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Joseph Berkson: Limitations of the Application of
Fourfold Table Analysis to Hospital Data.
Biometrics 1946; 2:47-53.

Berkson's 1946 article, "Limitations of the Application of Fourfold Table Analysis to Hospital Data," is the earliest algebraic analysis of an epidemiologic selection bias of which I am aware. In one sense Berkson was far ahead of his time: though his article became famous within the field during the three decades covered by this collection, over the same period I could find no algebraic analyses of other selection bias phenomena (although reviews of Berkson's arguments were common).

Described in modern terminology, Berkson studied the phenomenon that diseases can appear associated in a hospital-based case-control study solely on account of higher admission rates among persons with multiple conditions, even if the conditions affect admission rates independently. This phenomenon came to be known as "Berkson's bias," a term rumored to have been deployed by Berkson since it suggested that Berkson committed the bias, rather than discovered it.

An unfortunate aspect of the history of Berkson's paper has been a tendency to overlook the fact that the phenomenon described by Berkson was *not* a general problem of case-control studies. Kraus [1954] was perhaps the earliest author to indicate the limitations of Berkson's argument. For Berkson's bias to occur, it was necessary that both the outcome under study *and* the putative risk factor independently affect hospitalization rates. Kraus pointed out that typical study factors are not active diseases, and therefore are unlikely to affect hospitalization rates; thus Berkson's bias would not be a threat in most studies.

Although the practical importance of the specific phenomenon studied by Berkson remains debatable, some empirical evidence for its occurrence has been offered [Roberts et al., 1978], and there can be little doubt that Berkson's contribution helped stimulate many of the more recent analyses of selection and response biases.

References:

- Kraus AS. The use of hospital data in studying the association between a characteristic and a disease. *Pub Health Rep* 1954; 69:1211-1214.
- Roberts RS, Spitzer WO, Delmore T, Sackett DL. An empirical demonstration of Berkson's bias. *J Chron Dis* 1978; 31:119-128.