Boundaries of Perception and Knowledge for Risk Assessment in Epidemiology

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The intention of the paper is to introduce the concept of thresholds or boundaries of perception and knowledge in epidemiology, especially in the context of risk assessment. The notion of causal scores is introduced. A risk pictogram is proposed as a standardized way of presenting and comparing various risks.

There are thresholds of knowledge in every science. We need effective ways to state borderlines of knowledge. In epidemiology we must separate the safe conclusions of knowledge from areas of speculation. The following will review some of the important aspects on this with reference to low-risk lung cancer.

Criteria have been evolved for judging the causality of associations demonstrated through epidemiological research. Several criteria must be fulfilled in order to conclude from epidemiological data that a causal connection exists between exposures and effect. The criteria first proposed by Bradford-Hill have been widely used and have been modified to some extent since they were proposed. The original criteria include the consistency of the association, the strength of the association, the specificity of the association, the presence of a dose-response relationship, a proper time relationship between exposure and response, consistency among studies, biological plausibility, coherence, experimental evidence and analogy.

Considering such criteria, the IARC has proposed four different levels of evidence when evaluating the existence of a causal relationship regarding carcinogenicity.

Sufficient evidence: There is a causal relationship between exposure and human cancer.

Limited evidence: A causal relationship is credible, however, alternative explanations (such as chance, bias and confounding) cannot be adequately excluded.

Inadequate evidence: There are few pertinent data or the available studies, while showing evidence of an association, do not exclude chance, bias or confounding.

No evidence: Several adequate studies are available which do not show evidence of carcinogenicity.

The criteria for a causal relationship as described above have been discussed and criticized recently with the proposal that causal inference is not a matter of science. However, such convincing concepts should not be dropped just because the results do not fit the expectations. Perhaps by applying these criteria with more rigour, a more certain threshold for causal evidence from epidemiology can be established.

HOW CAN EMPIRICAL BOUNDARIES OF PERCEPTION IN EPIDEMIOLOGY BE IMPROVED?

Causal Scores

Indicators for a causal connection could be elaborated in a more formal way. I propose as an example that a causal score could be composed from the above criteria for a causal relationship.

Criteria for a causal connection might be set up in the form of ten questions answered by YES or NO (Table 1). An answer counts one point towards the total score (first column) and a NO counts zero. The maximum total score is 10 when all questions are answered by YES and it is 0 when all questions are answered by NO. One might assign five possible evaluations to the total causal score as indicated in Table 2.

Every indicator is necessarily somehow arbitrary. The total causal score weights all questions in the same way and requires a YES/NO decision for ten difficult questions. This will lead to a certain variance in the

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The second instrument to improve boundaries of perception is a standardized way of presenting risk. There are four basic risk measures used in epidemiology: the incidence in the control group \( I_0 \), the incidence in the exposed group \( I_1 \), the relative risk, which is the ratio of \( I_1 \) to \( I_0 \), the attributable risk, which is the difference of \( I_1 \) and \( I_0 \).

By definition, the basic risk measurements are interconnected. Three of them contain all the information and can be presented in a standardized way in one graph. I have called this a risk pictogram (Figure 1).

To the right is the relative risk or the odds ratio. On the vertical axis, the attributable risk \( A \), i.e., the number of people additionally affected, a certain population has to be referred to. The risk pictogram uses a population of 100 million exposed people which can easily be converted to other population sizes, for example, one million or ten million exposed.

The curves show the mathematical relation between relative risk, the basic incidence \( I_1 \) in the non-exposed group and the number of additionally affected people. With a relative risk of three and a basic incidence of \( 10^{-5} \), about 1000 people are additionally affected in a population of 100 million exposed people. With one million exposed people, the attributable risk would be 10 people.

When the basic incidence and the relative risk is known, the attributable risk can be read from this graph. It can be used as a standardized way of presenting risk from epidemiological data by drawing individual risk points for various risks.

