## Comments and Responses

### Are Organic Foods Safer or Healthier?

**TO THE EDITOR:** Smith-Spangler and colleagues' meta-analysis (1) found significant differences for only 1 of 6 groups of secondary metabolites in plant foods (Table 1), which contrasts with the findings of a previously published meta-analysis that showed significant differences for 4 of 6 groups (2). Several aspects of the methodology used by Smith-Spangler and associates seem insufficiently justified or inconsistent, affecting the quality of the meta-analysis.

Five issues require clarification. First, the meta-analysis method used is valid only if appropriate sample sizes are used for the calculations (1). Recognized standards for good practice (3) emphasize that "coding of data from the articles" should be "specified and objective." However, no procedure for allocation of sample sizes was presented (1), and a comparison with the design descriptions in the papers included in Smith-Spangler and coauthors' review shows no consistent patterns. For example, for reference 217, the "sample size" in Smith-Spangler and colleagues' online Supplement 4 equals the numbers of independently analyzed subsamples (corresponding with the reported averages and SDs, so probably appropriate). However, for reference 260, the "sample size" is the total number of subsamples from all plots and years, even though results were reported separately per year and the "sample size" for references 240 and 151 (1) are the total numbers collected of tomatoes and leaves, respectively, regardless of how many had been analyzed together.

Second, the authors should explain the choices and definitions of groups of secondary metabolites, particularly why the flavanols were divided into 3 separate groups (increasing the type 2 error) and why most relevant groups other than "total phenols" and "β-carotene" (for example, phenolic acids) were excluded.

Third, most details about study exclusion and data extraction are missing, making it impossible to reproduce the analysis or detect errors. Best practice in terms of transparency would have been to publish these details online, as in Brandt and colleagues' (2) and Seufert and associates' (4) papers.

Fourth, despite stating that only peer-reviewed, English-language studies were eligible for inclusion (in contrast to Stroup and colleagues' recommendations [3]), the authors included data from reference 143 (which was not peer-reviewed) and 239 (which is in Polish) in the calculations (1).

Finally, it is not explained why data on secondary metabolites from 14 included studies (Smith-Sprangler and colleaques' online Supplement 4) were not included in the calculations (their Supplement 2).

Clear explanation and justification of procedures plus publication of the full extracted data set are necessary to assess why the results of the 2 meta-analyses (1, 2) differ and which methodology is best suited for this type of data.

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**Potential Conflicts of Interest:** *Grant (money to institution):* Sheepdrove Charitable Trust (£11 250 in 2010); Soil Association (£1000 in 2007); *Support for travel to meetings for the study or other purposes:* American Society of Agronomy; *Other:* Other industry-related funding to Dr. Brandt's institution for her research (£145 197 since 2004) is for projects not related to organic food (for example, from Danone and Asda [part of WalMart]). Most of the author's public grant income is also not related to organic food. Dr. Brandt is the corresponding author on one of the cited articles (2).

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**TO THE EDITOR:** In their Methods section, Smith-Spangler and colleagues (1) state that they "evaluated the extent to which the organic–conventional comparison pairs were of the same cultivar or breed, grown on neighboring farms, and harvested during the same season." However, in their Results section, they admitted that they included a significant percentage of pairs in their meta-analysis that compared different cultivars and that did not come from neighboring fields ("Among produce studies, 59% . . . and 65% . . . compared food pairs from neighboring farms or the same cultivar, respectively."). Thus, 41% of the pairs were not grown on neighboring farms and 35% did not compare identical cultivars.

Genetics and environmental factors are known to influence plant metabolism and, hence, accumulation of phytonutrients. Lester and Saftner (2) clearly noted the importance of this, yet the authors did not rigorously screen for only valid pairs that compared identical cultivars, growing in comparable soils and microenvironments. If the authors had carefully screened for cultivar and environmental factors, they may have found significant *P* values and homogeneity (that is, a nonsignificant heterogeneity statistic) for several nutrients reported in Table 1.

