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Boundaries of Perception and Knowledge for Risk Assessment in Epidemiology

KARL K ÜBERLA

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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[1] 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[2] 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[3,4] 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

Institut fur Medizsinische Informationsverarbeitung, Biometrie und Epidemiologie der Universität, Marchionistrasse 15, D-8000 Munich, West Germany.

TABLE 1 *Construction of causal scores*

Question included in causal score	Weights used for 'Yes'		
	Total score	Basic score	Supporting score
Undoubtful consistency and replicability	1	1	–
Exposure measure reliable and valid (r>0.7)	1	–	1
Outcome measure reliable and valid (r>0.7)	1	–	1
Main bias factors sufficiently excluded	1	–	1
Main confounding factors sufficiently excluded	1	–	1
Statistical significance p<0.05, two-sided	1	1	–
Strength of association: RR greater than 2–3	1	1	–
Dose-response relationship: p<0.05, two-sided	1	1	–
Intervention effect shown	1	–	–
Biological plausibility likely	1	–	–
Maximum score	10	4	4

score. Other weights and other scores can be proposed. In the second and third column of Table 1, a basic causal score and a supporting causal score are proposed which can be used independently or which can be combined to a unified evaluation as indicated in Table 3. The biological plausibility has been left out of the basic and the supporting score since it is difficult to estimate. Also, intervention effects are left out as such data are frequently unavailable. Table 3 shows the evaluation of the outcome of the basic and the supporting causal score.

Risk Pictogram

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 is indicated using a logarithmic scale. To get the attributable risk A, ie 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_0 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 ten 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.

The curves in the risk pictogram are mathematical consequences of the definitions and contain no statistical consideration. Confidence intervals can be attached to them. It can be seen that the basic incidence I_0 in the non-exposed group is more important for the attributable risk than the relative risk. When the relative risk is varied, only two dimensions in the attributable risk change, whereas the incidence variation over several dimensions leads to a corresponding large variation in the attributable risk.

Meta-analysis

To strengthen the evidence from studies with low-risk

TABLE 2 *Evaluation of the outcome of the total causal score*

Causal score <5:	No indication of causal connection
Causal score 6:	Some weak hint of causal connection
Causal score 7:	Causal connection possible
Causal score 8:	Causal connection likely
Causal score 9:	Causal connection existent

TABLE 3 *Possible evaluation of the outcome of the basic and the supporting causal score*

		Supporting causal score				
		0	1	2	3	4
Basic causal score	0	–	–	–	–	–
	1	–	–	–	–	+
	2	–	–	–	+	++
	3	–	–	+	++	+++
	4	–	+	++	+++	++++

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 extists.

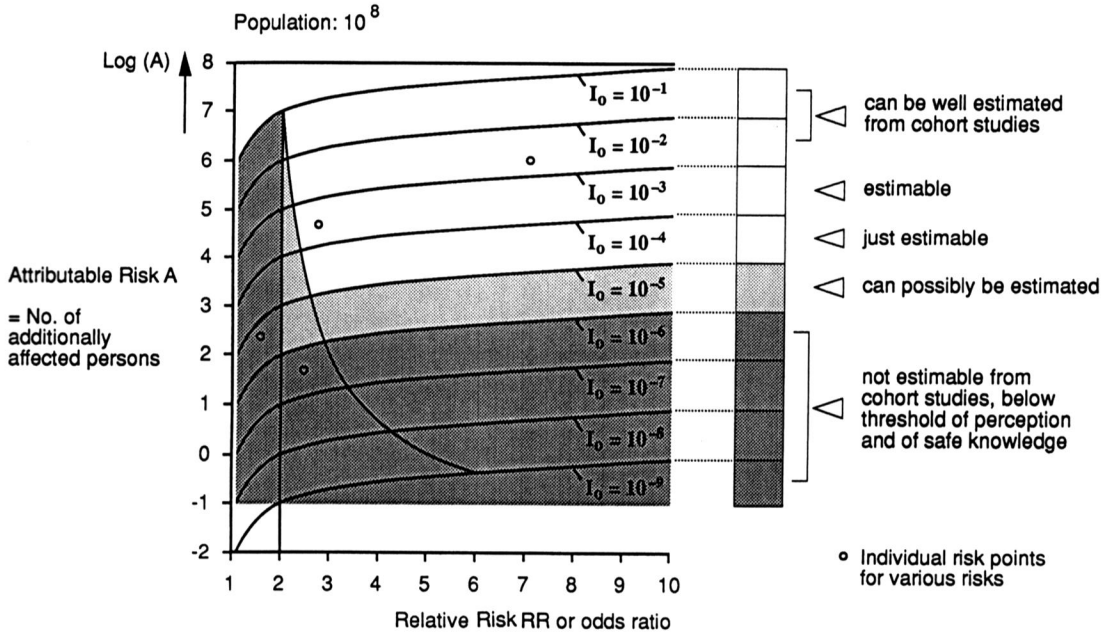

FIGURE 1 *Risk—Pictogram. Relative Risk RR and incidence I_0 in their relation to the Attributable Risk A.*

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.[6,7] 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.[7]

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.

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