Dear Editor:

Vieira et al. (2011) noted that, across 11 countries, “Resistance in E. [Escherichia] coli isolates from food animals (especially poultry and pigs) was highly correlated with resistance in isolates from humans. This supports the hypothesis that a large proportion of resistant E. coli isolates causing bloodstream infections in people may be derived from food sources.” Is this causal interpretation of ecological correlations justified?

Consider the following hypothetical analogy: a study examines levels of radioactivity in animals and humans in 11 countries, observes that some countries have higher levels of radioactivity in both humans and poultry than others, and concludes that, “This supports the hypothesis that a large proportion of radioactivity in people may be derived from food sources” (or, with equal logical validity, that “a large proportion of radioactivity in poultry may be derived from people.”) Either inference is a non sequitur: an alternative explanation is that both animals and people have higher levels of radiation in countries with higher background levels. The same logic applies to resistant E. coli. An ecological correlation is unsurprising, given the global prevalence of multidrug resistance plasmids, even in areas and epochs without anthropogenic influence (Singer et al., 2006b; D’Costa et al., 2011).

Vieira et al. (2011) stated that “when usage of antimicrobials in humans was analyzed with antimicrobial resistance among human isolates, only correlations between fluoroquinolones (r = 0.90) and third-generation cephalosporins (r = 0.75) were significant.” One might equally well explain the significantly correlated resistance prevalences between the human and animal isolates by assuming that use of these critically important antibiotics in humans selects for resistance in human isolates of E. coli, which are then disseminated into animal production units, as by assuming transmission from animals to people.

The authors also asserted that, “Studies have shown (1) that multi-resistant E. coli can be frequently found in food animals… (2) widespread carriage of multi-resistant E. coli in the community with no healthcare association…, and (3) indications that most resistant E. coli in the bowel of people are derived from food animals…” (p. 1296), but these studies do not address directionality of transmission. The one-directional flow posited by the authors is not the only—or most likely—pattern consistent with the data (Singer et al., 2006a). Correlations of resistances warrant no such causal interpretation.

Methods for sound causal inference, and guidance for refuting plausible alternative explanations, have been extensively developed in epidemiology (e.g., Maclure, 1985). It would be well to apply them before announcing causal interpretations of ambiguous ecological correlations.

References


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