Impact numbers: measures of risk factor impact on the whole population from case-control and cohort studies

R F Heller, A J Dobson, J Attia, J Page

Objective: To describe new measures of risk from case-control and cohort studies, which are simple to understand and relate to numbers of the population at risk.

Design: Theoretical development of new measures of risk.

Setting: Review of literature and previously described measures.

Main results: The new measures are: (1) the population impact number (PIN), the number of those in the whole population among whom one case is attributable to the exposure or risk factor; (2) the case impact number (CIN) the number of people with the disease or outcome for whom one case will be attributable to the exposure or risk factor; (3) the exposure impact number (EIN) the number of people with the exposure among whom one excess case is attributable to the exposure; (4) the exposed cases impact number (ECIN) the number of exposed cases among whom one case is attributable to the exposure.

Conclusions: These new measures should help communicate the impact on a population, of estimates of risk derived from cohort or case-control studies.
All those people with the disease, that is, cases

This is a subset of the entire population, see figure 1. The CIN, is “the number of people with the disease for whom one case will be attributable to the exposure or risk factor”. The excess risk attributable to the risk factor for this population is the population attributable fraction (PAF), the fraction of disease in a population attributable to the particular exposure. The CIN is the reciprocal of the PAF and can be written as:

\[
\text{CIN} = \frac{1}{\text{PAF}}
\]

3 All those with the risk factor or exposure

This represents a different subset of the entire population (see fig 1). The EIN, is “the number of individuals with the exposure amongst whom one excess case is due to the exposure”. This is the reciprocal of the absolute risk difference or attributable risk and can thus be written as:

\[
\text{EIN} = \frac{1}{\text{ARD}}
\]

These measures should be qualified by an appropriate timeframe; for example, number of cases per year.

**Examples of the ECIN, EIN, CIN, and PIN in cohort studies**

As an example, let us look at the risk from cigarette smoking on two outcomes, CHD, and lung cancer. In this study, about 30% of the population were smokers (table 1).

For coronary heart disease, the numbers are interpreted as follows:

- **PIN**: for every 1302 people in the community, there is on average one CHD death attributable to smoking per year.
- **EIN**: For every 391 people who smoke, there is on average one death from CHD attributable to the smoking per year.
- **CIN**: For every 6.4 people who die from CHD, on average one is attributable to smoking.
- **ECIN**: For every 2.6 smokers who die from CHD, on average one is attributable to their smoking, or for about every five smokers who die from CHD, two are attributable to their smoking.

For lung cancer, the numbers are interpreted as follows:

- **PIN**: for every 2564 people in the community, there is on average one lung cancer death attributable to smoking per year.
- **EIN**: For every 769 people who smoke, there is on average one death from lung cancer attributable to the smoking per year.
- **CIN**: For every 1.26 people who die from lung cancer, on average one death is attributable to smoking, or for about every five people who die from lung cancer, four are attributable to smoking.
- **ECIN**: For every 1.08 smokers who die from lung cancer, on average one death is attributable to smoking, or for every 14 smokers who die from lung cancer, 13 are attributable to smoking.

**Extending the ECIN, EIN, CIN, and PIN to case-control studies**

In using data from case-control studies, it is necessary to approximate the relative risk, RR, in the formulas by the odds ratio, OR (with the usual assumption that the outcome is
Although we have considered only dichotomous risk factors in the population of interest, the RR, and not on the incidence of the disease or risk factor. We can use the same RR of 1.62 from the previous formulas given above, PIN becomes 1302, EIN becomes 68.67/100000, CIN becomes 9.63, and EIN becomes 9.06 (instead of 6.38), respectively. We have used as an example, the risks of atrial fibrillation and cigarette smoking for stroke in a population based case-control study, where there were 267 cases of stroke in a year among a population of 100,000 aged under 80 years (the rate being 68.66/100000 per 100,000 per year).

Despite the greater risk associated with atrial fibrillation than heavy smoking, suggested by the odds ratios, these new measures indicate that in the total population (PIN), and the population with stroke (CIN), the numbers of people among whom one stroke is attributable to the risk factor are fairly similar; this is because the lower odds ratio for smoking is counter-balanced by the higher prevalence of exposure (table 2). The impact numbers for the exposed populations (EIN) however differ substantially reflecting the differences in odds ratios. The impact numbers for populations with stroke and exposure to each of the risk factors (ECIN) are unaffected by incidence of disease or prevalence of exposure and do not strongly reflect the differences in odds ratios because the odds ratios occur in both the numerator and the denominator.

### Applying the ECIN, EIN, CIN, and PIN to another population

You may wish to use estimates of risk from an observational study to apply to your own setting. Provided that the generalisation is appropriate, you may use the relative risk or odds ratio estimate from the study, with the disease incidence and risk factor prevalence for your own population of interest to calculate the various impact numbers.

