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## **Initial Reflections on the *Annals of Internal Medicine* Paper “Are Organic Foods Safer and Healthier Than Conventional Alternatives? A Systematic Review”**

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### **Overview**

In a comprehensive paper published in the September 4, 2012 issue of the *Annals of Internal Medicine* (Smith-Spangler et al., Vol. 157, Number 5: pages 349–369), a Stanford University Medical School team surveys the global literature for evidence of differences between the nutritional quality and safety of organic and conventional foods. The team’s two major conclusions are that:

“The published literature lacks strong evidence that organic foods are significantly more nutritious than conventional foods.”

“Consumption of organic foods may reduce exposure to pesticide residues and antibiotic-resistant bacteria.”

The analysis supporting these conclusions is flawed in several ways. The basic indicators used to compare the nutritional quality and safety of organic versus conventional food consistently understate the magnitude of the differences reported in high-quality, contemporary peer-reviewed literature. In the case of pesticides and antibiotics, the indicator used—the percent of samples of organic food with a trait minus the percent of conventional samples affected—is not a valid indicator of human health risk.

In its analysis the team does not tap extensive, high quality data from the USDA and Environmental Protection Agency (EPA) on pesticide residue levels (USDA Pesticide Data Program, 2012), toxicity and dietary risk (Office of Inspector General, 2006 a and 2006b; Benbrook, 2011a; Benbrook, 2008b), as well as a persuasive body of literature on the role of agricultural antibiotic use in triggering the creation of new antibiotic resistant strains of bacteria, and the genes conferring resistance (Looft et al., 2012).

The team’s answer to the basic question, “Is organic food more nutritious or safer?,” is based on their judgment of whether published studies provide evidence of a clinically significant impact or improvement in health. Very few studies are

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designed or conducted in a way that could isolate the impact or contribution of a switch to organic food from the many other factors that influence a given individual's health. Studies capable of doing so would be very expensive, and to date, none have been carried out in the U.S.

For most people, just switching to organic fruits and vegetables, or organic dairy products or meat, in the absence of other changes in food choices and overall diet quality, would not be expected to trigger a clinically significant improvement in health, especially in the relatively short time periods assessed in the dietary-intervention or human-health studies reviewed by the Stanford team. The one exception in the literature—studies spanning the duration of a woman's pregnancy and the first few years of a child's life—provide encouraging evidence that organic food can reduce the odds of some adverse health impacts, including birth defects, neuro-behavioral and learning problems, autism, and eczema (Arbuckle, et al., 2001; Bellinger, 2012; Bouchard, et al., 2011; Engel, et al., 2011; Garry et al.; 2002; Rauh, et al., 2011; Schreinemachers, 2003).

When an individual decides to switch to healthy dietary choices from clearly unhealthy ones, and also consistently chooses organic foods, the odds of achieving "clinically significant" improvements in health are substantially increased (Benbrook, 2011b). The most significant, proven benefits of organic food and farming are: (1) a reduction in chemical-driven, epigenetic changes during fetal and childhood development, especially from pre-natal exposures to endocrine disrupting pesticides (Crews et al., 2012; Vandenberg, et al., 2012), (2) the markedly more healthy balance of omega-6 and -3 fatty acids in organic dairy products and meat, and (3) the virtual elimination of agriculture's significant and ongoing contribution to the pool of antibiotic-resistant bacteria currently posing increasing threats to the treatment of human infectious disease (Aarestrup, 2012; Looft, et al., 2012).

The Stanford team's study design precluded assessment of much of the evidence supporting these benefits, and hence their findings understate the health benefits that can follow a switch to a predominantly organic diet, organic farming methods, and the animal health-promoting practices common on organically managed livestock farms.

### **Putting The Stanford Findings In Perspective**

The findings of this study are ripe for overstatement and misinterpretation. From the study's summary and press materials, it is easy to see why many stories will start with a clear and unequivocal statement like—"New Study Undermines Health Benefits of Organic Food." While the study reports a lack of evidence of "clinically significant" benefits, it acknowledges several benefits that fall short of the team's undefined threshold of "significant."

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The study design also prevented the Stanford team from connecting the dots across multiple bodies of evidence from several disciplines that help shed light on the mechanisms through which organic farming and the consumption of organic food can enhance human health outcomes.

