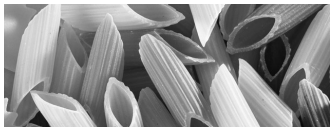

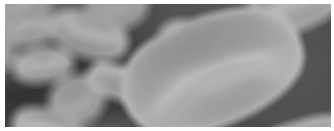

Science and Pseudoscience in Adult Nutrition Research and Practice

Human nutrition research and practice is plagued by pseudoscience and unsupported opinions. A scientific analysis separates reliable nutrition facts from nutritional pseudoscience and false opinion.

REYNOLD SPECTOR

In recent years, nutrition research and practice have lagged behind many other biological and medical fields.[1–5] In part, this lag is due to many pseudoscientific beliefs and practices mistakenly regarded as being based on scientific methods.[1–5] By nutrition I mean all the foods, fluids, and "natural" supplements humans ingest.[1, 2] By pseudoscience, I mean the use of inappropriate methods that frequently yield wrong or misleading answers for the type of question asked. In nutrition research, such methods also often misuse statistical evaluations.[4] My purpose here is to definitively (wherever possible) or tentatively (where the data are incomplete or nonexistent) answer a series of key questions about adult human nutrition using relevant rigorous scientific principles

and methods. The data clearly show that much current advice about dietary pyramids, food supplements, megavitamins, and weight loss regimens is frequently unproven, erroneous, or even harmful and is often based on pseudoscience or derivative incorrect professorial opinion.[1–7]

But before coming to the answers, we should frame the general questions precisely:

1. What do we know about adult human nutrition that meets the standards for truth?
2. Is there an optimum body weight? Is the ancient wisdom of Aristotle correct? He preached a sound mind in a sound body and, most importantly, moderation in all things, including diet. Or are current (immoderate) claims that large amounts of certain nutrients (e.g., vitamins, lycopene, fruits, and vegetables) and avoidance of others (e.g., saturated fats like butter, rapidly absorbed carbohydrates like rice and potatoes) the "way" to prevent bodily harm and promote health?[1, 2, 6, 7]
3. Why are there so many confusing or contradictory data and opinions in the literature, news media, and books on the following points?[1–5]

- Are food supplements such as megavitamins—defined as greater than five times the recommended daily allowance (RDA)—helpful? Specifically, are megavitamins E, C, and carotene healthful or harmful? That is, will they prevent disease and aging alone or in combination? Is there even one supplemental nutrient (nutraceutical) proven to prevent disease and possibly prolong life?
- Are certain common foods (in moderation) harmful? For example, are dietary saturated fats really harmful? Or are such fats useful fuel burned in the body to harmless carbon dioxide and water to provide energy as described in the biochemistry textbooks? Are processed rice and potatoes really bad for you? Do rice and potatoes really strain insulin production by the pancreas and lead to diabetes as alleged?[6] Or are rice and potatoes a reasonable source of calories ingested by billions without harm? In other words, are there some nutrients that can cause disease and others that can prevent disease and illness?[1, 2, 6] Are there "fountain of youth" nutritional approaches or do the body's homeostatic mechanisms counteract "over-consumption" or "under-consumption" of most nutrients? Obviously, everything can be harmful in excess, even salt and water.
- Are there comparative studies that show that certain classes of foods are better or worse than others for adult human health? Are diets high in saturated fats worse than diets high in rapidly absorbed carbohydrates or animal proteins?
- Which weight-loss diets, if any, *work*?

4. Why are there so many erroneous or uninterpretable nutritional experiments (pseudoscience) in the literature? Why do so many scientifically contradicted claims persist in the literature?[3–5, 7] Why are certain long-term epidemiology/observation studies (EOS) continued in spite of the persistent publication of pseudoscience from these studies?[1–5, 7]

To answer these four general questions, we need to understand the methods required to prove hypotheses conclusively in human nutrition and human health. We must apprehend the assumptions, methods to establish causality, clinical trial design, hierarchies of evidence, and statistical concepts so we can evaluate nutritional studies correctly,[3–5, 8] i.e., to separate pseudoscience from science, falsehood from truth. Also, we need to understand the methods involved in extrapolating data from nutritional studies to inferences about populations. For example, data in children or young adults may not be transferable to the elderly (e.g., milk tolerance and vitamin B-12 absorption are different in children than in the elderly).