To use the example of smoking and CHD mortality given above: assume that in your population of interest, the CHD death rate among non-smokers is 300 per 100,000 per year (instead of 413) and the prevalence of smokers is 20% (instead of 30%). We can use the same RR of 1.62 from the previous study. When we calculate the impact numbers using the formulas given above, PIN becomes 2689 (instead of 1302), CIN becomes 9.06 (instead of 6.38), EIN becomes 538 (instead of 390.6), and the ECIN remains at 2.6 (as it depends solely on the RR, and not on the incidence of the disease or risk factor in the population of interest).

### Extension to continuous risk factors

Although we have considered only dichotomous risk factors (present/absent) the method can easily be extended to risk factors with multiple levels of exposure. If, for example, you wanted to look at the public health impact of homocysteine on CHD deaths, one could use the same formulas and the information for PIN, EIN, CIN, and ECIN to exposed cases. The impact number reflects the number of people in each of those populations among whom one outcome is attributable to the particular risk factor.

### Statistical characteristics

The NNT is a way of reporting benefit (or risk). As a statistic it has rather poor properties; in particular confidence intervals may be difficult to interpret when the difference in effectiveness between treatments is small. The numbers described here have the same limitations. For example, because the formulas use reciprocals if the estimate of excess risk is near zero the impact number will be very large and can be affected strongly even by rounding in the calculations. Also, if the “risk” factor is protective so that the estimate of excess risk is negative, the impact number should be interpreted in terms of outcomes prevented. Confidence limits for impact numbers also have these problems. When the risk estimate is large and positive, it is possible in principle to obtain easily interpretable confidence limits for the impact number. This would entail the calculation of standard errors, taking into account the variability in risk factor prevalence, disease incidence proportions, and relative risks, and use of an appropriate transformation so that the statistic is approximately normally distributed. Thus the calculation of confidence limits entails many assumptions and approximations so that the nominal probability levels may be misleading.

From a public health perspective interval estimates of impact obtained from sensitivity analyses are likely to be more useful than confidence intervals. For instance, various plausible values for the prevalence of exposure and disease incidence in the study population could be used with published estimates of relative risk or odds ratios (and possibly the confidence limits of these parameters) to calculate estimates of excess risk. Provided the estimates are positive and not very small they can be inverted to produce valid impact numbers. If they are negative then the impact numbers describe protective effects. If they are very small then the impact numbers will be very large. The range of impact numbers calculated in this way illustrates the impact of the risk factor under plausible scenarios.

### DISCUSSION

We have proposed four measures, based conceptually on the NNT, to express the impact of a risk factor on the incidence of disease, each measure reflecting the impact on a different population. The nomenclature was chosen to indicate the relevant population: PIN refers to the entire population, CIN to those who are cases with the disease, EIN to people with the exposure, and ECIN to exposed cases. The impact number reflects the number of people in each of those populations among whom one outcome is attributable to the particular risk factor.

The advantages of these measures are the same as those of the NNT; they are intuitively easier to understand than their

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Impact numbers for stroke in a case-control study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Past medical history of atrial fibrillation</td>
</tr>
<tr>
<td>Proportion controls exposed, P_c</td>
<td>0.022</td>
</tr>
<tr>
<td>Odds ratio, OR*</td>
<td>5.4</td>
</tr>
<tr>
<td>Annual incidence in unexposed group, I_u</td>
<td>68.67/100000</td>
</tr>
<tr>
<td>Case impact number, CIN</td>
<td>11.33</td>
</tr>
<tr>
<td>Population impact number, PIN</td>
<td>15044</td>
</tr>
<tr>
<td>Exposed case impact number, ECIN</td>
<td>123</td>
</tr>
<tr>
<td>Exposure impact number, EIN</td>
<td>331</td>
</tr>
</tbody>
</table>

*Derived from adjusted OR in study; †Estimated as incidence in the total population, as the risk factor is relatively uncommon.
Key points

- We describe new measures of risk from case-control and cohort studies, which relate to numbers of the population at risk and likely to be easily understood by policy makers, health care providers, and consumers.
- The population impact number (PIN) is the number of those in the whole population among whom one case is attributable to the exposure of risk factor (this is equivalent to the reciprocal of the population attributable risk).
- The case impact number (CIN) is the number of people with the outcome for whom one case will be attributable to the exposure of risk factor (this is equivalent to the reciprocal of the population attributable fraction).
- The exposure impact number (EIN) is the number of people with the exposure among whom one excess case is attributable to the exposure (this is equivalent to the reciprocal of the attributable risk).
- The exposed cases impact number (ECIN) is the number of exposed cases among whom one event is attributable to the exposure (this is equivalent to the reciprocal of the aetiological fraction).

reciprocals. We anticipate that they will be useful in communicating the population impact of various risk factors to public health professionals, administrators, those involved in public policy, and the lay public.

