The principles of evidence-based review have found broad application, ranging from health insurance coverage decisions and clinical practice guideline development to informing the development of biomedical research agendas and public policy (1). For each application, there are unique challenges, advantages, and limitations associated with incorporating evidence-based reviews into existing decision-making processes.

In this issue of the Journal, Kavanaugh et al. (2) describe the approach that the U. S. Food and Drug Administration (FDA) has used to incorporate evidence-based review principles into the challenging area of evaluating qualified claims for health benefits of foods and food components that are marketed as dietary supplements (2). The particular topic of this paper was qualified health claims for tomatoes and for lycopene, a constituent of tomatoes that is marketed as a dietary supplement, in reducing the risk of some forms of cancer, including prostate cancer. FDA’s systematic review of the relevant literature followed the rules that are crucial to evidence-based review and, as such, exemplifies the transparency and neutrality of an evidence-based review approach in evaluating the strength of the available evidence in an area where the expectation of risk reduction sometimes results in a biased interpretation of the evidence. However, there are several issues that must be taken into account when considering the processes that FDA was obliged to use to meet its needs.

First, the literature relating tomatoes and/or lycopene to the incidence of cancer is heterogeneous, and there are few clinical trials of any great size. Instead, clues about whether lycopene or tomatoes might be associated with a reduced risk of cancer have come from preclinical and observational studies and from small trials, which together have suggested that lycopene is associated with a reduced risk of prostate cancer (and, perhaps, of other forms of cancer). The systematic review performed by FDA, which was restricted to clinical intervention trials and observational studies, indicates that although some study results support an association between lycopene and prostate cancer risk reduction, there is little reliable and robust evidence in favor of that conclusion.

A second concern about FDA’s evidence review is that tomatoes and lycopene are a conventional food and a food constituent that is available as a dietary supplement, respectively. Because neither is a drug, there is no requirement that people seek medical advice before ingesting them, and both are freely available on store shelves. Whereas healthcare providers are the key audience for results of reviews of clinical practice guidelines, the major audience for FDA review of qualified claims for health benefits of foods and food components is the general public. Advice to the public needs to be appropriately framed to reflect the certainty or uncertainty of the evidence supporting claims of benefits to health. FDA concluded that the following statements could be made: that there was “no credible evidence” for an association between lycopene intake and a reduced risk of any of the cancers in question; that there was “no credible evidence” for an association between tomato consumption and a reduced risk of lung, colorectal, breast, cervical, or endometrial cancers; and that there was “very limited evidence” to support an association between tomato consumption and a reduced risk of prostate, ovarian, gastric, or pancreatic cancers. Conveying the complexity and sometimes subtle differences between such messages to the public is challenging, and there is evidence that consumers have not really understood the language of qualified health claims (3).

Neither of these concerns, however, diminishes the importance of using evidence-based review principles to evaluate important diet–health relationships. In fact, it may be argued that evaluating a diet–health relationship is precisely the circumstance in which systematic review techniques can be most appropriate and effective because they are transparent and objective, and the search and review strategies could be exactly reproduced by others. The key questions to be answered in any systematic review are identified at the beginning, and a decision is made about which studies and study designs are relevant to answering those questions. There may be considerable differences of opinion about whether or not an association does exist, and hence what to recommend to the public, but transparency of the processes for gathering and evaluating the available, relevant evidence assures that decisions are reached in an open and even-handed way.

An additional value of the evidence-based review approach is that a systematic review can readily be updated to include emerging relevant data. It is possible, for example, that FDA could revisit the qualified health claim for tomatoes and lycopene and risk reduction for cancer if new studies were published that appeared to shed further light on the topic. In a field such as this, new data appear regularly (4).

References


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