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From measures of effects to measures of potential impact

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Epidemiology identifies associations between exposure and outcomes by comparing occurrences of outcomes among the exposed and the unexposed. To measure the strength of an association "measures of effect" or "measures of association" are used. These measures do not provide information about the total burden of the public health impact of an exposure in a specific population. "Measures of potential impact" are necessary to translate epidemiological results into policy relevant information.

This Hints & Kinks synthesizes the concepts, assumptions and calculations of measures of impact. It extends basic concepts of risk quantification addressed in two previous articles in this series[1,2]. Table 1 summarizes common, alternative and extended formulas found in basic epidemiology text books[3,4] adapted with a standardized nomenclature[5]. Table 2 presents a made-up numeric example for the tobacco exposure to illustrate the calculation and use of these measures.

Concept, underlying assumptions and caution

At the center of all measures of potential impact is the concept of attributable risk and attributable fraction. These measures allow researchers to answer the question "how much of the risk can be attributed to an exposure?" Attributable risks and fractions can be derived for an exposed group, for those with the disease, or for the total population.

The use of impact measures assumes a causal relationship between the exposure and the outcome with the underlying assumption that this outcome would be prevented if the exposure was removed. Unless based on experimental studies, impact measures should thus exclusively interpreted as predictive measures. The validity of the prediction depends on the quality of the design of the studies on which impact measures are derived (i. e. relative risk), such as the correct control for potential confounders. Because the incidence of almost all diseases is the result of several factors (or exposures) rather than one single factor, there will always be some residual incidence in a group of individuals (background risk). Thus, the use of impact measures also assumes that both the exposed group and the unexposed group have an equal amount of background risk. Validity of this assumption should be tested when using these measures. Caution should also be taken when dealing with multiple exposures, where cases attributable to one risk factor added to other risk factor may explain more than 100 % of all cases. Competition between risk factors is not well understood but necessary for the correct interpretation of impact results. While "attributable numbers", the translation of attributable fractions into case number for a specific population, can be derived for all health outcomes, it should be emphasized that the approach is flawed for mortality given that death can only be postponed rather than prevented. Expression of the risk burden in terms of life years is thus preferable[6].

Attributable risk and fraction for an exposed group

The attributable risk in an exposed group (AR_{exp}), or the incidence of a disease that is attributable to the exposure in an ex-

Table 1. Measures of potential impact [a, b].

Measure	Formula	Measure	Formula
Exposed			
AR_{exp} Attributable risk *or excess risk*	$AR_{exp} = I_1 - I_0$	**EIN** Exposure Impact Number	$EIN = \frac{1}{AR_{exp}}$
Incidence of cases among the exposed attributable to the exposure		*Number of exposed amongst whom one case is due to exposure*	
AF_{exp} Attributable fraction (exposed) [c] *or attributable risk percent or etiologic fraction among the exposed* *or relative risk reduction*	$AF_{exp} = \frac{I_1 - I_0}{I_1}$ or $AF_{exp} = \frac{(RR - 1)}{RR}$	**ECIN** Exposed Case Impact Number	$ECIN = \frac{1}{AF_{exp}}$
Proportion of cases among the exposed attributable to the exposure		*Number of exposed cases amongst whom one case is due to the exposure*	
Total population			
PAR Population attributable risk	$PAR = I - I_0$ or $PAR = AR_{exp} \cdot p_p$	**PIN** Population Impact Number	$PIN = \frac{1}{PAR}$
Incidence of cases observed in the population that are attributable to the exposure		*Number of those in the whole population amongst whom one case is attributable to exposure*	
AF_{pop} Population attributable fraction [c] *or population attributable risk percent*	$AF_{pop} = \frac{I - I_0}{I}$ or $AF_{pop} = \frac{p_p \cdot (RR - 1)}{p_p \cdot (RR - 1) + 1}$ or $AF_{pop} = p_c \cdot AF_{exp}$	**CIN** Case Impact Number	$CIN = \frac{1}{AF_{pop}}$
Proportion of cases in the population attributable to the exposure		*Number of people with the disease in the population for whom one case will be attributable to the exposure factor*	

[a] Nomenclature as in [3]; Impact Number as in [5].
[b] Definitions of abbreviations as follows:
- I_1: Incidence of outcome among the exposed
- I_0: Incidence of outcome among the unexposed
- I: Incidence of outcome in the total population (exposed and unexposed)
- p_p: fraction population exposed
- p_c: fraction cases exposed

[c] For continuous exposure, formulae become:

$$AF_{exp} = \Sigma \frac{(RR_x - 1)}{RR_x} \quad \text{and} \quad AF_{pop} = \frac{\Sigma p_{(x)} \cdot (RR_x - 1)}{\Sigma p_{(x)} \cdot (RR_x - 1) + 1}$$

