].

By drawing on the reference literature on epidemiological measures and using mathematical derivations, this paper attempts to fill the knowledge gap on a global framework of standard equations. The first aim of this study is to propose a classification of relative excess measures of effect that is functional for health impact assessment. The second objective is to propose a standard and general framework for estimating health impacts in different situations. The third goal is to propose different approaches to calculating health impacts when using data at different spatial resolutions.

METHODS

Rationale and assumptions

The present work builds on and extends the definitions of effect measures provided by leading epidemiology texts in an attempt to establish a standard and general framework [9-12]. Concepts and equations are based on a counterfactual framework. Namely, one population of size N is considered under two alternative scenarios, baseline – or actual or factual – and counterfactual. The reported definitions are referred to as counterfactual or potential-outcome definitions because at least one of

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the two conditions is contrary to fact. The population may be exposed or non-exposed. If the population is exposed, then the non-exposed condition is counterfactual, and if it is non-exposed, then the exposed condition is counterfactual. Association measures are referred to as effect measures after assuming reasonable absence of bias in the estimation of the exposure-response functions. Strictly speaking, we could never observe a true effect measure. In fact, a true effect measure compares what would happen to one population under two possible but different conditions, only one of which can occur. It is a theoretical – some would say "metaphysical" – concept in that it is logically impossible to observe the population under both conditions, and therefore logically impossible to see the magnitude of the effect directly. In contrast, we necessarily use measures of association from studies that compare what happened in different populations. Identifying these measures with measures of effect in a single population is an approximation that assumes there is no bias in the estimation of the measure. A further assumption is the transportability of the measures from the populations observed in the analytical studies to the population to which the effect measures are applied. The terms "exposure" and "non-exposure" denote the index and reference conditions respectively. Only adverse outcomes are considered in the present study. For simplicity reasons, only risk measures are considered in this study. In the present study, the term "cases" is used to denote the incident cases (new cases) that occur in a given period of time in a population at risk of size *N* at the beginning of the period. Similar effect measures can be calculated using rate or odds measures, and an analogous health impact assessment methodology can be applied by using these measures under the rare disease assumption [1-24].

Classification and calculation of relative excess measures of effect

In a population of size *N*, the attributable risk (*AR*) or risk difference (*RD*) or excess risk (*ER*) represents the quantity which is added to the risk by the exposure (absolute effect measure or excess measure of effect). By using the risks in the exposed (*R*1) and non-exposed (*R*0), or the number of cases in the exposed (*C*1) and non-exposed (*C*0), or the number of attributable cases (*AC*), it is defined according to equation 1.

The relative risk (*RR*) or risk ratio (*RR*) represents the quantity by which the risk is multiplied by the exposure (relative effect measure or ratio measure of effect). It is defined according to equation 2.

Sometimes, it could be useful to consider the negative attributable risk (–*AR*) or preventable risk (*PR*), the negative attributable cases (–*AC*) or preventable cases (*PC*), and the reciprocal relative risk (1/*RR* or *RRR*) according to equations 3 and 4.

Further definitions are provided in *Note 1 available online as Supplementary Materials*. Relative excess measures of effect can be calculated by dividing an absolute effect measure by (relative to) the non-exposed or exposed risk. These definitions have been used in the present work to provide, using mathematical derivations, a simple and systematic classification of the relative excess measures of effect that could be functional for health impact assessment [1-24]. New effect measures (preventable risk, reciprocal relative risk and excess reciprocal relative risk) have been proposed.

Classification and calculation of health impacts

Health impact assessment can be thought as a "reverse" study design. In a classical analytical study, outcome data under two exposure scenarios are compared to estimate an effect measure. In health impact assessment, an estimated effect measure and the outcome data under one exposure scenario (baseline) are combined to estimate the change in outcome data (health impacts) under an alternative exposure scenario (counterfactual) [1-24].

The functional classification of relative excess measures of effects, in conjunction with the literature, has been used in the present work to develop a simple and standard framework for the classification and calculation of attributable and preventable cases in health impact assessment [1-24]. This approach combines the baseline data with one of the four relative excess measures of effects, based on the nature of the exposure and the imagined change in exposure. The nature of the

$$AR = R1 - R0 = \frac{C1}{N} - \frac{C0}{N} = \frac{C1 - C0}{N} = \frac{AC}{N} \quad (1)$$

$$RR = \frac{R1}{R0} = \frac{\frac{C1}{N}}{\frac{C0}{N}} = \frac{C1}{C0} \quad (2)$$

$$-AR = PR = R0 - R1 = \frac{C0}{N} - \frac{C1}{N} = \frac{C0 - C1}{N} = \frac{PC}{N} \quad (3)$$

$$\frac{1}{RR} = RRR = \frac{R0}{R1} = \frac{\frac{C0}{N}}{\frac{C1}{N}} = \frac{C0}{C1} \quad (4)$$

exposure refers to the expected effect of the exposure in relation to the non-exposure: harmful or beneficial to human health. The imagined change in the exposure refers to the counterfactual exposure in relation to the baseline exposure: an increase if the baseline exposure is the non-exposure and the counterfactual exposure is the exposure, or a decrease if the baseline exposure is the exposure and the counterfactual exposure is the non-exposure. The attributable or preventable cases estimated according to the proposed methodology can also be used to calculate other forms of health impacts, such as the attributable or preventable years lived with disability (YLD) or years of life lost (YLL), the calculation of which is beyond the scope of this paper.

Calculation of health impacts using data at different spatial resolutions

Health impact assessments often combine different sources and types of data, so it is common to use data with different spatial levels of measurement. Often, baseline outcome data are available with lower spatial resolution with some degree of statistical aggregation (area level, less detailed) [25], while population and exposure data are available with higher spatial resolution (population level, more detailed) [8, 22, 23, 26]. For example, the total number of deaths (baseline outcome data) could be available for the municipal level (less detailed, lower resolution), while residential greenness (population and exposure data) can be available at the infra-municipal level (more detailed, higher resolution) [8, 25, 26]. Basically, there are different exposure values for the same baseline outcome value. When population and exposure data are more detailed than the baseline outcome data, two main approaches can be used to calculate the measures of effect [8, 9, 11, 13, 19, 20, 22, 23].

One approach is to use the more detailed data to calculate the population-weighted exposure (PWE), which can be used to calculate the effect measure for the less detailed level. Another possible approach is to calculate the effect measures for the more detailed level, and to combine them for the less detailed level. In both approaches, the calculated relative effect measure can ultimately be used to estimate the impacts at a less detailed level, where the baseline outcome data are available [8].