The authors also neglected to include a 2010 study (3) that compared organically and conventionally grown strawberries in California in which cultivar and environmental factors were meticulously controlled. This study found increased concentrations of vitamin C and total phenolic compounds, as well as higher antioxidant capacity, in organic strawberries. (For the sake of full disclosure, I am a coauthor of this study.) Smith-Spangler and colleagues' inclusion of invalid organic–conventional comparisons (that is, those of different cultivars or growing in different soils and microenvironments) and omission of Reganold and associates' study, which Dr. Smith-Spangler admitted was "erroneously" omitted (4), calls into question the results of this meta-analysis and the authors' conclusions about nutritional differences between organic and conventional produce. Interested readers should compare these results with those of another meta-analysis (5), in which organically grown fruits and vegetables had significantly higher concentrations of the same nutrients.



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**TO THE EDITOR:** As an internist who relies on the *Annals* to publish articles that are free from bias and for which authors' potential conflicts of interest are clearly stated, I was dismayed that Smith-Spangler and colleagues' article on organic food (1) did not indicate that some of the authors are affiliated with Stanford's Freeman Spogli Institute for International Studies, which receives funding from agribusiness and agricultural chemical companies, such as Cargill and Monsanto. These affiliations may explain why the title, abstract, and conclusions emphasize that "[t]he evidence does not suggest marked health benefits from consuming organic versus conventional foods" (1). In actuality, the data show that organic foods have significantly fewer pesticide and toxic chemical residues and antibiotic-resistant bacteria than conventionally grown food. Why were these important findings not highlighted?

The President's Cancer Panel Report, released in April 2010 (2), states that exposure to U.S. Environmental Protection Agency–approved agricultural chemicals has been linked to cancer in most organ systems. The report advises persons to reduce cancer risk by minimizing exposure to environmental toxins. The Recommendations section states, "Individuals and families have many opportunities to reduce or eliminate chemical exposures. For example . . . [e]xposure to pesticides can be decreased by choosing, to the extent possible, food grown without pesticides or chemical fertilizers" (2). Given the Panel's recommendation, why did the authors not highlight this important evidence of the benefits of organic food, rather than bury it in the body of the article where journalists and other readers are less likely to notice it?

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**Potential Conflicts of Interest:** Dr. Davison has made donations to Washington Sustainable Food and Farming Network, Food Democracy Now, and the Neighborhood Farmers Market Alliance.

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**TO THE EDITOR:** Smith-Spangler and colleagues (1) chose the frequency of residues in conventional versus organic food as their basic metric to assess pesticide-related health benefits of organic food. This choice was inappropriate: Frequency of residues does not indicate risk. Pesticide dietary risk is a function of many factors, including the number and levels of residues and pesticide toxicity.

An appropriate assessment would use the extensive, high-quality data on pesticide residues in organic and conventional food from the U.S. Department of Agriculture's Pesticide Data Program (2). These publicly accessible data allow comparisons of residue frequency, levels, and chronic risks. Using a measure of chronic risk based on assessment methods from the Environmental Protection Agency, I calculated that the average pesticide risk level is approximately 90% lower in the organic versus conventional fruit and vegetable samples tested in 2010 and that the average odds ratio is 32.7 (average conventional risk–average organic risk), indicative of a highly significant difference.

The authors used 6 multiple-food residue studies in their meta-analysis. The studies vary greatly in quality, foods tested, analytic methods, and limits of detection. Five of the studies tested European food, and the only study focusing on the U.S. food supply analyzed residue data more than 10 years old. Given how dramatically pesticide use patterns and residues in food have changed since the passage of the Food Quality Protection Act of 1996 (3), the pesticide "risk" findings in Smith-Spangler and associates' review are essentially irrelevant to what American consumers are now facing.

Organic farming largely eliminates the human health risks associated with both pesticides in food and animal agriculture's use of antibiotics. I agree with Smith-Spangler and coworkers that more science is needed to fully quantify these risks, but strong evidence (4, 5) shows that dramatically reducing them would be of clinical significance.