Finally, we must understand what the U.S. Food and Drug Administration (FDA) and other regulators require for assessing and approving nutritional claims and drugs.[3–5, 8] Within the limits of its jurisdiction (see below), the FDA generally evaluates claims of the type "X causes Y" based on rigorous scientific standards before accepting a causal claim.[1–4, 8] This is in contrast to many journal editors, academic and governmental nutritional committees (e.g., the Department of Agriculture), and the media, which often have weak scientific standards.[1, 2] I will briefly review the FDA standards below.

With a rigorous scientific approach, we can then distinguish "true" nutritional claims with some certainty—separate facts and reasonable inferences from false claims and unproven hypotheses where there is inadequate, incorrect, or misinterpreted data.

In an accompanying document entitled "Methodological and Statistical Issues in Adult Nutritional Research," available on the SKEPTICAL INQUIRER Web site, I describe in some detail the relevant methodological and statistical issues. This analysis is critical to understanding the results of much nutritional research, and I recommend it to interested readers. For example, many EOS widely used to assess causality (e.g., that megavitamin E decreases cardiovascular risk) are methodologically unable to do so.[4, 5, 7] Yet they are frequently performed and published. I explain this strange phenomenon and other methodologically important issues in the "Methodological and Statistical Issues . . ." document.

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What Do We Know?

In fact, we know a lot about adult human nutrition. As shown in Table 1, there are a number of nutrients and minerals humans must ingest for health and well being throughout life. For most adults, except as noted below, these nutrients and minerals are readily obtained from a balanced diet without the need for supplements.[9] Lack of these will lead to poor health and even death. However, it is true that in four- to six-week experiments in obese subjects, only water, vitamins, and minerals, especially potassium chloride, were required. In fact, very

obese patients can survive in excellent health for many months on only water, vitamins (in RDA doses), and potassium chloride.[1] Potassium is required to make up for its obligatory loss through the kidney. In these starving, obese people, calories are mainly obtained through fat mobilization with attendant weight loss. But over the long term, the nutrients and minerals in Table 1 must be ingested. As noted in Table 1, however, the need for calories (fuel) can mainly come from carbohydrate, fat, protein, or combinations of these three. The need for the essential substances in Table 1 is not controversial.[1, 6, 9]

Table 2 shows three important principles of biochemical and physiological nutrition. First, a healthy person (given RDA intake of the substances in Table 1) can proceed with a normal (see below), stable weight by eating predominantly fat or carbohydrates or protein or various combinations of these because of the body's ability to interconvert and utilize carbohydrates, fats, and proteins (amino acids) as needed. In other words, fat, carbohydrate, or protein can serve as the principal source of calories.

Second, the body has a remarkable ability to maintain relatively constant blood levels (homeostasis) of many nutrients. Even more remarkable is the ability of the central nervous system, testicles, and ovaries to maintain nutrient homeostasis. For example, in two carefully studied cases, even huge fluctuations in (orally) ingested potassium or vitamin C barely changed the concentrations of these substances in cerebrospinal fluid (CSF) or the brain.[10] We now understand the biochemical, molecular, and genetic bases for such remarkable homeostasis in the CSF and brain.[10,11] This has profound implications for attempting to prevent cognitive decline with certain nutrients as discussed below.

Finally, with aging, there are large changes in nutritional needs and metabolism. For example, there is approximately a 1 percent decrease per year in energy requirements after age thirty. As we age, there are also major changes in many functions in some individuals, for example, decreases in the enzyme lactase (in the gastrointestinal tract), which splits lactose to easily absorbed galactose and glucose. Also, in some elderly persons, the ability to absorb certain essential substances, such as vitamin B-12, declines. These changes must be understood when talking about diets in the young versus in the elderly.