The measures only make sense when causality between exposure and outcome has been shown, with causality judged according to the usual criteria. The choice of which of these measures should be used, will depend on the purpose. Taking as an example the development of an antismoking education programme, the PIN and the EIN could help the policy maker decide on funding the project from the viewpoint of the potential benefit to the whole population and the numbers of smokers to be targeted to potentially prevent one death respectively. The CIN and ECIN could comprise part of the message given to cigarette smokers to express the risks they run.

These measures are linked to the incidence of disease and the proportion of the population with exposure to a specific risk factor. Therefore, they are not transportable from one population to another, in the same way that the RR or the OR are. Rather than being a drawback, this is an advantage, as users can tailor their estimates to reflect their population of interest. Estimating these numbers reliably depends on local population based registers. This highlights the type of information required to implement these aids.

In an environment of limited financial resources, it is even more important that policy makers have access to tools that will allow them to assess the relative impact of risk factors in their population. This will permit more appropriate allocation of resources to identifying those factors that are most important in the given setting.

APPENDIX

In the same way that NNT is the reciprocal of the attributable risk, we have defined our new measures as the reciprocals of the excess risk at a population level. As discussed in the paper we can define the population in at least four ways:

1. The entire community from which those with and without disease are drawn. For cohort studies, the excess risk attributable to the risk factor for this population is the PAR or population attributable risk, and the reciprocal of this value is the population impact number, PIN.

   \[ \text{PIN} = \frac{1}{\text{PAR}} \]

   \[ \text{PIN} = \frac{1}{\text{AR} \times P_e} \]

   \[ \text{PIN} = \frac{1}{I_e - I_u} \times P_e \]

   \[ \text{PIN} = \frac{1}{I_u \times P_e \times (\text{RR} - 1)} \]

   where \( I_e \) is the incidence proportion in the exposed group, \( I_u \) is the incidence proportion in the unexposed group and \( P_e \) is the proportion of the population that is exposed to the risk factor. Therefore, where \( \text{RR} = \frac{I_e}{I_u} \), is the relative risk. The PAR is the proportion of people with disease attributable to the risk factor and its reciprocal, the PIN, is “the number of those in the whole population amongst whom one case is attributable to the exposure”.

2. All those with disease; that is, cases. For cohort studies, the excess risk attributable to the risk factor for this population is the population attributable fraction (PAF), and the reciprocal of this is the case impact number, CIN.

   \[ \text{CIN} = \frac{1}{\text{PAF}} \]

   \[ \text{CIN} = \frac{1}{\text{AR} \times P_e} \]

   \[ \text{CIN} = \frac{1}{(I_e - I_u)} \times P_e \]

   \[ \text{CIN} = \frac{(P_e \times I_e) + (1 - P_e)}{(\text{RR} - 1) \times P_e} \]

   If both the numerator and denominator are divided by \( I_e \) we obtain

   \[ \text{CIN} = \frac{P_e \times \text{RR}}{(\text{RR} - 1) \times P_e} \]

   The PAF is the proportion of people with the disease in the population in whom the disease attributable to the particular exposure and so its reciprocal, the CIN, is “the number of people with the disease for whom one case will be attributable to exposure to the risk factor”.

3. All those with the risk factor or exposure. The excess risk for this population is the absolute risk difference (AR), and the reciprocal of this is the exposure impact number, EIN.

   \[ \text{EIN} = \frac{1}{I_e - I_u} \]

   \[ \text{EIN} = \frac{1}{I_u \times (\text{RR} - 1)} \]

   The AR is the excess incidence proportion of cases among those with the exposure, and its reciprocal, the EIN, is “the number of people with the exposure among whom one excess case is attributable to the exposure or risk factor”.

4. All those with both the risk factor or exposure and the disease (the exposed cases). The excess risk attributable to the risk factor in this population is the aetiological fraction, and its reciprocal is the exposed case impact number, ECIN.

   \[ \text{AF} = \frac{1}{\text{AR} \times P_e} \]

   and
Divide both the numerator and denominator by $I_u$ to obtain

$$\text{ECIN} = \frac{I_e}{I_e - I_u}$$

The aetiological fraction is the proportion of all cases in the exposed group that is attributable to the exposure, and its reciprocal, the ECIN, is “the number of exposed subjects with disease among whom one case is attributable to the exposure”.

To highlight the relation between these various measures, we can see that:

$$\text{CIN} = \text{PIN} \times I,$$
$$\text{EIN} = \text{PIN} \times P_e.$$

**Authors’ affiliations**

R F Heller, Evidence for Population Health Unit, The Medical School, The University of Manchester, UK

A J Dobson, School of Population Health, The University of Queensland, Queensland, Australia

J Attia, Centre for Clinical Epidemiology and Biostatistics, Faculty of Medicine and Health Sciences, The University of Newcastle, New South Wales, Australia

J Page, Department of Epidemiology, Harvard University School of Public Health, Boston, USA

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