Finally, the risk difference (RD) measure is misleading. The authors report an approximately −30% pesticide RD between organic and conventional foods (approximately 7% of organic samples contained residues compared with approximately 38% of conventional samples). As presented, this finding was often understandably interpreted as referring to pesticide health risk. It does not. Plus, the construct of this metric obscures the real magnitude of differences. If 90% of conventional and 60% of organic samples had residues (instead of 38% and 7%), one would get the same RD of −30%, which is equivalent to a modest 34% reduction in residue frequency. The authors' reported −30% RD is actually an 82% reduction in frequency.



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**Potential Conflicts of Interest:** *Employment:* The Organic Center, Center for Sustaining Agriculture and Natural Resources, Washington State University; *Other:* Dr. Benbrook served as the chief scientist of The Organic Center, a nonprofit organization focusing on the health benefits of organic food and farming, from 2005 to June 2012.

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**TO THE EDITOR:** I read Smith-Spangler and colleagues' review (1) with great interest. Their laudable goal was to give "information that people can use to make their own decisions based on their level of concern about pesticides, their budget, and other considerations" (2). Unfortunately, the authors' reporting went badly awry about the "risks" (incidences) of pesticide residues and antibiotic-resistant bacteria. Their Discussion section greatly understates the findings, stating that "conventional produce has a 30% higher risk for pesticide contamination than organic produce" (1). A Stanford School of Medicine online article (2) includes a similar understatement, and one or the other miscue appeared in most major news stories.

In usual terminology, the actual "risk" (incidence) in conventional foods was more than 5 times higher, not 30% higher. The authors found a 38% incidence in conventional foods compared with only 7% in organic foods. Their "30%" comes from their unfamiliar RD metric, calculated as (approximately) 38% − 7%. Their discussion and the Stanford article drop the word "difference" and make statements certain to be misinterpreted, such as "organic produce had a 30 percent lower risk of pesticide contamination than conventional fruits and vegetables" (2).

As for antibiotic-resistant bacteria in chicken and pork, Smith-Spangler and colleagues' Figure 5 shows an RD of 33%; however, in the Results section, "difference" is again dropped: "The risk for isolating bacteria resistant to 3 or more antibiotics was 33% higher among conventional chicken and pork than organic alternatives" (1). Not so. The authors did not report the separate "risks" (incidences) for conventional and organic meats, but Figure 5 suggests incidences of approximately 49% for conventional chicken and pork and 16% for organic (a "difference" of 33%). Thus, the actual incidence was approximately 3 times higher in the conventional meats, not 33% higher as stated by the authors and duly reported by the Associated Press, Reuters, and others.

The authors were careless and misleading in their reporting, with the predictable result that many journal readers and certainly the public did not receive accurate information for making their own decisions about pesticides and bacteria.

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**Potential Conflicts of Interest:** *Consultancy:* The Organic Center and Center for Sustaining Agriculture and Natural Resources, Washington State University; *Other:* Dr. Davis is a retired research scientist from the University of Texas.

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**IN RESPONSE:** There has been considerable attention from the media, medical and agricultural research communities, and the general public since the publication of our review, including several comments posted on the *Annals* Web site. Many of these inquiries asked similar questions, and we would like to share our responses in summary for interested readers. At the end of this letter, we respond to specific comments posted by Dr. Brandt and Dr. Andrews.

## Purpose of the Study

We were interested in the evidence of whether organic foods are more nutritious, safer, or healthier than conventional alternatives. Although consumers are probably most interested in whether consumption of organic food improves health or reduces disease, we identified only 17 studies of humans consuming organic and conventional foods and only 3 of these studies examined a very small number of clinical outcomes. Given this limited literature, we next examined indirect measures of health and disease (such as nutrient levels and risk for contamination among organic and conventional products) to understand differences between organic and conventional foods that may influence health and disease.