Where:
RR_x: Relative risk for the health outcome in category c of exposure
$p(_x)$: fraction of the population in category c of exposure

posed group, can be calculated as the incidence in the exposed group (I_1) minus the incidence in the non exposed group (I_0), the latter reflecting the background risk. AR_{exp} can be interpreted as the incidence of cases due to the exposure (among the exposed). To express AR_{exp} as a fraction- the attributable fraction among the exposed (AF_{exp})- it is necessary to divide AR_{exp} by the incidence of the exposed group. AF_{exp} represents the proportion of cases among the exposed attributable to the exposure (see formula in Table 1). In our made-up example we found that 5 of the 30/1,000 (30/1,000 –25/1,1000) incident cases of lung cancer in smokers are attributable to the fact that their smoke. This represents 17 % (5/1,000 divided by 30/1,000) of all lung cancer cases among smokers. I_1 divided by I_0 is also the relative risk (RR), the measure of association between exposed and non exposed provided by epidemiological studies. Transforming AR_{exp} by replacing RR in the AF_{exp} formula, provides an alternative formula for this measure. Attributable risk among the exposed group is generally used when there is a positive causal association between the exposure and the outcome (i.e. RR > 1). If exposure prevents the outcome (RR < 1), one can calculate the preventable fraction as 1–RR.

Table 2. Numeric hypothetical example of impact evaluation.

Example: cases of lung cancer due to smoking			
Incidence in smokers (I_1): 30/1,000 Incidence in non smokers (I_0): 25/1,000 Incidence in population (I): 28/1,000 Relative risk, RR: 1.2 Fraction of smokers in population (p_p): 0.62 Fraction of smokers among cases with lung cancer (p_c): 0.64			
Impact measures		**Results**	**Interpretation**
Exposed	Attributable risk among exposed (AR_{exp})	5/1,000	5 of the 30/1,000 incident cases of lung cancer in smokers are attributable to the fact that their smoke
	Exposure impact number (EIN)	200	for every 200 persons who smoke, there is on average one case of lung cancer attributable to smoking
	Attributable fraction among exposed (AF_{exp})	0.17	17% of cases of lung cancer among smokers are attributed to smoking and could be prevented if their exposure was removed
	Exposed cases impact number (ECIN)	6	for every 6 smokers who have lung cancer, on average one case is attributable to smoking
Total population	Population attributable risk (PAR)	3/1,000	3 of the 28/1,000 incident cases of lung cancer observed in the population are attributable to smoking
	Population impact number (PIN)	333	for every 333 people in the population there is on average one case of lung cancer attributable to smoking per year
	Population attributable fraction (AF_{pop})	0.11	11% of the cases of lung cancer in the population are attributable to smoking
	Case impact number (CIN)	9	for every 9 persons with lung cancer, on average one case is attributable to smoking.

Attributable risk and fraction for the total population

The population attributable risk (PAR) is calculated as the incidence in the population (I) minus the background risk (I_0) and represents the incidence of cases observed in the population that are attributable to the exposure. The population attributable fraction (AF_{pop}) is the ratio of the PAR to the incidence of the outcome in the population (I) and expresses the proportion of cases attributable to the exposure in the population. If one knows or can estimate the total number of cases in a specific population, it is then possible to obtain the number of attributable cases due to exposure. In our example, 3 of the 28/1,000 (28/1,000–25/1,000) incident cases of lung cancer observed in the population are attributable to smoking which represents 11 % (3/1,000 divided by 28/1,000) of all cases of lung cancer in the population. Depending on the data available, alternative formulas to derive AF_{pop} exist. As done for AF_{exp}, the AF_{pop} can be expressed in terms of the RR (Levin´s formula). This formula shows that the impact of the exposure depends on its prevalence among the population. An exposure with a high prevalence may have greater impact than an exposure with a low prevalence even if the RR is smaller. If everybody in a population is exposed, then AF_{pop} is equal to AF_{exp}. AF_{pop} can also be obtained by multiplying AF_{exp} by the fraction of exposed cases (p_c).

Impact numbers

Clinicians often use the number needed to treat (NNT) to express the impact of an intervention. NNT represents how many people need to be treated to prevent one additional outcome of interest. Similar measures called “impact numbers” have been proposed[7] to express attributable risk and fraction in terms of number of events prevented. These measures are based on taking the reciprocal of the attributable measures. Depending on the denominator used impact numbers have different meanings.

The reciprocal of the AR_{exp} is the exposure impact number (EIN) or “the number of individuals with the exposure amongst whom one excess case is due to exposure”. In our made-up example, we found an EIN of 200 meaning that for every 200 persons who smoke, there is on average one case of lung cancer attributable to smoking. The reciprocal of AF_{exp} is the exposed case impact number (ECIN), or “the number of exposed cases amongst whom one case is due to the exposure”, i.e. for every 6 smokers who have lung cancer, on average one case is attributable to smoking. The reciprocal of PAR is the population impact number (PIN) or “the number of those in the whole population amongst whom one case is attributable to exposure to the risk factor”. In our example, we found a PIN of 333 meaning that there is on average one case of lung cancer attributable to smoking per year for every 333 persons. Finally, the reciprocal of the AF_{pop} is the case impact number (CIN), or "the number of people with the disease in the population for whom one case will be attributable to the exposure or risk factor". The CIN in our example was 9; for every 9 persons with lung cancer, on average one case is attributable to smoking.

Extension to continuous exposure

The measures presented above use two levels of exposure (absent/present). These measures can be extended to risk factors with several levels of exposure by summing the attributable risk and proportion derived using each exposure category versus a reference category.

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