The framing of this study's findings also drives home the acute need for an open dialogue among scientists, clinicians, nutritionists, the food industry, the government, and consumers about what constitutes a "significant" benefit from *any* health-promoting life-style intervention, how such benefits should be quantified, and then weighed against the costs entailed in achieving them.

I am among a small group of people who, by virtue of professional interests and responsibilities over the last decade, have read over 200 of the 298 references cited in the Stanford paper. I have analyzed the results of dozens of them and carried out meta-analyses on this body of literature (Benbrook, 2008b). My goal has been to integrate into a public-health context the insights gained from research in several disparate fields.

Over time, I believe that unbiased analysis coupled with modern-day science is likely to show with increasing clarity that growing and consuming organic food, especially in conjunction with healthy diets rich in fresh, whole foods, is one of the best health-promotion investments we can make today as individuals, families, and a society.

For people with unhealthy diets lacking in fruits and vegetables and prone to excess caloric, salt, sugar, and fat intakes, the switch to a healthier diet is the most important intervention (Benbrook, 2011b).

For individuals already adhering to and benefitting from a balanced and healthy diet composed of conventionally grown food, including ample servings of fresh fruit and vegetables, the strategic selection of organic foods can help them further tip the odds toward good health (Benbrook, 2011b), particularly at certain stages of life when humans are particularly vulnerable to the adverse impacts of pesticides and animal drugs, i.e. before and during pregnancy, thru the first few years of a child's life, when battling a degenerative disease, and after age 60.

### **Is Organic Food More Nutritious?**

The Stanford team does not define empirically what it means by a food being "significantly more nutritious" than another food. To me, such a food would need to deliver at least 50% higher levels of several important nutrients per calorie or serving, while also not delivering substantially lower concentrations of other essential nutrients. But a food does not need to be 50% more nutrient dense (i.e. "significantly" more nutritious) to deliver important health-promoting benefits. Achieving even a 10% increase in the levels of key nutrients in commonly consumed foods would bring about tangible health benefits across the U.S. population.

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In carefully designed studies comparing organic and conventional apples, strawberries, grapes, tomatoes, milk, carrots, grains, and several other raw foods, organic farming leads to increases on the order of 10% to 30% in the levels of several nutrients, but not all. Vitamin C, antioxidants, and phenolic acids tend to be higher in organic food about 60% to 80% of the time, while vitamin A and protein is higher in conventional food 50% to 80% of the time.

A large team of plant and food scientists carried out the most sophisticated meta-analysis of the “organic-versus-conventional food” nutrient-content literature. The team was led by Kirsten Brandt, a scientist at the Human Nutrition Research Center, Newcastle University in the United Kingdom, and included individuals with extensive expertise in designing, carrying out, and interpreting these sorts of studies. Their analysis was published in *Critical Reviews in Plant Sciences* in 2011, under the title, “Agroecosystem Management and Nutritional Quality of Plant Foods: The Case of Organic Fruits and Vegetables” (Vol. 30: 177–197).

The Stanford paper cites this analysis but does not mention its findings, remark on the study’s scope and sophisticated methodology, nor acknowledge the major differences in the conclusions reached.

The Brandt team covered essentially the same literature as the Stanford team. They used different and more rigorous criteria to judge whether a published study was properly designed and conducted and produced reliable results. Still, the studies included in their meta-analysis largely overlaps with those analyzed by the Stanford team.

The Brandt et al. study both documents significant differences in favor of organically grown food and explains the basic farming system factors leading to the differences. They conclude that increasing the amount of plant-available nitrogen, as typically occurs in conventional farming, “...reduces the accumulation of [plant] defense-related secondary metabolites and vitamin C, while the contents of secondary metabolites such as carotenes that are not involved in defense against diseases and pests may increase.”

They found that secondary plant metabolite-based nutrients in fruits and vegetables are 12% higher, on average, in organic food compared to conventionally grown food. A subset of nutrients composed of plant secondary metabolites that are involved in plant defense against pests and response to stress were, on average, 16% higher. This subset encompasses most of the important, plant-based antioxidants that promote good health through multiple mechanisms.

The team went on to estimate that consumption of organic fruits and vegetables, by virtue of their average 12% higher nutrient levels, would extend life expectancy by 17 days for women and 25 days for men. Are such extensions of life expectancy “clinically significant”?