Our comparison of pesticide contamination or antibiotic-resistant bacteria among organic and conventional foods, for example, was not designed to, and is not able to, assess the safety of current pesticide levels in produce or antibiotic-resistant bacteria on meat products but instead to provide information to consumers about differences in these outcomes between organic and conventional products. The outcomes of greatest importance vary among consumers: Some consumers are interested in whether certain foods are more nutritious than others (for example, contain higher vitamin or mineral levels), whereas others are more concerned about food safety issues (such as bacterial or pesticide contamination). Thus, we presented the evidence for various outcomes of interest so that individual consumers could make preference-sensitive decisions.

Furthermore, as we mention in our review, there are numerous valid reasons why consumers might chose organic over conventional foods, including concerns about the environment, animal welfare, farm worker health, taste, and cost. Our study did not address these



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issues; instead, we sought to synthesize the evidence on nutrient levels, contamination, and known health effects of the decision to consume organic versus conventional foods.

## Project Funding

Study authors did not receive funding from any agricultural, chemical, or food organization or business for this project, and authors do not have other work funded by these organizations or businesses. Ms. Pearson (who was an undergraduate at the time of the project) was supported by a Stanford Undergraduate Research Grant for 1 summer. Dr. Smith-Spangler (who was a postdoctoral fellow during the time of this project) was supported by the Veterans Affairs Physician Post-Residency Fellowship, a research training program. This study was supported by no other funding mechanisms, including grants or contracts.

Interested readers may examine the International Committee of Medical Journal Editors' disclosure of potential conflicts of interest statements, which are available from all authors at www.annals.org. To summarize these statements, the study authors, Stanford University, or any other institution affiliated with the study authors did not receive a grant, a consulting fee or honorarium, support for travel to meetings for the study or other purposes, fees for participation in activities, payment for writing or reviewing the manuscript, provision of writing assistance or equipment or administrative support, or other types of support from a third party to support any aspect of the submitted work. Furthermore, no authors have any financial relationships (for example, board membership, consultancy, employment, expert testimony, grants or grants pending, payment for lectures, and payment for manuscript preparation) with any entities (such as agricultural, chemical, or food organizations or businesses) that could be perceived to influence our published work.

## Methodological Questions

The 3 most common questions about our methods relate to our use of the absolute risk difference (RD) when comparing pesticide residues in organic and conventional produce; our presentation of *P* values and consideration of statistical significance in light of multiple comparisons; and how our methods differ from those of Dr. Brandt and colleagues (1), which we discuss at the end of this letter.

## Absolute RD

We have been asked whether our choice of the absolute difference in risk for exposure to any detectable pesticide residue is an appropriate effect size. We found a 30% reduction in absolute risk for contamination with any detectable pesticide residues among organic compared with conventional produce—a substantial reduction in risk.

We disagree with those who suggest that our use of absolute RD is misleading. We clearly described the use of absolute RD in both the Methods and Results sections. Furthermore, in epidemiology it is considered to be best practice to report absolute RDs rather than relative RDs, particularly when events are uncommon, as was the case with the included evidence. Indeed, for this reason we believe that using measures of relative risk reduction would have been misleading. In addition, we reported absolute RDs throughout the paper, not just for pesticide contamination but also for contamination with bacteria and antibiotic-resistant bacteria, for similar reasons.

We are aware that other outcomes related to pesticide contamination in foods are of interest to consumers, including the magnitude of levels of pesticide residues and exposure to multiple pesticide residues. However, we found only 9 studies comparing pesticide outcomes (and 3 of these were single-food studies). Data on pesticide levels and contamination with multiple pesticides were reported inconsistently among these studies; thus, we could not summarize results on absolute pesticide levels or contamination with multiple pesticides. However, 3 studies did report risk for contamination exceeding maximum allowed limits, which we assessed and reported in our review.