Table 1. Examples of Essential Substances for which Recommended Daily Allowances (RDA) are Known*[1, 6, 9]

1. "Calories" for fuel from carbohydrate, fat and/or protein (see text)**
2. Vitamins (water- and fat-soluble)
3. Minerals (e.g., potassium, magnesium, calcium, zinc, salt, trace metals)
4. Essential amino acids
5. Essential fatty acids
6. High-quality protein (animal or vegetable, e.g., amaranth)

*Many Nobel Prizes were awarded for the work done in this table, especially for the vitamin work.
**The number of calories for each individual should be sufficient to maintain a steady weight with a BMI between 20–25.

Table 2. Examples of Important Principles of Biochemical and Physiological Nutrition

1. Inter-conversion in the body of carbohydrates, fats, and proteins as necessary
2. Homeostasis of vitamins, minerals, amino acids, sugars, and fats
3. Change in some functions with age, e.g., slowing of metabolism

Is There an Optimum Weight for Adult Humans?

The answer is probably yes.[12] There is a large amount of epidemiological, pathological, and clinical data that suggests a body mass index (BMI) (defined as weight in kilograms divided by the square of height in meters) of approximately 20–25 is optimal. A BMI of greater than 30 is termed obese. There is also a large body of controlled evidence showing that animals fed a low-calorie diet (that keeps them "thin") live longer and are healthier than heavier animals fed an "ad libitum" diet. These human and animal data satisfy Hill's criteria noted

in the "Methodological and Statistical Issues" document.[2–4, 12] However, in humans there has never been a randomized controlled trial of food intake to keep BMI at 20–25 versus greater than 30 with morbidity (disease) and mortality the end points.[12] But, for this article, I accept the notion that obese humans, on average, are less healthy and/or die sooner than people with a BMI of 20–25, all other things being equal, although it is formally possible that obese individuals are "doomed" for reasons independent of obesity.

Table 3. Erroneous Epidemiology/ Observation Studies (EOS)[2–5, 7, 9, 13–21]

EOS	Clinical trial results
1. Agents claimed to reduce cardiovascular risk	
a) Hormone replacement therapy	False
b) Reduce blood homocysteine with B vitamins	False
c) Low fat diets	False
d) Megavitamin E	False
e) Omega-3 fat supplements	Uncertain [21]
2. Agents claimed to prevent cognitive decline	
a) Megavitamin E	False
b) Megavitamin C	False
c) High dose b-carotene	False
d) Vitamin A	False
e) Various combinations of a, b, c, and d	False
3. Agents claimed to prevent cancer	
a) Omega-3 fat supplements	False
b) Dietary Fiber (bowel cancer)	False*
c) Lycopene and Megavitamin E (prostate cancer)	Probably false**
d) Folic acid (bowel cancer)	False

*Dietary fiber does, however, improve bowel function in some people and may be useful functionally.
**Based on best available data[16, 24]

Controversial Questions Answered

Are food supplements helpful? Are there particular nutrients that will prevent illness and disease and possibly prolong life?

The answer, notwithstanding thousands of positive EOS and, in some cases, small inadequate clinical trials, is there is no rigorous scientific evidence for the utility of dietary supplements, including megavitamins in normal-weight (nonpregnant) adults with a stable BMI of 20–25 eating a diet containing adequate amounts of the nutrients in Table 1. See Table 3 for representative examples of false claims based on erroneous EOS.[2–5, 9, 13–21] As you can see, the EOS have been frequently in error, yielding false-positive results. In general the clinical trials in Table 3 are examples of controlled, randomized studies done with very large numbers of people often versus placebo. (It is true, however, that in certain populations the RDA of a few vitamins might be slightly higher than in normal adults, e.g., vitamin D and possibly calcium for nursing home residents and others who do not go out in the sun, and vitamin B-12 for elderly people or for those on proton pump inhibitor drugs.) In fact, there is some evidence in controlled trials that megavitamins (e.g., E, C, and A) may actually increase mortality.[14] Clear exceptions to the general lack of utility of megavitamins are extremely rare patients with genetic abnormalities, e.g., those with vitamin B_6-responsive seizures.[10,11] Yet, notwithstanding the lack of evidence of benefit and potential harm, megavitamins and supplements are still recommended by some nutrition "experts."[9] It is worth noting that the nutraceutical (supplement) industry is a multibillion-dollar enterprise.[9, 14] Dan Hurley summarizes the pseudoscience in this area in his excellent book *Natural Causes*.[9]