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That is a difficult question for which opinions are bound to differ. One relevant factor, however, is that a substantial and growing share of national health care expenditures are made at the end of life, a time when the medical care costs of sustaining life for another 17 to 25 days are, on average, very significant.

### **Pesticide Exposures and Food Safety**

The Stanford team reports that “Organic produce had 30% lower risk for contamination with any detectable pesticide residue than conventional produce.” The use of the term “risk” in this context is confusing and inappropriate, since many readers are likely to associate “risk” with the probability of an adverse health outcome.

The Stanford team’s analysis of pesticide-related “risk” is based on an incidence metric they call the “RD,” or “Risk Difference.” The “RD” from a given study of the incidence of one or more pesticide residues in food samples, or an average (“summary”) RD across multiple studies, is the absolute *difference* between the percent of organic samples found to contain a residue and the same percent in a study’s corresponding, conventional samples.

But the “RD” has little to do with actual, clinical risk, defined as the odds that a given exposure to a pesticide increases the likelihood of an adverse health outcome. Most conventional fruit and vegetable samples contain two to five residues, and in several important crops, about 10% of samples contain eight or more residues. Fortunately, residues are much less frequent in produce with a thick peel or shell (e.g., sweet corn, pineapples, and bananas), as well as in some crops grown in the ground (e.g., onions).

An enormous body of evidence compiled by the EPA during the course of conducting pesticide dietary risk assessments shows that the number of high-risk samples in any given year, for any given food, is driven by the presence of relatively high levels of the most toxic pesticides, rather than the absolute number of residues detected in the food.

The Stanford team’s RD results for nine studies comparing the incidence of one or more pesticide residues in conventional and organic food appear in their Figure 2. They conclude that the average (“summary”) RD value is –30%, suggesting that there is a 30% lower chance of an organic sample having one or more residues, compared to a conventional food sample.

However this “30% lower risk” is an unusual and unfamiliar metric that will likely be misunderstood by many readers, on two levels. The usual way to express the difference between organic and conventional samples testing positive for a pesticide residue would subtract the organic percent positive from the conventional percent positive, and divide the result by the conventional percent positive. By this familiar

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measure, the overall reduction in frequency of residues in organic food is 81%, a much larger decrease than suggested by the Stanford team's RD metric.

To illustrate the misleading nature of the RD metric in more detail, consider the first study shown in the authors' Figure 2. Four of 81 organic samples had a detectable residue, a 5% risk of contamination ("incidence" seems a more accurate term than "risk"). In the same study, 1354 of 4069 conventional samples had a detectable residue, a risk or incidence of 33%. Thus the incidence is only 15% as high in the organic samples compared to conventional samples (5%/33%), and in common, practical terminology we would most likely say that there was an "85% lower risk or incidence" in the organic compared to the conventional samples. But in the unfamiliar terminology of RD, Figure 2 shows only a "28% lower risk" ( $RD = 5\% - 33\% = -28\%$ ). A similar analysis applies to the other studies in Figure 2 and to the authors' summary RD across the nine studies. Their seemingly unimpressive finding of "30% lower risk" corresponds to an overall 81% lower risk or incidence of one or more pesticide residues in the organic samples compared to the conventional samples.

The second level of potential misunderstanding arises because the potential *health risk* of pesticide residues in organic foods compared to conventional foods typically averages 10 to 20-times smaller than that in conventional foods. This is because: (a) most residues in organic food occur at much lower levels than in conventional food, (b) residues are not as likely in organic foods, (c) multiple residues in a single sample are rare in organic food but common in conventional produce, and (d) high-risk pesticides rarely appear as residues in organic food, and when they do, the levels are usually much lower than those found in conventional food (especially the levels in imported produce).

In terms of more sophisticated measures of pesticide health risk, the typical reduction from choosing organic foods, especially fresh produce, is even greater than the authors' actual reduced incidence near 80%. For example, I recently completed an assessment of relative pesticide health risks from residues in six important fruits—strawberries, apples, grapes, blueberries, pears, and peaches. Using the latest data from USDA's Pesticide Data Program (USDA, 2012) on these foods, I found that the overall pesticide risk level in the conventional brands was 17.5-times higher than in the organic brands (see table below). The differences translate into a 94% reduction in health risk  $[(0.2507-0.0143)/0.2507]$  from the selection of organic brands.