Using an epidemiological terminology and referring to the level of calculation of the relative risk, the present work proposes to define these two approaches as "marginal" and "conditional" with respect to the population (i.e., the more detailed level of measure). Standard analytical solutions with mathematical derivations are elaborated for the two approaches. Two different spatial units are considered, with the area unit representing the less detailed level (e.g., the municipality) and the population unit the more detailed level (e.g., the census tract or the population polygon or point) [8, 20, 25, 26].

RESULTS

Classification and calculation of relative excess measures of effect

Relative excess measures of effect can be calculated for a harmful or beneficial exposure and on the basis of non-exposed or exposed risk. A graphical representation of these measures with numerical examples is shown in *Figure 1*. Attributable risk (*AR*) is used to obtain a positive relative excess measure of effect when the exposure under consideration has a harmful effect ($R1>R0$). Negative attributable risk (*–AR*) or preventable risk (*PR*) is used to obtain a positive relative excess measure of effect when the exposure under consideration has a beneficial effect ($R1<R0$). These measures can be expressed by using relative risk (*RR*) or reciprocal relative risk (1/*RR* or *RRR*).

Excess relative risk

The excess relative risk (*ERR*) is the attributable risk (*AR*) divided by the non-exposed risk (*R*0). It is defined as the amount of risk that is attributable to the exposure relative to the non-exposed risk, according to equations 5 and 6.

Attributable fraction

The attributable fraction (*AF*) or attributable risk fraction (*ARF*) is the attributable risk (*AR*) divided by the exposed risk (*R*1). It is defined as the amount of risk that is attributable to the exposure relative to the exposed risk, according to equations 7 and 8.

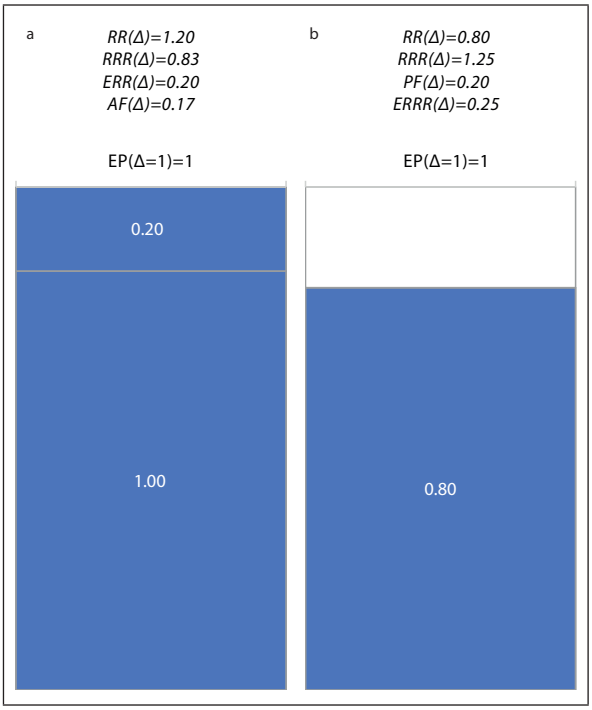

Figure 1

Relative excess measures of effect for a harmful exposure (charts a) and for a beneficial exposure (b). For each chart, the coloured area represents the risk in the exposed and the sum of white numbers is the relative risk. Relative risks are hypothetical.

AF: attributable fraction; *EP*: exposure prevalence; *ERR*: excess relative risk; *ERRR*: excess reciprocal relative risk; *PF*: preventable fraction; *RR*: relative risk; *RRR*: reciprocal relative risk; *X-axis*: population exposed; *Y-axis*: risk of the outcome; *Δ*: difference between exposure and non-exposure.

Preventable fraction

The preventable fraction (*PF*) or preventable risk fraction (*PRF*) is the negative attributable risk (*–AR*) or preventable risk (*PR*) divided by the non-exposed risk (*R0*). It is defined as the amount of risk that is preventable by the exposure relative to the non-exposed risk, according to equations 9 and 10.

Excess reciprocal relative risk

The excess reciprocal relative risk (*ERRR*) is the negative attributable risk (*–AR*) or preventable risk (*PR*) divided by the exposed risk (*R1*). It is defined as the amount of risk that is preventable by the exposure relative to the exposed risk, according to equations 11 and 12.

Classification and calculation of health impacts

Health impacts can be calculated for a harmful or beneficial exposure and on the basis of non-exposed or exposed risk. Attributable cases (*AC*) or attributable incident cases (*AIC*) can be estimated for an increase in a harmful exposure in a non-exposed population or for a decrease in a harmful exposure in an exposed population. Preventable cases (*PC*) or preventable incident cases (*PIC*) can be estimated for an increase in a beneficial exposure in a non-exposed population or for a decrease in a beneficial exposure in an exposed population. The proposed framework for the classification and calculation of health impacts is reported in *Figure 2* and in *Table 1*. Further details on the exposure-response

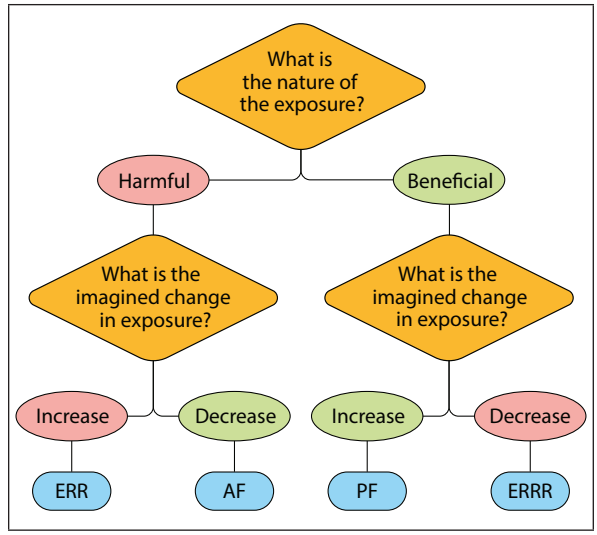

Figure 2
Classification and calculation of health impacts: general framework.
AF: attributable fraction; *ERR*: excess relative risk; *ERRR*: excess reciprocal relative risk; *PF*: preventable fraction.