Focusing on the lack of scientific rationale for so many nutritional claims, many people ask why and how this sad state of affairs developed. For example, based on what has been known for over thirty years about brain and CSF vitamin homeostasis, how could so many EOS investigators hypothesize and then accept EOS (Table 3) that suggested that megavitamin E, C, and/or B could prevent cognitive decline in adults on diets adequate in the essential substances in Table 1?[10, 11] Consumers and the public correctly ask: If you can't increase brain levels of these vitamins by even large oral doses, how could they "work?" The Hill criterion for biological plausibility is clearly negative.[3–5] In fact, after spending hundreds of millions of dollars on scientific controlled trials, it is now clear that megavitamins do not work (Table 3).

What then is the reason for so many erroneous EOS? Is there a systematic bias? First, as discussed in the "Methodological and Statistical Issues" document, because they are not randomized, EOS are prone to bias and confounding. In many studies, one type of bias is healthy-person bias. In other words, healthier, more health-conscious people tend to take supplements. These people tend to have less disease regardless of the supplements. So, in such EOS it looks like the supplements help. If randomized studies had been conducted, this would not happen (Table 3).

Are certain foods, minerals, or supplements harmful?

Excess amounts of anything can be harmful. Especially noteworthy are vitamins A and D, which can be very toxic in high doses. Aristotle was generally correct—all things should be in "moderation." He actually took this advice from an inscription on the temple of Apollo in Delphi, Greece. As I noted earlier, even widely used supplements such as vitamins E, C, and carotene in "standard mega-doses" (greater than five times the RDA) may indeed be harmful.[14] The potential for harm for many other types of supplements has not been systematically studied, although there are convincing data that certain supplements may damage the liver, kidney, or heart or alter drug metabolism.[9] For example, the amino acid tryptophan (used to induce sleep) and ephedrine-containing herbs (for asthma) were removed from the over-the-counter market because of severe toxicity, including deaths in some people.[9] Unfortunately, the FDA does not generally evaluate supplement claims for safety and efficacy nor does not it regulate the content of most supplements.[9] Hence, it is difficult to know the true content of these supplements. Moreover, when carefully measured, there are many examples of supplement labels not reflecting the true content, a deplorable situation.[9]

Are certain classes of foods better or worse than others?

In healthy people who ingest the essential nutrients in Table 1 and have a normal stable weight (BMI approximately 20–25), there is no convincing comparative outcome evidence (as I defined above) that common foodstuffs, e.g., saturated fats like butter, rapidly absorbed carbohydrates like white rice and potatoes, or animal proteins, are especially helpful or harmful. The notion that some diets (e.g., low-fat or low-carbohydrate) are better than others is not based on sound science but instead on flawed EOS.[1] The USDA food pyramid of the past (which prescribed what you should eat, how many portions, and disparaged certain nutritious foods like eggs and butter) was unscientific.[1, 2, 6] That food pyramid was based, in part, on EOS so flawed as to be almost ludicrous.[1, 2] Specifically, there are no scientific outcome data (as defined above) that five daily servings of fruits or vegetables as per the original USDA food pyramid are better than two or that apples are better than pears (notwithstanding Ben Franklin) in normal-weight adults who consume the essential nutrients in Table 1. Let the proponents of such dietary advice prove the value of their advice with real outcome data from well-managed randomized controlled trials. Similarly, recent attempts to create new food pyramids are also flawed, for example, those that disparage rapidly absorbed carbohydrates (e.g., processed rice and potatoes) and recommend megavitamin E.[6] Let the anti-potato and anti-rice proponents scientifically prove to billions of normal-weight adults or millions of older citizens with delayed gastric emptying (on diets adequate in the essential nutrients in Table 1) that potatoes or white rice per se are more harmful than whole wheat in scientific controlled outcome trials.

