

A strategy for bounding attributable risk: a lung cancer example.

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Response to Sander Greenland's Critique of Bounding Analysis

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1. RESPONSE TO THE CRITIQUE

1.1. Bounding Analysis is Not an Alternative to Standard Risk Assessment

Greenland misses the point of our method. He suggests that we have proposed "bounding analysis as an alternative to probabilistic risk assessment, or even as a standard to judge the latter." This is not correct. Our opening paragraphs and our previously published qualitative arguments on this same subject[(1)] clearly explain that we are *only* proposing this approach to deal with situations in which the existing data are insufficient to support standard methods of risk assessment. The idea is to use the parts of the problem that can be characterized using conventional probabilistic risk analysis to back out an upper bound on the contribution made by the causes for which there are scanty data.

The application of conventional probabilistic methods to such poorly understood causes can yield broad probability distributions, which, when added to the better defined estimates of cases due to the well-known causes, yield an estimate of the sum that includes many more cases than the number that is known to have occurred. In such circumstances we argue that it should be possible to bound the estimate of the number of deaths from poorly understood causes.

When adequate science is available to characterize all the exposures that contribute to a specific health endpoint, clearly one should adopt conventional risk analysis. But in the case when some of the exposures contributing to a risk are poorly understood it is simply not possible to follow Greenland's prescription of applying advanced methods such as meta-analysis, or the "specification of a joint prior for all unknown parameters."

The reasoning based on order-of-magnitude arguments and bounding methods is common in many fields of science and engineering. The point of such methods is *not* to produce a precise answer, but to get the answer into the right ballpark. We believe that there are some circumstances in which such methods should also be applied in risk analysis.

1.2. A Bound is Not a Confidence Interval

Greenland complains that we have no operational definition of bounds or reliable means for measuring them. Our definition of bounds is simply the highest and lowest fraction of lung cancer mortality that the expert believes could be caused by each factor, singly and in combination with other exposures. Since these bounds *cannot* be directly measured experimentally, we ask for the expert's informed opinions. This is the kind of situation for which expert elicitation is most appropriate.[(2)]

Greenland's extended discussion of whether a bound is 0.69, 0.70, or 0.71 reframes the question in terms of confidence intervals. Our elicitation protocol poses questions such as "What is the *highest* value that you believe the total fraction of lung cancer mortality due to this factor could be?" We seek an upper bound, not a 90% or 98% confidence interval. Greenland criticizes a number we used in our worked example (a lower bound of 0.70 on the fraction of lung cancer mortality due to smoking) as being lower than

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literature values. But that is what the lower bound is supposed to be: a number that we believe the real fraction must exceed. It is neither the best estimate nor a $(1 - \alpha)$ lower confidence limit. The numerical example provided in the article was only intended to illustrate the method. As might be expected, results from the expert elicitations we are now conducting are different from the values used in the example.

To assure that the elicited bounds meet our definition, at the end of our elicitation protocol we ask the experts to systematically revisit all the bounds they have set and consider reassessing some if they are not similarly confident about all of them. We understand that experts may be overconfident and we make no claim that our method can produce estimates that are highly precise. Our claim is that bounding arguments can set a first-order limit on the upper bound of the residual that can be used to gauge the plausibility of estimates of the impacts of the poorly documented causes. In this context, an elaborate treatment of second-order uncertainty strikes us as inappropriate and probably not helpful.

1.3. Expert Elicitation is Not a Substitute for Doing the Science

Greenland is disparaging of the use of expert subjective judgment. We agree that expert judgment is inferior to directly relevant high-quality scientific evidence and analytical methods whenever the latter are available. We also agree that expert judgment is subject to a variety of biases produced by cognitive heuristics. It is for that reason that more than a decade ago one of us argued[2] that "the use of expert subjective judgment is not a substitute for proper scientific research. Expert judgment can be helpful in policy analysis when decisions must be made before all the necessary science is known. In most cases, however, having made initial decisions on the basis of expert judgment, one should follow up with the appropriate science, to assure that in the future, policy is more firmly rooted in physical reality." We continue to hold this view. However, when directly relevant high-quality scientific evidence is lacking, we believe that expert judgment, carefully informed by whatever scientific evidence and analytical models are available, is often the best alternative.

In our article we indicated that we plan to illustrate the method of bounding by conducting a series of expert elicitations. We have now begun to perform these elicitations. In addition to presenting the experts with summaries of the relevant literature, we encourage them to turn to all available evidence to inform their judgments. We conduct the interviews in the experts' offices so that their reference materials are readily available. During one recently completed elicitation, the expert, who was the director of a major research group, paused on several occasions during the process to phone colleagues to ask them to perform supporting analysis, or to check data in the literature. Could the results be biased? Of course. However, we are not aware of a better feasible alternative.

Greenland implied that we are forcing a consensus on the experts. Our method does not demand or seek consensus among experts. The results of individual elicitations are not combined, and will be presented independently, as they have been in previous elicitations we have conducted.[3–5] Indeed, the range of the resulting bounds should provide additional insight on our state of understanding or ignorance.

1.4. Mathematical Development

One of the important lessons we have learned about applied policy analysis is that methods proposed in theory need to be refined through application. As we have begun to apply our ideas to a real problem we have discovered issues that required refinement or correction. For example, after running our first elicitation we determined that it is not necessary to disallow three-way and higher interaction terms, or to impose the full set of $2|\Omega| + 2$ coherence constraints (Equation (6)). Since we are only interested in the upper bound on the residual, only the coherence constraint pertaining to it (a) and consistency (b) need be satisfied in order to determine the upper bound on the residual.

$$\overline{f}(X) + \sum_{s_j \neq X} \underline{f}(s_j) = 1 \quad s_j \in \Omega, 1 \leq j \leq |\Omega|, \qquad \text{(a)}$$

$$\sum_{s_j} \underline{f}(s_j) \leq 1 \quad s_j \in \Omega, 1 \leq j \leq |\Omega| \qquad \text{(b)}$$

The method described in the article produced a full set of coherent bounds (quantifying all the interaction terms) implied by the expert's original bounds—which involved unnecessary detail. Our simplification allows the direct calculation of the upper bound on the residual without requiring an optimization program maximizing unspecificity. We still stand by our development of the mathematical theory, but now focus exclusively on the portion that defines the bounds on the residual. Greenland asked where and how Laplace's Principle of Insufficient Reason was used to calculate the bounds. Though our current solution

method does not require this, we were referring to the choice of objective function of the optimization, which searched for the most unspecific set of bounds compatible with the elicited bounds (Equation (5)).

2. CONCLUSION

We appreciate the considerable effort that Greenland has made in developing his critique. We certainly will follow his advice that we continue to refine and improve the work. We hope that this exchange will prompt others to explore alternative ways to apply order-of-magnitude and bounding methods, so common in many other fields, to relevant applications in risk analysis.

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