$$ERR = \frac{AR}{R0} = \frac{R1 - R0}{R0} = \frac{R1}{R0} - 1 = RR - 1 \quad (5)$$

$$ERR = \frac{AR}{R0} = \frac{R1 - R0}{R0} = \frac{\frac{R1 - R0}{R1}}{\frac{R0}{R1}} = \frac{1 - \frac{R0}{R1}}{\frac{R0}{R1}} = \frac{1 - \frac{1}{RR}}{\frac{1}{RR}} = \frac{1 - RRR}{RRR} \quad (6)$$

$$AF = \frac{AR}{R1} = \frac{R1 - R0}{R1} = \frac{\frac{R1 - R0}{R0}}{\frac{R1}{R0}} = \frac{\frac{R1}{R0} - 1}{\frac{R1}{R0}} = \frac{RR - 1}{RR} \quad (7)$$

$$AF = \frac{AR}{R1} = \frac{R1 - R0}{R1} = 1 - \frac{R0}{R1} = 1 - \frac{1}{RR} = 1 - RRR \quad (8)$$

$$PF = \frac{-AR}{R0} = \frac{PR}{R0} = \frac{R0 - R1}{R0} = 1 - \frac{R1}{R0} = 1 - RR \quad (9)$$

$$PF = \frac{-AR}{R0} = \frac{PR}{R0} = \frac{R0 - R1}{R0} = \frac{\frac{R0 - R1}{R1}}{\frac{R0}{R1}} = \frac{\frac{R0}{R1} - 1}{\frac{R0}{R1}} = \frac{\frac{1}{RR} - 1}{\frac{1}{RR}} = \frac{RRR - 1}{RRR} \quad (10)$$

$$ERRR = \frac{-AR}{R1} = \frac{PR}{R1} = \frac{R0 - R1}{R1} = \frac{\frac{R0 - R1}{R0}}{\frac{R1}{R0}} = \frac{1 - \frac{R1}{R0}}{\frac{R1}{R0}} = \frac{1 - RR}{RR} \quad (11)$$

$$ERRR = \frac{-AR}{R1} = \frac{PR}{R1} = \frac{R0 - R1}{R1} = \frac{R0}{R1} - 1 = \frac{1}{RR} - 1 = RRR - 1 \quad (12)$$

Table 1
Classification and calculation of health impacts: detailed framework

Type of health impact assessment	Nature of the exposure	Baseline exposure and outcome (reality)	Counterfactual exposure and outcome (what-if)	Imagined change in exposure	Relative excess measure of effect	Health impacts
1)	Harmful	Non-exposed	Exposed	Increase	Excess relative risk	Attributable cases (they would be attributable and in excess)
2)	Harmful	Exposed	Non-exposed	Decrease	Attributable fraction	Attributable cases (they are attributable and a fraction)
3)	Beneficial	Non-exposed	Exposed	Increase	Preventable fraction	Preventable cases (they are preventable and a fraction)
4)	Beneficial	Exposed	Non-exposed	Decrease	Excess reciprocal relative risk	Preventable cases (they would be preventable and in excess)

functions and example equations using the natural logarithm are reported in *Note 2 available online as Supplementary Materials*. Practical examples of calculation of health impacts using meta-analytic relative risks [27, 28] are reported in *Table 2* and commented in *Note 3 available online as Supplementary Materials*.

The relative risk (*RR*) and the reciprocal relative risk (1/*RR* or *RRR*) to be used in calculating the relative excess measures of effect can be estimated for the difference (*Δ*) between the exposure and the non-exposure by using an exposure-response function (*f*). The exposure difference (*Δ*) is between the counterfactual exposure (*CE*) and the baseline exposure (*BE*) when imagining an increase in exposure, and between the baseline (*BE*) exposure and the counterfactual exposure (*CE*) when imagining a decrease in exposure (equations 13 and 14).

Attributable cases when imagining an increase in exposure (excess)

This type of health impact assessment imagines an increase in a harmful exposure, from non-exposure to exposure. The excess relative risk (*ERR*) could be calculated by using the estimated relative risk or reciprocal relative risk (*RR*–1 or (1–*RRR*)/*RRR*) for the difference (*Δ*) between the counterfactual exposure (the counterfactual level of exposure that is imagined, the exposure corresponding to *R*1) and the baseline exposure (the actual level of exposure that is observed, the non-exposure corresponding to *R*0) in the same population of size *N*. Basically, here the baseline scenario refers to the non-exposure (reality) and the counterfactual scenario refers to the exposure (what-if).

Considering the baseline cases (*BC*, which are the non-exposed cases *C*0), the baseline risk (*BR*, the non-exposed risk *R*0), the counterfactual cases (*CC*, the exposed cases *C*1) and the counterfactual risk (*CR*, the exposed risk *R*1), the excess relative risk can be defined according to equations 15 and 16.

The attributable cases (*AC*) can be calculated by using the excess relative risk and the baseline risk or cases according to equations 17 and 18.

These attributable cases (excess) represent the cases that do not occur under the baseline exposure (non-exposure) and that would be caused by the difference (*Δ*) between the counterfactual exposure (exposure) and the baseline exposure (non-exposure). Under the counterfactual exposure, these cases would be attributable to this difference and in excess of the baseline cases.

Attributable cases when imagining a decrease in exposure (fraction)

This type of health impact assessment imagines a decrease in a harmful exposure, from exposure to non-exposure. The attributable fraction (*AF*) could be calculated by using the estimated relative risk or reciprocal relative risk ((*RR*–1)/*RR* or *1–RRR*) for the difference (*Δ*) between the baseline exposure (the actual level of

Table 2
Classification and calculation of health impacts: practical examples

Type of health impact assessment	Nature of the exposure	Exposure variable	Baseline exposure (reality)	Baseline outcome (reality)	Counterfactual exposure (what if)	Exposure difference (Δ)	Relative risk [27, 28]	Relative excess measure of effect	Health impacts
1)	Harmful	$PM_{2.5}$ (air pollution)	15 μg/m³	1,000 deaths	25 μg/m³	10 μg/m³	1.08	ERR=1.08–1=0.080	AC=80 deaths
2)	Harmful	$PM_{2.5}$ (air pollution)	15 μg/m³	1,000 deaths	5 μg/m³	10 μg/m³	1.08	AF=(1.08–1)/1.08=0.074	AC=74 deaths
3)	Beneficial	NDVI (greenness)	0.3	1,000 deaths	0.4	0.1	0.96	PF=(1–0.96)=0.040	PC=40 deaths
4)	Beneficial	NDVI (greenness)	0.3	1,000 deaths	0.2	0.1	0.96	ERRR=(1–0.96)/0.96=0.042	PC=42 deaths

AC: attributable cases; *AF*: attributable fraction; *ERR*: excess relative risk; *ERRR*: excess reciprocal relative risk; *NDVI*: normalized difference vegetation index; *PC*: preventable cases; *PF*: preventable fraction; *PM*: particulate matter; Time: 1 year; *Δ*: difference between exposure and non-exposure.

exposure that is observed, the exposure corresponding to $R1$) and the counterfactual exposure (the counterfactual level of exposure that is imagined, the non-exposure corresponding to $R0$) in the same population of size N. Basically, here the baseline scenario refers to the exposure (reality) and the counterfactual scenario refers to the non-exposure (what-if).