<b>Conventional versus Organic Dietary Risk</b>		
	<b>Domestic Conventional FS-DRI Most Recent Year of PDP Data</b>	<b>Domestic Organic FS-DRI Most Recent Year of PDP Data</b>
Strawberries	0.482	0.007
Apples	0.274	0.0098
Grapes	0.1182	0.0635
Blueberries	0.165	0.0002
Pears	0.197	0.0036
Peaches	0.268	0.0017
<b>Average</b>	<b>0.2507</b>	<b>0.0143</b>
<b>Ratio Conventional to Organic =</b>		<b>17.5</b>

A 17.5-fold difference in pesticide risk levels, corresponding to a 94% reduction in health risk, is certainly much more clinically significant than is suggested by a “30% lower risk” based on RD, a metric that makes little practical or clinical sense. People should be concerned about pesticide *health* risk, not just the number of residues they are exposed to. Assessing pesticide-driven health risks is more complicated, but it can be done (Bellinger, 2012; Bouchard et al., 2011; Benbrook, 2011a and 2011b; Office of Inspector General, 2000b). The published literature doing so, however, rarely mentions farming systems or organic food, and hence was not included in the studies analyzed by the Stanford team.

The presence of a pesticide residue in a given food is just one of several factors that determine risk. The others are the level of the residue, the age of the exposed person, the tissues that are exposed, the pesticide’s innate toxicity, what else the person is exposed to and the presence of any synergistic effects, and whether the individual has normal or constrained ability to metabolize pesticides and/or deal with the toxic insult caused by the residues.

One other shortcoming in the Stanford analysis of pesticide risks is worth noting. There is now strong evidence that pre-natal exposures to organophosphate (OP) insecticides increase the risk of a range of neuro-developmental deficits (Crews et al., 2012; Engel, et al., 2011; Rauh, et al., 2011; Bouchard et al., 2011), including reduced IQ (Bellinger, 2012). Untimely OP exposures during pregnancy also increase a child’s risk of autism, ADHD, and asthma (Vandenberg et al., 2012). The studies cited above report relatively consistent relationships between levels of OP metabolites in the blood and urine of women during pregnancy, and in umbilical cord blood upon birth, and the prevalence of birth defects and developmental

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impacts that can lead to retarded motor function, intelligence, and aberrant behavior as children grow up.

Moreover, the level of OP metabolites in a woman's blood that are associated with a heightened risk of developmental disorders is comparable to the average level found in the most heavily exposed 25% of woman of child-bearing age (Rauh et al., 2011). In other words, the risk of possibly significant, adverse developmental outcomes from pre-natal OP exposures is not restricted to a small segment of the population facing unusual and/or occupational OP exposures.

### **Alex Lu's Research**

The Stanford paper surveys the findings of the approximately 10 published studies on the impacts of organic food on pesticide exposures. One-half of these studies are by teams including or led by Chensheng (Alex) Lu, now at the Harvard School of Public Health.

Lu's work is well known and provides compelling and consistent evidence that when school-age children switch to a predominantly organic diet, exposures to organophosphate (OP) insecticides are virtually eliminated—an effect far larger than that suggested by the Stanford team's summary RD statistic and stated indicator of pesticide contamination "risk."

Lu et al. conducted two dietary intervention studies in and around Seattle, Washington, and a third in Atlanta, Georgia (Lu, et al., 2006, Lu et al., 2008). Each shows that it takes only a couple of days on an organic diet for metabolites of OP insecticides to virtually disappear from a child's urine, and then it takes only a couple of days back on a conventional diet for the OP metabolite levels to return to pre-intervention levels.

The remarkable consistency of the findings between multiple cycles of going onto, and then off a predominantly organic diet across these three studies, involving three different groups of children, gives a high level of confidence in Lu et al.'s basic conclusion that consuming mostly organic food dramatically reduces, and indeed can nearly eliminate, OP dietary exposures.

The Stanford team, however, is subdued in its interpretation of Dr. Lu's work, and states that:

"Although these studies suggest that consumption of organic fruits and vegetables may significantly reduce pesticide exposure in children, they were not designed to assess the link between the observed urinary pesticide levels and clinical harm."