## Statistical Significance and Multiple Comparisons

We presented CIs and *P* values for all reported outcomes. The *P* values presented are those after correction for multiple comparisons. Multiple comparisons increase the likelihood of finding significant differences when none exists (false-positives).The problem of multiple comparisons occurs when one examines numerous outcomes, particularly when the outcomes come from the same samples, which are not independent but instead correlated, as is the case in our review. We believe that our conservative approach to calculating the *P* values is justified on the basis of the multiple comparisons and substantial heterogeneity among studies. Moreover, there was some concern that presenting the unadjusted *P* values would have confused readers accustomed to a threshold of $P = 0.05$ as the standard measure of statistical significance at which a given effect was considered not meeting statistical significance.

## Reporting on Outcomes of Interest

In the text, tables, and figures of our review (2), we presented detailed information about the abstracted data and our analyses to allow interested parties to interpret the data for themselves and to facilitate replication of our results. In addition to the data provided with the main text, we provided more than 70 pages of supplemental material about our methods and included studies (available at www.annals.org). We have been criticized for deemphasizing the importance of some key results of interest—most notably the reduction in absolute risk for contamination with any detectable pesticide residues and antibiotic-resistant bacteria among organic products. These are some of the most important findings of our study, and we highlighted the substantial reduction in absolute risk for exposure to any detectable pesticide residues and to multidrug-resistant bacteria in selected organic foods in the abstract, Discussion section, and multiple figures (2).

## Heterogeneity

As we noted in the discussion, there are multiple sources of heterogeneity (variability) among the included studies that should be kept in mind when interpreting our results. Study methods (for example, organic standard applied) varied considerably among the included articles both by geography and over time (included articles were from many countries and spanned many years, over which time organic standards have evolved). The foods that were evaluated (such as the specific cultivars) could have affected the measured outcomes (for example, nutrients).

Environmental factors, such as differences in harvesting, storage, and processing, can affect the outcomes of interest. Finally, farming practices can vary greatly among organic farmers (3). Any of these sources of variability could have obscured the ability to detect true differences between organic and conventional foods. However, consumers generally do not have specific information about the exact practices followed by farmers, such as harvest date; weather condi-



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tions; fertilizer type, concentration, or schedule; or cultivar or breed of animal. Thus, it seems appropriate to combine studies with these types of heterogeneity because they reflect the information available to consumers faced only with an organic or conventional label to guide their consumption decision.

### Response to Dr. Brandt and Dr. Andrews

Dr. Brandt raises several questions about differences in the methods that we used in our analysis and those that she and her colleagues used (1). In their review, Brandt and associates found significantly higher levels of total phenolics, "other (plant) defense compounds" (tannins, alkaloids, chalcones, stilbenes, flavanones and flavanols, hop acids, coumarins, and aurones), flavones and flavonols, and vitamin C. Differences were not significant between organic and conventional samples among the remaining groups that they examined, carotenes and "other non-defense compounds" (anthocyanins, tocopherols, and volatiles).

Some of our results were similar to those of Brandt and coworkers: We both found that organic produce had significantly higher levels of total phenols but no differences in $\alpha$-tocopherol or $\beta$-carotene levels. We did not examine "other plant defense compounds" as a group. However, we found no significant difference in the vitamin C content of organic and conventional foods and significant heterogeneity in the summary effect estimate, whereas Brandt and colleagues found a small but statistically significant higher level of vitamin C among organic produce than conventional alternatives (1).

Supporting our finding of no significant differences in vitamin C content, of all the studies comparing vitamin C levels in organic and conventional produce (including those reporting results incompletely so that statistical tests could not be conducted and hence the studies could not be included in summary effect calculation [our Table 1]), only 23 of the 113 comparison pairs had significant differences favoring organic produce. In 78 comparisons, differences between organic and conventional produce were not significant.

Our study differed substantially from that of Brandt and associates (1) in 2 important ways: by formally considering both within-study and between-study heterogeneity (variability) and including a correction for multiple comparisons (see previous discussion). Our study accounted for within-study variation by including the variance reported by each of the studies in summary effect calculations, whereas Brandt and coworkers did not seem to include this information in their calculations. When information about within-study variance is not included, more weight is given to studies with high variability.