Considering the baseline cases (BC, which are the exposed cases $C1$), the baseline risk (BR, the exposed risk $R1$), the counterfactual cases (CC, the non-exposed cases $C0$) and the counterfactual risk (CR, the non-exposed risk $R0$), the attributable fraction can be defined according to equations 19 and 20.

The attributable cases (AC) can be calculated by using the attributable fraction and the baseline risk or cases according to equations 21 and 22.

These attributable cases (fraction) represent the cases that would not occur under the counterfactual exposure (non-exposure) and that are caused by the difference (Δ) between the baseline exposure (exposure) and the counterfactual exposure (non-exposure). Under the baseline exposure, these cases are attributable to this difference and a fraction of the baseline cases.

Preventable cases when imagining an increase in exposure (fraction)

This type of health impact assessment imagines an increase in a beneficial exposure, from non-exposure to exposure. The preventable fraction (PF) could be calculated by using the estimated relative risk or reciprocal relative risk (1–RR or (RRR–1)/RRR) for the difference (Δ) between the counterfactual exposure (the counterfactual level of exposure that is imagined, the exposure corresponding to $R1$) and the baseline exposure (the actual level of exposure that is observed, the non-exposure corresponding to $R0$) in the same population of size N. Basically, here the baseline scenario refers to the non-exposure (reality) and the counterfactual scenario refers to the exposure (what-if).

Considering the baseline cases (BC, which are the non-exposed cases $C0$), the baseline risk (BR, the non-exposed risk $R0$), the counterfactual cases (CC, the ex-

$$RR = \frac{R1}{R0} = f(BE, \Delta) \tag{13}$$

$$RRR = \frac{R0}{R1} = \frac{1}{f(BE, \Delta)} \tag{14}$$

$$ERR = \frac{AR}{R0} = \frac{R1 - R0}{R0} = \frac{\frac{C1 - C0}{N}}{\frac{C0}{N}} = \frac{\frac{AC}{N}}{\frac{C0}{N}} = \frac{AC}{C0} \tag{15}$$

$$ERR = \frac{AR}{BR} = \frac{CR - BR}{BR} = \frac{\frac{CC - BC}{N}}{\frac{BC}{N}} = \frac{\frac{AC}{N}}{\frac{BC}{N}} = \frac{AC}{BC} \tag{16}$$

$$AC = \frac{AC}{N} \times N = AR \times N = \frac{AR}{R0} \times R0 \times N = ERR \times R0 \times N = ERR \times BR \times N \tag{17}$$

$$AC = \frac{AC}{C0} \times C0 = ERR \times C0 = ERR \times BC \tag{18}$$

$$AF = \frac{AR}{R1} = \frac{R1 - R0}{R1} = \frac{\frac{C1 - C0}{N}}{\frac{C1}{N}} = \frac{\frac{AC}{N}}{\frac{C1}{N}} = \frac{AC}{C1} \tag{19}$$

$$AF = \frac{AR}{BR} = \frac{BR - CR}{BR} = \frac{\frac{BC - CC}{N}}{\frac{BC}{N}} = \frac{\frac{AC}{N}}{\frac{BC}{N}} = \frac{AC}{BC} \tag{20}$$

$$AC = \frac{AC}{N} \times N = AR \times N = \frac{AR}{R1} \times R1 \times N = AF \times R1 \times N = AF \times BR \times N \tag{21}$$

$$AC = \frac{AC}{C1} \times C1 = AF \times C1 = AF \times BC \tag{22}$$

posed cases *C*1) and the counterfactual risk (*CR*, the exposed risk *R*1), the preventable fraction can be defined according to equations 23 and 24.

The preventable cases (*PC*) can be calculated by using the preventable fraction and the baseline risk or cases according to equations 25 and 26.

These preventable cases (fraction) represent the cases that occur under the baseline exposure (non-exposure) and that would be prevented by the difference (*Δ*) between the counterfactual exposure (exposure) and the baseline exposure (non-exposure). Under the baseline exposure, these cases are preventable by this difference and a fraction of the baseline cases.

Preventable cases when imagining a decrease in exposure (excess)

This type of health impact assessment imagines a decrease in a beneficial exposure, from exposure to non-exposure. The excess reciprocal relative risk (*ERRR*) could be calculated by using the estimated relative risk or reciprocal relative risk ((1-*RR*)/*RR* or *RRR*-1) for the difference (*Δ*) between the baseline exposure (the actual level of exposure that is observed, the exposure corresponding to *R*1) and the counterfactual exposure (the counterfactual level of exposure that is imagined, the non-exposure corresponding to *R*0) in the same population of size *N*. Basically, here the baseline scenario refers to the exposure (reality) and the counterfactual scenario refers to the non-exposure (what-if).

Considering the baseline cases (*BC*, which are the exposed cases *C*1), the baseline risk (*BR*, the exposed risk *R*1), the counterfactual cases (*CC*, the non-exposed cases *C*0) and the counterfactual risk (*CR*, the non-exposed risk *R*0), the excess reciprocal relative risk can be defined according to equations 27 and 28.

The preventable cases (*PC*) can be calculated by using the excess reciprocal relative risk and the baseline risk or cases according to equations 29 and 30.

These preventable cases (excess) represent the cases that would occur under the counterfactual exposure (non-exposure) and that are prevented by the difference (*Δ*) between the baseline exposure (exposure) and the counterfactual exposure (non-exposure). Under the counterfactual exposure, these cases would be preventable by this difference and in excess of the baseline cases.

