A Strengthening Programme for Weak Associations


In many cases discordant results from different epidemiologic studies are attributed to statistical variation or simply to unknown factors. This paper offers conceptual insights into the interpretation of differing results and indicates ways to strengthen findings by taking steps that will result in stronger effect measures. This advice was not meant as a subterfuge, but rather as a way to magnify real effects by taking into account the principles that lead to variation or underestimation of study results.

First, the paper focuses on relating the concept of strength of association with the sufficient-component cause model of causation. One of the basic principles that emerges from this consideration is that causal effects appear stronger when the disease outcome is rare, because in this situation, the cause in question is more likely to account for a large proportion of cases. The strong associations between diethylstilboestrol and adenocarcinoma of the vagina, vinyl chloride and angiosarcoma of the liver, and thalidomide and phocomelia were cited as examples.

This principle can be exploited by studying causal effects in low-risk populations, in which causal associations usually appear stronger than in high-risk populations. Exceptions, such as causal interactions, and drawbacks, such as a limited number of cases, were also discussed.

The other important principle that is useful for strengthening associations is the reduction of nondifferential misclassification, especially of exposure. The importance of specifying a reasonable induction period that takes into account the timing between exposure and disease is discussed, along with the general principle of aiming to increase the specificity of exposure metrics as opposed to improving the sensitivity of such measures.