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Supplementary Materials for

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

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This PDF file includes:

Supplementary Notes 1, 2, 3 and 4

SUPPLEMENTARY MATERIALS

Supplementary note 1

In a population of size N, the reciprocal of the attributable risk (AR) or risk difference (RD) or excess risk (ER) is the number needed to harm (NNH) and represents the number of people needed to be exposed to a harmful exposure to cause an attributable case (AC). By using the risks in the exposed ($R1$) and non-exposed ($R0$), or the number of cases in the exposed ($C1$) and non-exposed ($C0$), or the number of attributable cases (AC), it is defined according to supplementary equation 1 [1-5]:

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

In a population of size N, the reciprocal of the negative attributable risk ($-AR$) or preventable risk (PR) is the number needed to benefit (NNB) and represents the number of people needed to be exposed to a beneficial exposure to prevent a negative attributable case ($-AC$) or preventable case (PC). By using the risks in the exposed ($R1$) and non-exposed ($R0$), or the number of cases in the exposed ($C1$) and non-exposed ($C0$), or the number of negative attributable cases ($-AC$) or preventable cases (PC), it is defined according to supplementary equation 2 [1-5]:

$$NNB = \frac{1}{-AR} = \frac{1}{PR} = \frac{1}{R0 - R1} = \frac{1}{\frac{C0}{N} - \frac{C1}{N}} = \frac{1}{\frac{C0 - C1}{N}} = \frac{N}{C0 - C1} = \frac{N}{-AC} = \frac{N}{PC} \quad (2)$$

When the exposure is a treatment, the negative attributable risk ($-AR$) or preventable risk (PR) can be defined as the absolute risk reduction (ARR), and the number needed to benefit (NNB) can be defined as the number needed to treat (NNT) [1-5].

Supplementary note 2

Different exposure-response functions (f) could be used depending on the shape of the relationship between exposure and health outcome and on the study design and analysis. A general notation for different functions is proposed. Exposure-response functions could also be specific to the area unit a (f_a) or to the population unit p_a included in a (f_{p_a}).

When the exposure-response function is natural-log-linearly modelled and the effect of exposure is assumed to be homogeneous across strata, the relative risk for Δ or for $PW\Delta_a$(marginal approach) or for Δ_{p_a}(conditional approach) can be estimated by using the relative risk for unitary exposure (RR_1) according to supplementary equations 3-5 [6, 7]:

$$RR = exp(ln(RR_1) \times \Delta) \quad (3)$$

$$RR_a = exp(ln(RR_1) \times PW\Delta_a) \quad (4)$$

$$RR_{p_a} = exp(ln(RR_1) \times \Delta_{p_a}) \quad (5)$$

Supplementary note 3

In the following the examples presented in *Table 2* are discussed, according to *Table 1* and *Figure 2*. All examples consider a hypothetical population of size *N* with 1,000 baseline cases (BC) of all-cause deaths, a baseline exposure (BE) to $PM_{2.5}$ (fine particulate matter, air pollution) of 15 µg/m^3, and a baseline exposure (BE) to the normalized difference vegetation index (NDVI, greenness) of 0.3.

In example 1, it is imagined an intervention (e.g., opening of a new plant) to increase the harmful baseline exposure (BE) to $PM_{2.5}$ to the counterfactual exposure (CE) of 25 µg/m^3. The exposure difference (Δ) is 10 µg/m^3. The relative risk (RR) is 1.08 [8]. The excess relative risk (ERR) is 0.080. The attributable cases (AC) are 80. This corresponds to type 1 in *Table 1*, and to the scenario of an increase in a harmful exposure in *Figure 2*, using equations 13, 14 and 15 to 18.

In example 2, it is imagined an intervention (e.g., closing of an existing plant) to decrease the harmful baseline exposure (BE) to $PM_{2.5}$ to the counterfactual exposure (CE) of 5 µg/m^3. The exposure difference (Δ) is 10 µg/m^3. The relative risk (RR) is 1.08 [8]. The attributable fraction (AF) is 0.074. The attributable cases (AC) are 74. This corresponds to type 2 in *Table 1*, and to the scenario of a decrease in a harmful exposure in *Figure 2*, using equations 13, 14 and 19 to 22.

In example 3, it is imagined an intervention (e.g., planting of new trees) to increase the beneficial baseline exposure (BE) to NDVI to the counterfactual exposure (CE) of 0.4. The exposure difference (Δ) is 0.1. The relative risk (RR) is 0.96 [9]. The preventable fraction is (PF) is 0.040. The preventable cases (PC) are 40. This corresponds to type 3 in *Table 1*, and to the scenario of an increase in a beneficial exposure in *Figure 2*, using equations 13, 14 and 23 to 26.

In example 4, it is imagined an intervention (e.g., cutting of existing trees) to decrease the beneficial baseline exposure (BE) to NDVI to the counterfactual exposure (CE) of 0.2. The exposure difference (Δ) is 0.1. The relative risk (RR) is 0.96 [9]. The excess reciprocal relative risk ($ERRR$) is 0.042. This corresponds to type 4 in *Table 1*, and to the scenario of a decrease in a beneficial exposure in *Figure 2*, using equations 13, 14 and 27 to 30.

