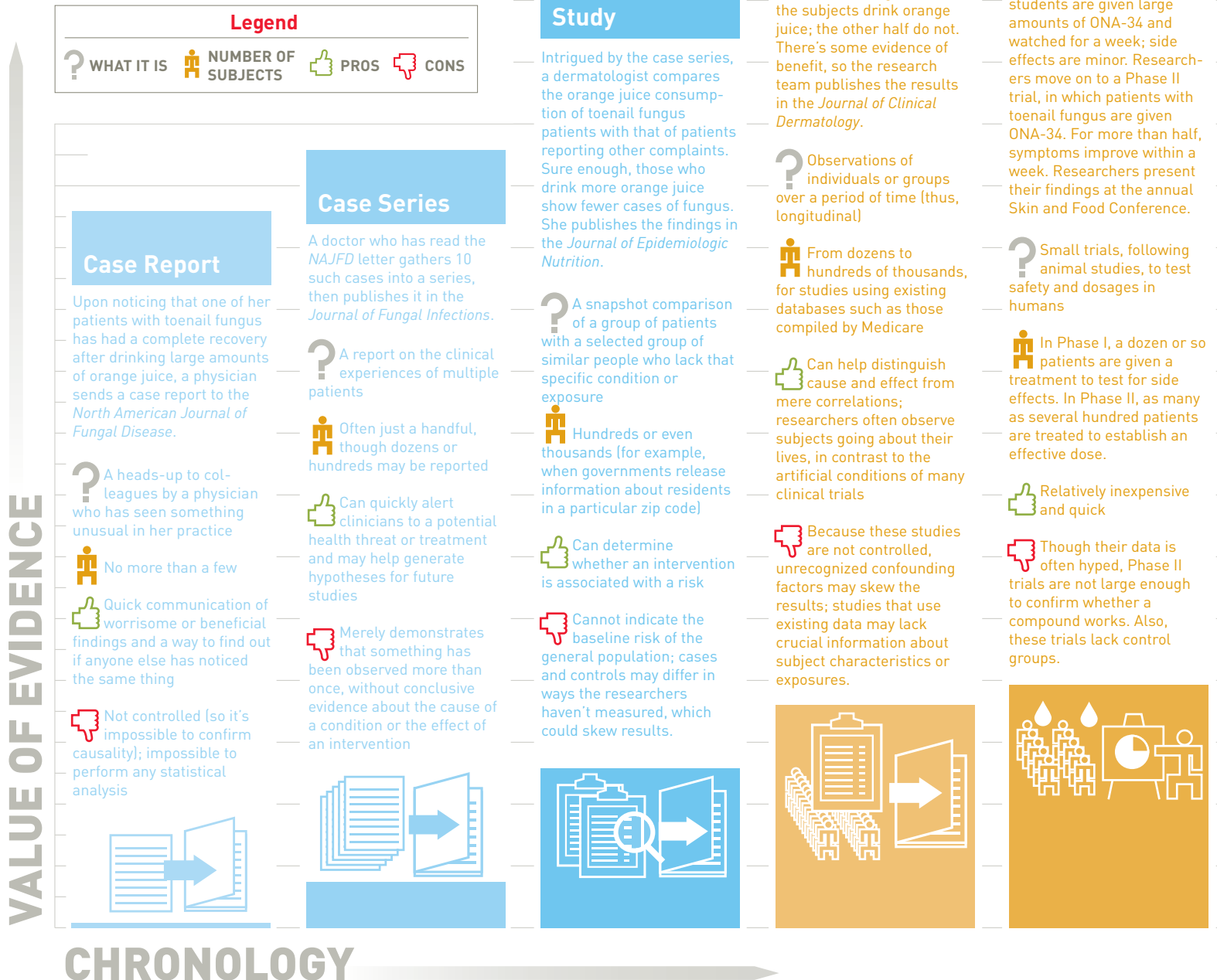


INFOGRAPHIC //

Body of Evidence

■ BY IVAN ORANSKY AND ANDREW HOLTZ // INFOGRAPHIC BY FLYING CHILLI

When a headline shouts “New Study Shows...,” many readers accept the story that follows as fact and expect the latest medical finding to translate quickly into treatment. But the reality is that the quality of studies’ evidence can vary widely, and the journey from discovery to clinical application is a long, hard slog. Here, in a hypothetical example, we describe how research progresses through the medical literature—and how evidence stacks up along the way.