To most experts in the field of pesticide toxicology and human health, the Lu studies do far more than "...suggest..." that reductions in exposure occur. Moreover, there have been several extensive analyses of differences in the frequency of residues,

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residue levels, and health risk in conventional versus organic food. These studies, including several conducted by The Organic Center (Benbrook, 2008a; Benbrook, 2011b), draw on the 400,000-plus samples of food tested by USDA for pesticide residues since the early 1990s in its Pesticide Data Program (PDP) (USDA, 2012). The results of PDP-based studies support and broaden Lu's basic finding. Choosing mostly organic fruits and vegetables will dramatically reduce anyone's exposure to pesticides via the diet.

As noted above, quantifying differences in human pesticide health risk is far more complex than quantifying differences in the frequency of residues or the number of residues in food. Risk levels for adverse outcomes like cardiovascular disease, diabetes (Lim, et al., 2009), cancer, reproductive problems (Arbuckle, et al., 2001), arthritis, dementia, and developmental deficiencies in children are hard to quantify (Bellinger, 2012). It is even harder to isolate the impact of a single risk factor or life-style change, like choosing organic food, on the genesis of these disorders and diseases. Despite such unavoidable complexity, it is widely accepted that reductions in pesticide exposures usually translate into roughly comparable reductions in risk.

### **Antibiotic Resistance**

The authors of the *Annals of Internal Medicine* paper write that "The risk for isolating bacteria resistant to 3 or more antibiotics was 33% higher among conventional chicken and pork than organic alternatives..." As in their similar analysis of pesticide residues in Figure 2, this 33% from Figure 5 refers to their summary absolute RD of -32.8%, an unfamiliar metric that is not very meaningful in practical terms. Few readers will realize that in usual terminology, the (relative) risk for isolating bacteria resistant to 3 or more antibiotics was actually about 300% higher in conventional meats compared to organic meats (risk about 48% in conventional and 16% in organic).

The authors go on to write that "Bacteria isolated from retail samples of organic chicken and pork had 35% lower risk for resistance to ampicillin." This 35%, too, refers to their absolute "risk" difference, RD = -34.9%, and it, too, is a misleading metric.

In usual terminology, the relative reduction in the incidence of bacteria resistant to ampicillin was about 66%, not 35%, and it corresponds to an increased relative "risk" of about 290% in the conventional samples (about 52% risk) compared to organic samples (18% risk). These summary differences have high statistical significance and they seem to support a stronger statement than the authors' bland conclusion that organic chicken and pork "may" reduce exposure to antibiotic-resistant bacteria.

In fact, organic farmers are not allowed to use antibiotics to treat animals producing organic food. If treatment with an antibiotic is necessary to save an animal from a life-threatening infection, current U.S. National Organic Program and European

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rules require the farm operator to treat the animal prior to selling it off the farm to a conventional producer, or shipping it for slaughter as conventional food. As a result, organic livestock farmers simply cannot in any way contribute to the problems that doctors face when treating an infection caused by antibiotic resistant bacteria.

The Stanford team concludes, tepidly, that the “...increased prevalence of antibiotic resistance may be related to the routine use of antibiotics in conventional animal husbandry.” This conclusion, based on understated RDs, sells dramatically short the proven benefits of organic livestock farming regarding bacterial susceptibility to antibiotics used to treat human infections. The authors grant that farm use of antibiotics “may be related” to the problem of antibiotic resistance, but they go on to assert that “...inappropriate use of antibiotics in humans is the major cause of antibiotic-resistant infections in humans.”

It is true that the epidemiological literature highlights the role of antibiotic use in humans in spreading antibiotic resistant infections across the human population. But this begs the question of where did the initial antibiotic-resistant genes come from?

My read of the global literature points to an important, five-decade-long role of sub-therapeutic antibiotic use for growth promotion and disease prevention on chicken and pig farms (Aarestrup, 2012; Looft et al., 2012)). Such uses have created a major “well” from which antibiotic-resistant bacteria first arise. Once created on the farm in the gastrointestinal tract of a pig or chicken, antibiotic-resistant bacteria, and the genes conferring resistance, can and do move in myriad ways, first to other bacteria, then from animals to man, and over time within the human population. Continued human use of antibiotics that are no longer fully effective surely does hasten the spread of resistant bacteria in humans, and exacerbates the health complications left in their wake. This dynamic *obscures* the role of agricultural uses of antibiotics in the initial creation of antibiotic-resistant genes and bacteria, but does not render them insignificant.

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