Supplementary note 4

All examples in *Figure 3* consider two hypothetical exposed population units (two columns) with exposure prevalences (EP) of 0.5 and 0.5 and differences (Δ) between exposure and non-exposure of 1 and 0, respectively. For each chart and column (exposed population unit), the coloured area represents the risk in the exposed ($R1$) and the sum of white numbers is the relative risk (RR). In charts *a* and *c* a harmful exposure is considered, in charts *b* and d *a* beneficial exposure. In chart *a* the same non-exposed risk ($R0$) is assumed, so that the non-exposed risks have the same height and the 1.0 component of the RR in the first population unit corresponds to the 1.0 component of the RR in the second population unit. In chart *b* the same non-exposed risk ($R0$) is assumed, so that the non-exposed risks have the same height and the 1.0 component of the RR in the first population unit corresponds to the 1.0 component of the RR in the second population unit. In chart *c* the same exposed risk ($R1$) is assumed, so that the exposed risks have the same height and the 1.2 component of the RR in the first population unit corresponds to the 1.0 component of the RR in the second population unit. In chart *d* the same exposed risk ($R1$) is assumed, so that the exposed risks have the same height and the 0.8 component of the RR in the first population unit corresponds to the 1.0 component of the RR in the second population unit. The exposure-response functions are hypothetical and assumed to be natural-log-linearly modelled. All reported measures can be calculated using equations 31 to 61, and supplementary equations 4 and 5.

All the scenarios shown in *Figure 3* could be assessed using the marginal approach. The conditional approach can be applied to different situations, but it requires more assumptions than the marginal approach. Assuming that risks are homogeneously influenced by the other factors not considered and that the variability of risks in the area depends mainly on the exposure under consideration, the type of assessment according to *Tables 1* and *2* and *Figure 2* can determine the choice of conditional approach to be used.

If the counterfactual exposure (CE) is the same in all population units in the area, the same risk in the non-exposed ($R0$) is assumed using equations 53 and 55 when the counterfactual scenario is the non-exposure (*Figure 3*, charts *a* and *b*, respectively). A hypothetical situation for using equation 53 could be the assessment of an intervention (e.g., closing of an existing plant) to decrease a harmful baseline exposure to $PM_{2.5}$ to a counterfactual exposure, that is equal in all population units in the area (type 2 in *Tables 1* and *2*). A hypothetical situation for using equation 55 could be the assessment of an intervention (e.g., cutting of existing trees) to decrease in each population unit the beneficial baseline exposure to NDVI to a counterfactual exposure, that is equal in all population units in the area (type 4 in *Tables 1* and *2*).

If the counterfactual exposure (CE) is the same in all population units in the area, the same risk in the exposed ($R1$) is assumed using equations 58 and 60 when the counterfactual scenario is the exposure (*Figure 3*, charts *c* and *d*, respectively). A hypothetical situation for using equation 58 could be the assessment of an intervention (e.g., opening of a new plant) to increase in each population unit a harmful baseline exposure to $PM_{2.5}$ to a counterfactual exposure, that is equal in all population units in the area (type 1 in *Tables 1* and *2*). A hypothetical situation for using equation 60 could be the assessment of an intervention (e.g., planting of new trees) to increase in each population unit a beneficial baseline exposure to NDVI to a counterfactual exposure, that is equal in all population units in the area (type 3 in *Tables 1* and *2*).

If the baseline exposure (BE) is the same in all population units in the area, the same risk in the non-exposed ($R0$) is assumed using equations 52 and 54 when the baseline scenario is the non-exposure (*Figure 3*, charts *a* and *b*, respectively). A hypothetical situation for using equation 52 could be the assessment of an intervention (e.g., opening of a new plant) to increase in each population unit a harmful baseline exposure to $PM_{2.5}$, that is equal in all population units in the area, to a counterfactual exposure (type 1 in *Tables 1* and *2*). A hypothetical situation for using equation 54 could be the assessment of an intervention (e.g., planting of new trees) to increase in each population unit a beneficial baseline exposure to NDVI, that is equal in all population units in the area, to a counterfactual exposure (type 3 in *Tables 1* and *2*).

If the baseline exposure (BE) is the same in all population units in the area, the same risk in the exposed ($R1$) is assumed using equations 59 and 61 when the baseline scenario is the exposure (*Figure 3*, charts *c* and *d*, respectively). A hypothetical situation for using equation 59 could be the assessment of an intervention (e.g., closing of an existing plant) to decrease in each population unit a harmful baseline exposure to $PM_{2.5}$, that is equal in all population units in the area, to a counterfactual exposure (type 2 in *Tables 1* and *2*). A hypothetical situation for using equation 61 could be the assessment of an intervention (e.g., cutting of existing trees) to decrease in each population unit a beneficial baseline exposure to NDVI, that is equal in all population units in the area, to a counterfactual exposure (type 4 in *Tables 1* and *2*).

All the scenarios in the examples provided could be assessed using the marginal approach.

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