Calculation of health impacts using data at different spatial resolutions

When the population and exposure data are more detailed (population level) than the baseline outcome data (area level), the effect measures to be used in the above equations (area level) can be estimated by using two different approaches, marginal or conditional. Equations using the natural logarithm are reported in *Note*

$$PF = \frac{-AR}{R0} = \frac{PR}{R0} = \frac{R0 - R1}{R0} = \frac{\frac{C0 - C1}{N}}{\frac{C0}{N}} = \frac{\frac{-AC}{N}}{\frac{C0}{N}} = \frac{\frac{PC}{N}}{\frac{C0}{N}} = \frac{PC}{C0} \quad (23)$$

$$PF = \frac{-AR}{BR} = \frac{PR}{BR} = \frac{BR - CR}{BR} = \frac{\frac{BC - CC}{N}}{\frac{BC}{N}} = \frac{\frac{-AC}{N}}{\frac{BC}{N}} = \frac{\frac{PC}{N}}{\frac{BC}{N}} = \frac{PC}{BC} \quad (24)$$

$$PC = \frac{PC}{N} \times N = PR \times N = \frac{PR}{R0} \times R0 \times N = PF \times R0 \times N = PF \times BR \times N \quad (25)$$

$$PC = \frac{PC}{C0} \times C0 = PF \times C0 = PF \times BC \quad (26)$$

$$ERRR = \frac{-AR}{R1} = \frac{PR}{R1} = \frac{R0 - R1}{R1} = \frac{\frac{C0 - C1}{N}}{\frac{C1}{N}} = \frac{\frac{-AC}{N}}{\frac{C1}{N}} = \frac{\frac{PC}{N}}{\frac{C1}{N}} = \frac{PC}{C1} \quad (27)$$

$$ERRR = \frac{-AR}{BR} = \frac{PR}{BR} = \frac{CR - BR}{BR} = \frac{\frac{CC - BC}{N}}{\frac{BC}{N}} = \frac{\frac{-AC}{N}}{\frac{BC}{N}} = \frac{\frac{PC}{N}}{\frac{BC}{N}} = \frac{PC}{BC} \quad (28)$$

$$PC = \frac{PC}{N} \times N = PR \times N = \frac{PR}{R1} \times R1 \times N = ERRR \times R1 \times N = ERRR \times BR \times N \quad (29)$$

$$PC = \frac{PC}{C1} \times C1 = ERRR \times C1 = ERRR \times BC \quad (30)$$

2 available online as Supplementary Materials. A graphical representation of these measures with numerical examples is shown in *Figure 3* and commented in *Note 4 available online as Supplementary Materials*.

The marginal approach

For the area unit (a), the population-weighted baseline ($PWBE_a$) and counterfactual ($PWCE_a$) exposures can be calculated as a weighted mean of the baseline (BE_{pa}) and counterfactual (CE_{pa}) exposures, respectively, in the n population units included in a (p_a). For the area unit (a), the population-weighted exposure difference ($PW\Delta_a$) can be calculated as a weighted mean of the difference (Δ_{pa}) between the counterfactual (CE_{pa}) and baseline (BE_{pa}) exposures when imagining an increase in exposure, or vice versa when imagining a de-