Randomized Controlled Clinical Trial

The Orange Growers' Association agrees to foot the bill for a Phase III trial, also known as a randomized controlled clinical trial. Two thousand people with toenail fungus receive an existing treatment; 2,000 more get ONA-34. It doesn't seem that ONA-34 is any better than the existing treatment. Results are published in the *Journal of the National Association of Doctors*. Meanwhile, the Orange Juice Association has sponsored its own trial using a different existing treatment.

? A trial in which some patients get the treatment or intervention being tested while others receive an existing treatment or a placebo (if it's ethical to withhold possible treatment or if no treatment yet exists). To minimize bias, neither the subject nor the researcher knows which treatment the subject is getting.

👤 Hundreds or even thousands

👍 Considered the gold standard of clinical evidence from a single trial; rigorous, well controlled and subject to close oversight

👎 High cost prevents researchers from testing every hypothesis; some experiments are ruled out by ethics (for example, the link between smoking and lung cancer could not be confirmed by randomly assigning some people to start smoking).



Editorial

A skeptical dermatologist writes an editorial accompanying the *JNAD* study, pointing out that the existing treatment given to the control group is not the best available, but that, if all it takes to cure toenail fungus is to drink orange juice, he's willing to recommend it to patients.

? Expert interpretation of the results of one or more studies

👤 None

👍 An independent expert analysis can highlight key strengths and limitations and suggest ways the results can be incorporated into clinical practice or further research.

👎 An editorial does not provide new data or other evidence. Also, the author may be biased.



Review Article

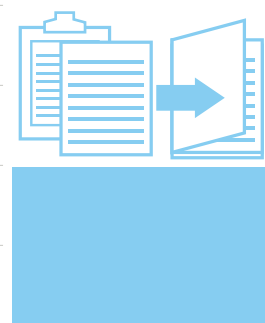
A nutritionist summarizes the data on ONA-34 in the *American Journal of Nutrition*. However, she fails to disclose that she has received hundreds of thousands of dollars in grant funding from the Orange Growers' Association.

? A review of the medical literature with conclusions by an expert author or authors

👤 None

👍 A review neatly summarizes the trials and other data and saves time that would be spent reading all those papers.

👎 Merely expresses an opinion, even if it is based on previous papers. In a number of recent instances, review articles have been ghostwritten by writers paid by drug companies, although it is unclear how often this happens.



Meta-Analysis

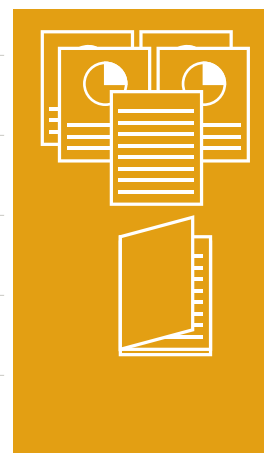
After publication of a third and fourth randomized controlled trial, a researcher analyzes all four studies and reports that there is, in fact, some benefit to ONA-34, but it's unclear whether there is enough in orange juice to make a difference. He suggests taking ONA-34 in pill form. This analysis is published in the *British Journal of Medicine*.

? A statistical analysis of data pooled from multiple randomized controlled clinical trials

👤 As many as tens of thousands, depending on the sizes of the original studies

👍 By merging data from multiple trials, a meta-analysis is less likely to be affected by random variations or unrecognized flaws that may skew the results of an individual trial.

👎 Researchers must depend on the quality of the original trials; sometimes, subjects enrolled in one trial center's protocol may end up in more than one published study, skewing results.



Evidence-Based Review

The Archibald Foundation draws up an evidence-based review in which it questions whether ONA-34 should be brought to market. The problem, the foundation says, is that each trial used a different method of comparing the treatment and control groups, as well as a different existing treatment. It suggests two new randomized controlled clinical trials using the most effective standard treatment on the control group.

? Systematic collection, evaluation and synthesis of existing studies to determine the sum of the evidence on a particular question. Frequently, reviews conclude that the evidence is insufficient.

👤 Often many thousands, depending on the size of the studies included

👍 When the underlying data are similar, the review can estimate the effect of an intervention to a greater degree of confidence than the original trials and may resolve contradictions between the conclusions of individual reports.

👎 The power of these reviews depends on the quality of the trials and the willingness of investigators to share unreported data. Also, not every expert may agree on the criteria for including trials in a review.