Meta-analysis

To strengthen the evidence from studies with low-risk

<table>
<thead>
<tr>
<th>Supporting causal score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic causal score</td>
<td>-</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

Legend:
- : No indication of causal connection
+ : Some weak hint of causal connection
++ : Causal connection possible
+++ : Causal connection likely
++++ : Causal connection existent

When an intervention effect is shown, a causal connection always exists.

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### Table 1: Construction of causal scores

<table>
<thead>
<tr>
<th>Question included in causal score</th>
<th>Weighted for 'Yes'</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total score</td>
</tr>
<tr>
<td>Undoubtedly consistent and replicability</td>
<td>1</td>
</tr>
<tr>
<td>Exposure measure reliable and valid ( r&gt;0.7 )</td>
<td>1</td>
</tr>
<tr>
<td>Outcome measure reliable and valid ( r&gt;0.7 )</td>
<td>1</td>
</tr>
<tr>
<td>Main bias factors sufficiently excluded</td>
<td>1</td>
</tr>
<tr>
<td>Main confounding factors sufficiently excluded</td>
<td>1</td>
</tr>
<tr>
<td>Statistical significance ( p&lt;0.05 ), two-sided</td>
<td>1</td>
</tr>
<tr>
<td>Strength of association: ( RR ) greater than 2-3</td>
<td>1</td>
</tr>
<tr>
<td>Dose-response relationship: ( p&lt;0.05 ), two-sided</td>
<td>1</td>
</tr>
<tr>
<td>Intervention effect shown</td>
<td>1</td>
</tr>
<tr>
<td>Biological plausibility likely</td>
<td>1</td>
</tr>
</tbody>
</table>

Maximum score: 10 | 4 | 4 |

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### Table 2: Evaluation of the outcome of the total causal score

<table>
<thead>
<tr>
<th>Causal score</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causal score 5:</td>
<td>No indication of causal connection</td>
</tr>
<tr>
<td>Causal score 6:</td>
<td>Some weak hint of causal connection</td>
</tr>
<tr>
<td>Causal score 7:</td>
<td>Causal connection possible</td>
</tr>
<tr>
<td>Causal score 8:</td>
<td>Causal connection likely</td>
</tr>
<tr>
<td>Causal score 9:</td>
<td>Causal connection existent</td>
</tr>
</tbody>
</table>

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### Table 3: Possible evaluation of the outcome of the basic and the supporting causal score

<table>
<thead>
<tr>
<th>Supporting causal score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
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<td>-</td>
<td>+</td>
<td>++</td>
<td>+++</td>
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</tr>
</tbody>
</table>

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When an intervention effect is shown, a causal connection always exists.
Figure 1: Risk—Pictogram. Relative Risk RR and incidence $I_0$ in their relation to the Attributable Risk $A$. 

increases the use of ‘meta-analysis’ has been suggested. Basically, the relative risks from several studies are summed up using certain weights, for instance, sample sizes. A point estimate of relative risk and its confidence interval are obtained. Meta-analyses have several limitations, however.

By summarizing many studies, one may obtain large numbers and statistically significant results. However, attaining statistical significance is distinct from determining the validity and biological significance of the findings.

The results of meta-analyses may vary. We have shown this by repeating the meta-analysis of Wald. Depending on the principles for inclusion of studies and data, depending on the quality of studies used, or on the scenario of misclassification, different results may be obtained.

Meta-analyses do not add anything to the empirical evidence—they only represent a new dimension of manipulation. When applying meta-analyses, different sets of studies should always be used, in order to get a feeling for the corresponding variation in results.

CONCLUSIONS

There is no established formal method to separate certain knowledge from uncertain in epidemiology. The currently employed approaches might lead to conflicting results. This situation could be improved by

— the development of causal scores and related concepts
— the use of a standardized way of presenting risks in a risk pictogram.

REFERENCES