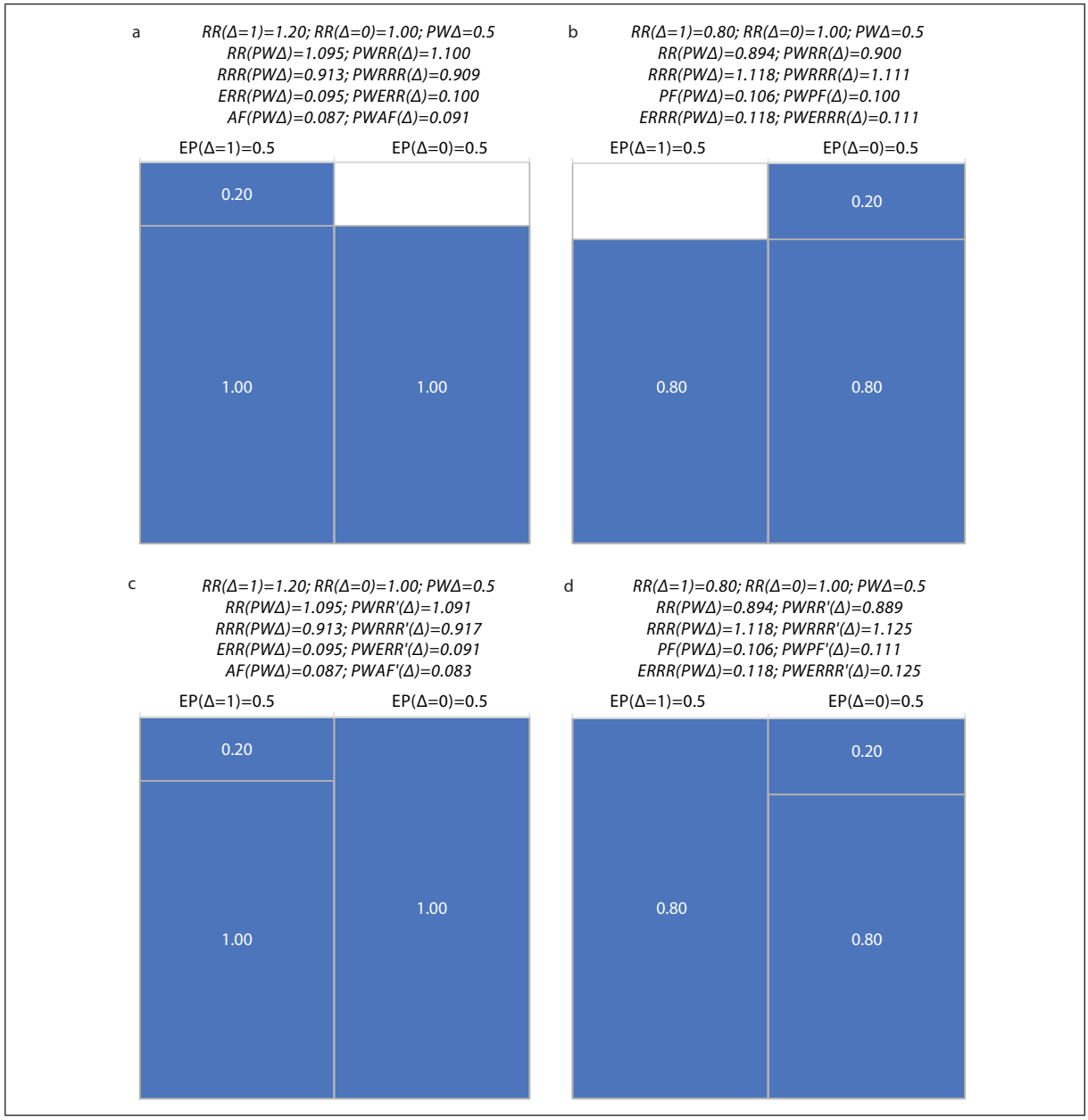

Figure 3

Relative excess measures of effect from marginal approach (PWΔ, RR, RRR, ERR, AF, PF, ERRR), conditional approach with same non-exposed risk (PWRR, PWRRR, PWERR, PWAF, PWPF, PWERRR), and conditional approach with same exposed risk (PWRR', PWRRR', PWERR', PWAF', PWPF', PWERRR'), for a harmful exposure (charts a and c) and for a beneficial exposure (b and d), by assuming in the conditional approach the same non-exposed risk (a and b) or the same exposed risk (c and d). For each chart and column (exposed population unit), the coloured area represents the risk in the exposed and the sum of white numbers is the relative risk. Relative risks are hypothetical and assumed to be natural-log-linearly modelled.

AF: attributable fraction; *EP*: exposure prevalence; *ERR*: excess relative risk; *ERRR*: excess reciprocal relative risk; *PF*: preventable fraction; *PW*: population-weighted; *RR*: relative risk; *RRR*: reciprocal relative risk; *X-axis*: population exposed; *Y-axis*: risk of the outcome; *Δ*: difference between exposure and non-exposure.

crease in exposure, in the n population units included in a (p_a). For each p_a, the weight of the weighted means is the population (POP_{pa}). This formulation is equivalent to using the exposure prevalence (EP_{pa}) corresponding to each p_a, which is the ratio of the population of p_a (POP_{pa}) to the total population of a (POP_a) (equations 31-37).

For the area unit (a), by using the exposure-response function (f_a), the relative risk (RR_a), the reciprocal relative risk ($1/RR_a$ or RRR_a) and the relative excess measures of effect (ERR_a,AF_a,PF_a,$ERRR_a$) can be estimated for the population-weighted exposure difference ($PW\Delta_a$). These effect measures can be interpreted in terms of non-exposed risk ($R0_a$) and exposed risk ($R1_a$) at the area level (a) (equations 38-43).

The conditional approach

For each population unit (p_a) included in the area unit (a), the difference (Δ_{pa}) between the counterfactual (CE_{pa}) and baseline (BE_{pa}) exposures when imagining an increase in exposure, or vice versa when imagining a decrease in exposure, can be calculated.

$$EP_{p_a} = POP_{p_a}/POP_a = POP_{p_a} \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) \tag{31}$$

$$\sum_{p_a=1}^{n} (EP_{p_a}) = 1 \tag{32}$$

$$PWBE_a = \sum_{p_a=1}^{n} (BE_{p_a} \times POP_{p_a}) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} (BE_{p_a} \times EP_{p_a}) \tag{33}$$

$$PWCE_a = \sum_{p_a=1}^{n} (CE_{p_a} \times POP_{p_a}) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} (CE_{p_a} \times EP_{p_a}) \tag{34}$$

$$PW\Delta_a = \sum_{p_a=1}^{n} (\Delta_{p_a} \times POP_{p_a}) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} (\Delta_{p_a} \times EP_{p_a}) \tag{35}$$

$$PW\Delta_a = \sum_{p_a=1}^{n} (\Delta_{p_a} \times EP_{p_a}) = \sum_{p_a=1}^{n} ((CE_{p_a} - BE_{p_a}) \times EP_{p_a}) = \sum_{p_a=1}^{n} (CE_{p_a} \times EP_{p_a}) - \sum_{p_a=1}^{n} (BE_{p_a} \times EP_{p_a}) = PWCE_a - PWBE_a \tag{36}$$

$$PW\Delta_a = \sum_{p_a=1}^{n} (\Delta_{p_a} \times EP_{p_a}) = \sum_{p_a=1}^{n} ((BE_{p_a} - CE_{p_a}) \times EP_{p_a}) = \sum_{p_a=1}^{n} (BE_{p_a} \times EP_{p_a}) - \sum_{p_a=1}^{n} (CE_{p_a} \times EP_{p_a}) = PWBE_a - PWCE_a \tag{37}$$

$$RR_a = \frac{R1_a}{R0_a} = f_a(PWBE_a, PW\Delta_a) \tag{38}$$

$$RRR_a = \frac{R0_a}{R1_a} = \frac{1}{f_a(PWBE_a, PW\Delta_a)} \tag{39}$$

$$ERR_a = RR_a - 1 = \frac{1 - RRR_a}{RRR_a} \tag{40}$$

$$AF_a = \frac{RR_a - 1}{RR_a} = 1 - RRR_a \tag{41}$$

$$PF_a = 1 - RR_a = \frac{RRR_a - 1}{RRR_a} \tag{42}$$

$$ERRR_a = \frac{1 - RR_a}{RR_a} = RRR_a - 1 \tag{43}$$

For each population unit (p_a) included in the area unit (a), by using the exposure-response function (f_{p_a}), the relative risk (RR_{p_a}), the reciprocal relative risk ($1/RR_{p_a}$ or RRR_{p_a}) and the relative excess measures of effect (ERR_{p_a},AF_{p_a},PF_{p_a},$ERRR_{p_a}$) can be estimated for the exposure difference (Δ_{p_a}). These effect measures can be interpreted in terms of non-exposed risk ($R0_{p_a}$) and exposed risk ($R1_{p_a}$) at the population level (p_a) (equations 44-49).

For the area unit (a), when assuming the same non-exposed risk ($R0_a$) in all the p_a, the population-weighted relative risk ($PWRR_a$), reciprocal relative risk ($PWRRR_a$) and relative excess measure of effect ($PWERR_a$,$PWAF_a$,$PWPF_a$,$PWERRR_a$) can be calculated by using the relative risks (RR_{p_a}) and the excess measures of effect relative to the non-exposed risk (ERR_{p_a},PF_{p_a}) in the n population units p_a. These population-weighted effect measures can be interpreted in terms of non-exposed risk ($R0_a$) and population-weighted exposed risk ($PWR1_a$) at the area level (a). For each p_a, the weight of the weighted means is the population (POP_{p_a}). This formulation is equivalent to using the exposure prevalence (EP_{p_a}) corresponding to each p_a, which is the ratio of the population of p_a (POP_{p_a}) to the total population of a (POP_a) (equations 50-55).