In addition, in contrast to Brandt and colleagues, we reported heterogeneity statistics for all findings (which examined between-study variability), conducted sensitivity analyses when possible to explore sources of heterogeneity (for example, testing method, study design, and organic standard applied), and conducted sensitivity analyses to detect influential studies (2)—all standard practices for the conduct of a meta-analysis.

Furthermore, we included each study only once in summary effect calculations to avoid correlation effects (that is, findings from the same study but different years that are likely to be correlated), whereas Brandt and associates assumed that samples from the same study but different years or seasons are independent.

Finally, our choice and grouping of outcomes reflect our different perspectives. We were principally interested in the outcomes that consumers use to inform their shopping decisions and those frequently reported in the literature (for example, ascorbic acid and $\alpha$-tocopherol levels). We would have liked to examine flavanol content, which has been implicated in the health benefits of chocolate (4), but too few studies reported on this group. Instead, we assessed a larger group of which flavanols are a part (flavonoids) and did not find significant differences between organic and conventional produce.

Dr. Brandt suggested that we did not provide sufficiently detailed information about our methods or results. We disagree. As described in our Methods section, we extracted the data (for example, means, variances, and sample sizes) from each study and used standard methods for combining results by using a commercially available software package, Comprehensive Meta-analysis, version 2 (Biostat, Englewood, New Jersey) (2). We provided more than 70 pages of detailed supplemental material about our methods and included studies (available at www.annals.org). For example, Supplement 4 describes each included study in detail, including sample sizes, outcomes measured, and a summary of key findings. In addition, we provided much of the raw data on key outcomes, such as risk for contamination, in the figures (such as Figures 2 to 5) (2).

We also described our inclusion and exclusion criteria in the Methods section and even listed the studies that reported results but did not report results completely, such that they could be included in statistical calculations (Supplement 2). For example, the 14 studies that Dr. Brandt mentioned did not report SDs or variances, so we could not include them in summary calculations (as described in the Methods section); however, Table 1 and Supplement 4 qualitatively summarize the results of these studies.

Furthermore, reference 239 (mentioned by Dr. Brandt) includes a summary with data in English about vitamin C, and our understanding is that reference 143 was peer-reviewed (results from reference 143 were included in analyses of vitamins C and A and quercetin); therefore, we included these articles in our review. However, as with all outcomes, we conducted sensitivity analyses in which each study was individually removed from the analysis to evaluate whether any 1 study substantially changed the reported findings. Removal of reference 143 or 239 did not alter our findings.

A final note about our statistical methods: Our paper was extensively reviewed, including by a statistical editor at the *Annals* and their statistical board to ensure that we adhered to standard methods of conducting and reporting meta-analyses.

We agree with Dr. Andrews that genetic and environmental factors influence plant metabolism, hence the accumulation of phytonutrients. However, consumers do not generally receive information about genetics or environmental factors when they purchase food and instead only have information about whether the food was organic or conventionally produced. Thus, to reflect the choices of consumers, we believe that it was fair to include all data comparing organic and conventional food.

We regret that Reganold and associates' study of organic and conventional strawberries (5) was not included in our analyses of organic and conventional foods because it was erroneously coded as a soil study. However, upon additional review, we find that their study has data that would meet criteria for inclusion. Our review did



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find significantly higher levels of total phenols among organic produce, similar to Reganold and coworkers' findings of higher levels among organic compared with conventional strawberries (5).

In contrast to Reganold and colleagues' study, our review did not examine antioxidant capacity as an outcome and we did not find significant differences in vitamin C levels between organic and conventional produce. Given that our review included 31 other studies in our summary effect calculation for vitamin C (and found a large *P* value of 0.48 [Table 1]), it is highly unlikely that inclusion of 1 more study would have substantially altered the results.

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