For the area unit (a), when assuming the same exposed risk ($R1_a$) in all the p_a, the population-weighted reciprocal relative risk ($PWRRR'_a$), relative risk ($PWRR'_a$), and relative excess measure of effect ($PWERR'_a$, $PWAF'_a$, $PWPF'_a$, $PWERRR'_a$) can be calculated by using the reciprocal relative risks ($1/RR_{p_a}$ or RRR_{p_a}) and the excess measures of effect relative to the exposed risk (AF_{p_a}, $ERRR_{p_a}$) in the n population units p_a. These population-weighted effect measures can be interpreted in terms of exposed risk ($R1_a$) and population-weighted non-exposed risk ($PWR0_a$) at the area level (a). For each p_a, the weight of the weighted means is the population (POP_{p_a}). This formulation is equivalent to using the exposure prevalence (EP_{p_a}) corresponding to each p_a, which is the ratio of the population of p_a (POP_{p_a}) to the total population of a (POP_a) (equations 56-61).

$$RR_{p_a} = \frac{R1_{p_a}}{R0_{p_a}} = f_{p_a}(BE_{p_a}, \Delta_{p_a}) \tag{44}$$

$$RRR_{p_a} = \frac{R0_{p_a}}{R1_{p_a}} = \frac{1}{f_{p_a}(BE_{p_a}, \Delta_{p_a})} \tag{45}$$

$$ERR_{p_a} = RR_{p_a} - 1 = \frac{1 - RRR_{p_a}}{RRR_{p_a}} \tag{46}$$

$$AF_{p_a} = \frac{RR_{p_a} - 1}{RR_{p_a}} = 1 - RRR_{p_a} \tag{47}$$

$$PF_{p_a} = 1 - RR_{p_a} = \frac{RRR_{p_a} - 1}{RRR_{p_a}} \tag{48}$$

$$ERRR_{p_a} = \frac{1 - RR_{p_a}}{RR_{p_a}} = RRR_{p_a} - 1 \tag{49}$$

$$PWRR_a = \sum_{p_a=1}^{n} \left(\frac{R1_{p_a}}{R0_a} \times POP_{p_a}\right) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} \left(\frac{R1_{p_a}}{R0_a} \times EP_{p_a}\right) = \frac{PWR1_a}{R0_a} = \sum_{p_a=1}^{n} (RR_{p_a} \times EP_{p_a}) \tag{50}$$

$$PWRRR_a = \frac{R0_a}{PWR1_a} = \frac{1}{PWRR_a} \tag{51}$$

$$PWERR_a = \sum_{p_a=1}^{n} (ERR_{p_a} \times POP_{p_a}) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} (ERR_{p_a} \times EP_{p_a}) = \sum_{p_a=1}^{n} \left((RR_{p_a} - 1) \times EP_{p_a}\right) = PWRR_a - 1 = \frac{1 - PWRRR_a}{PWRRR_a} \tag{52}$$

$$PWAF_a = \frac{PWRR_a - 1}{PWRR_a} = 1 - PWRRR_a \tag{53}$$

$$PWPF_a = \sum_{p_a=1}^{n} (PF_{p_a} \times POP_{p_a}) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} (PF_{p_a} \times EP_{p_a}) = \sum_{p_a=1}^{n} \left((1 - RR_{p_a}) \times EP_{p_a}\right) = 1 - PWRR_a = \frac{PWRRR_a - 1}{PWRRR_a} \tag{54}$$

$$PWERRR_a = \frac{1 - PWRR_a}{PWRR_a} = PWRRR_a - 1 \tag{55}$$

$$PWRRR'_a = \sum_{p_a=1}^{n} \left(\frac{R0_{p_a}}{R1_a} \times POP_{p_a}\right) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} \left(\frac{R0_{p_a}}{R1_a} \times EP_{p_a}\right) = \frac{PWR0_a}{R1_a} = \sum_{p_a=1}^{n} (RRR_{p_a} \times EP_{p_a}) \quad (56)$$

$$PWRR'_a = \frac{R1_a}{PWR0_a} = \frac{1}{PWRRR'_a} \quad (57)$$

$$PWERR'_a = \frac{1 - PWRRR'_a}{PWRRR'_a} = PWRR'_a - 1 \quad (58)$$

$$PWAF'_a = \sum_{p_a=1}^{n} (AF_{p_a} \times POP_{p_a}) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} (AF_{p_a} \times EP_{p_a}) = \sum_{p_a=1}^{n} ((1 - RRR_{p_a}) \times EP_{p_a}) = 1 - PWRRR'_a = \frac{PWRR'_a - 1}{PWRR'_a} \quad (59)$$

$$PWPF'_a = \frac{PWRRR'_a - 1}{PWRRR'_a} = 1 - PWRR'_a \quad (60)$$

$$PWERRR'_a = \sum_{p_a=1}^{n} (ERRR_{p_a} \times POP_{p_a}) \Big/ \sum_{p_a=1}^{n} (POP_{p_a}) = \sum_{p_a=1}^{n} (ERRR_{p_a} \times EP_{p_a}) = \sum_{p_a=1}^{n} ((RRR_{p_a} - 1) \times EP_{p_a}) = PWRRR'_a - 1 = \frac{1 - PWRR'_a}{PWRR'_a} \quad (61)$$

DISCUSSION

Health impact assessment can be thought as a "reverse" study design, where an exposure-response function and the outcome data under one exposure scenario are combined to estimate the change in outcome data under an alternative exposure scenario. This paper aims to fill gaps in the HIA literature by proposing a systematic classification of effect measures, reporting a standard conceptual framework, and addressing spatial resolution challenges. The present work proposes a simple approach with four situations based on the nature of the exposure and the imagined change in exposure. In addition, two possible approaches to the problem of different spatial resolutions are proposed. These contributions are expected to improve the robustness and applicability of health impact assessment in different contexts.

Furthermore, the proposed classifications are of epidemiological interest beyond health impact assessment. The functional classification of the four relative excess effect measures and the proposed definitions for preventable risk, reciprocal relative risk and excess reciprocal relative risk could potentially contribute to promoting standard epidemiological terminology. The marginal and conditional approaches were essentially based on and extended the definitions of attributable fractions for the exposed and population, respectively [11]. Our proposal sought to extend the framework to the other relative excess measures of effect. Furthermore, the common definition of the population attributable fraction basically assumed the same non-exposed risk among population units, whereas the present work also explores the assumption of the same exposed risk. In summary, the proposed epidemiological definitions aim to provide a comprehensive and general framework for the relative excess measures of effect.

From a practical point of view for HIA purposes, the difference between *AF* and *ERR*, or between *PF* and *ERRR*, may be negligible with relative risks close to one. Furthermore, it may not always be possible to use baseline outcome data that strictly match to the available non-exposure or exposure scenarios, e.g., non-exposure may be at time 1, baseline outcome data at time 2 and exposure at time 3. A possible solution could be to assume that the available baseline risk is equal to the non-exposed or exposed risk, whichever is assumed to be more similar. In addition, this work explicitly considers a single counterfactual scenario and a single exposure variable for each unit, but an analogous methodology could be applied to multiple counterfactuals and exposures. With regard to the different levels of measurement, the marginal approach may be more general and easier to apply, as it could be mathematically simpler to calculate and doesn't require specific assumptions about the distribution of risks across population units. This last point may be important because risks are, by their nature, highly variable across the population, depending on a whole range of unmeasured variables. The marginal approach can produce effect measures that are somehow an average of the estimates derived from the two possible conditional approaches. A recent work reported both marginal approach (main analysis) and conditional approach (sensitivity analysis) in calculating the mortality impacts of increasing residential greenness for the whole of Italy, with a difference of 1.3% in the estimates [8].

Our results are also consistent with several guidelines and publications [1-24]. While most of the HIA literature focuses on air pollution, the framework and methods developed in the present study can be extended virtually to all other environmental and social determinants of health. Future research could explore health impact assessment in areas such as noise pollution, urban planning, and climate change [29]. The versatility of the proposed framework allows it to be adapted to different types of exposures, thereby increasing its utility across different sectors. The main strength of the present study is that it proposes a simple, standardized

and general approach to health impact assessment that is applicable to virtually all exposures.

In this regard, advances in computational tools and technologies, such as geographic information systems, machine learning, and big data analytics, offer new opportunities to enhance health impact assessment. These tools can improve the accuracy of exposure and outcome assessments, facilitate the analysis of complex datasets, estimate more tailored and accurate exposure-response functions and provide more detailed spatial and temporal analyses. Future studies should explore the integration of these technologies into the HIA framework to improve its effectiveness and accuracy. For example, the Global Human Settlement (GHS) population grid is a European Commission product that shows the distribution of residential population, expressed as the number of people per cell [26]. When the GHS population grid is used for exposure assessment in conjunction with satellite exposure data, there is no need to georeferenced the local population or to address privacy concerns [8]. In fact, this makes it possible to approximate exposure at the municipal level using public population data thar are freely available worldwide at high resolution [8, 26]. The sole outcome information required can be used after aggregation to the municipal level [25]. With the most recent data provided by health and statistical agencies, the HIA can be applied worldwide.

Our proposed standard framework is in line with common HIA approaches reported by different guidelines and documents [1-8, 13-23]. For example, the same framework (use of meta-analytic relative risks to estimate health impacts) has been reported by WHO in the officially provided tools for HIA on air quality (AirQ+) [2]. The WHO HRAPIE (health risks of air pollution in Europe) document on exposure-response functions [3] recommended the same approach and basically provided for air pollutants a list of available metanalytic relative risks for air pollutants to be used in HIA. However, further research is essential and recommended for the future to explore the associations between multiple exposures and health and to provide more reliable exposure-response functions, thus enabling more accurate and complete assessments.

Indeed, there are limitations to the proposed approach, both in terms of the HIA framework and to the quality of the input elements (populations, exposures, outcomes, functions). The accuracy of the HIA is highly dependent on the quality and availability of data and functions. Poor quality of these elements can be a challenge. Future studies should focus on improving data harmonization, estimating exposure-response functions, and developing robust methodologies to fill data gaps. Collaboration between public health agencies, environmental monitoring agencies, and academic institutions is crucial to ensure comprehensive and high quality data for health impact assessment.

One limitation may be the uncertainty of the exposure estimation. The "original sin" of most environmental epidemiology studies may be to use residential exposure as a proxy for total individual exposure, even though people spend only part of their time at home. Another important limitation is the uncertainty in the estimates due to uncertainty in the exposure-response function estimation (confounding, selection and information bias, heterogeneity) and utilization (non-transportability) [9-12]. These limitations are related to the counterfactual definitions of effect measures and to the assumptions described in the *Methods* section. It is therefore crucial to use the more reliable and accurate exposure-response functions from properly conducted analytical studies and meta-analyses when conducting health impact assessment. However, due to the complex nature of the relationship between exposures and health outcomes, some degree of uncertainty remains inherent and unavoidable in health impact assessment. Therefore, future research should also focus on developing methods to quantify and communicate these limits in HIA results. In addition, the marginal and conditional approaches are essentially methods for calculating health impacts when the outcome data are not available at the same spatial detail as the population and exposure data. However, these outcome data could potentially be downscaled to some extent by using other variables not directly included in the health impact assessment. The potential of machine learning models could help in this sense in the future.

With these perspectives in mind, this paper can make an important contribution to the field of health impact assessment by providing a systematic classification of relative excess measures of effect, developing a standardized and evidence-based conceptual framework, and elaborating standard solutions for dealing with different spatial resolutions. Key findings and proposals include a clear and systematic classification that improves the understanding and use of relative excess measures in health impact assessment; a simple conceptual framework that addresses different research questions, making assessments more robust and applicable across different contexts and exposures, and the estimates comparable across different studies; and different analytical solutions for dealing with different levels of spatial detail in HIA that improve the accuracy and reliability of the health impact estimates.

By addressing all these aspects, the study fills existing gaps in the HIA literature and provides a foundation for future research and practice. The proposed methods and frameworks are designed to be applicable to a range of different situations, ensuring their relevance in various settings and applications. As health impact assessment continues to evolve, the insights and tools provided in this paper could help guide more effective and equitable health impact assessments, ultimately contributing to better public health decisions and outcomes.

Conflict of interest statement

The Author declares no competing interests.

Data availability

Not applicable.

Code availability

Not applicable.

Acknowledgments

Special thanks to Lucia Bisceglia, Ida Galise, Sante Minerba, and the Environmental Epidemiology Working Group of Apulia Region (Italy), whose work inspired me. The opinions expressed in this article are my own and do not necessarily reflect the views of the institutions with which the author is affiliated.

Received on 4 November 2024.
Accepted on 20 January 2025.

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