However, in obese individuals (BMI > 30), there is some evidence that not only do they eat too many calories but they may also be eating a diet (e.g., rapidly absorbed carbohydrates) that does not "satiate" them and leads to more rapid fat deposition.[1] This hypothesis remains to be proven.

Do weight-loss diets in obese people work?

None work well. On average, over the long term, obese humans do not lose much weight on voluntary low-calorie diets of any kind. (There are of course a few obese individuals who have "self discipline" and can lose weight and keep the weight off. Their "secret" is obscure.) There is, however, some evidence that low-carbohydrate diets "work" best at least for periods up to one year,[22] but this has not been replicated in a two-year study.[22a] Notwithstanding thousands of weight-loss articles and books, there has been very little progress in this area outside of surgical intervention.

Why is so much erroneous and pseudoscientific nutrition research and commentary published? Why do contradicted claims persist in the literature?

While the methodology to approach the truth in nutrition research has been known for decades, it is often either not followed or scientific data are resisted.[1–5, 7, 9] In attempts to understand why this happens, sociologists often employ a balanced analysis. A useful part of such an analysis is the question: who benefits from a particular event or behavior?[4, 5, 7] To begin to answer that question, it is necessary first to review past publication policies of leading medical journals.

In 1994, in a revealing editorial, the editors of the *New England Journal of Medicine* (who have published many erroneous EOS), in an Apologia in response to highly critical newspaper articles, attempted to justify publication of many conflicting (EOS) dietary studies on vitamins as chemo-preventive agents and the whole issue of dietary advice (e.g., butter vs. margarine).[23] Unfortunately, the editors did not claim that the goal of research should be the search for truth using the best available methods.[2–5, 23] They did not acknowledge the hierarchy of evidence and the great value of well-conceived and executed experiments.[2–5, 23] The editors seemed unaware that a few clear, convincing, well-conducted trials, when widely disseminated and followed, can change the practice of nutrition and medicine definitively, unlike hundreds of inconclusive studies, especially EOS.[2–5, 7, 23]

Table 4. Who Benefits from Current Publication Policies?[5, 9]

Category	How They Benefit
1. Editors and journals	A high volume of reports maintains sales, interest, advertising revenue, and so on.
2. Academicians	It's easy to publish almost anything; certain types of studies (e.g., case-control studies) require much less effort and resources than controlled trials to yield a publication.
3. Nutraceutical and certain agricultural/commercial interests	Sale of some foods, nutraceuticals, and supplements increase (e.g., megavitamin E therapy).
4. Selected news media	Controversy based on poor medical science increases sales of papers, magazines, and so on.

Instead, the editors stated, "Thus, nearly every clinical research study would be seen as preliminary. . . . Doctors know that clinical research rarely advances in one giant leap; instead, it advances incrementally."[23] The editors did not blame themselves (and other editors) for publishing low-quality or uninterpretable papers. Instead, the editors blamed the media, which should "improve the way they interpret science." Angell and Kassirer then stated that "the public at large needs to become much more sophisticated about clinical research, particularly epidemiology" because "what medical journals publish is not received wisdom but rather working papers."[23]

Thus, they as journal editors placed the burden on the student, nutritionist, medical scientist, physician, public, and media to determine what is valid, important, and meaningful, sometimes with the help of editorials.[23] This is not a realistic expectation as can be seen in the chaotic state of nutritional research and practice.[1–5, 7, 9]

Who benefits from such an editorial policy so profoundly dissonant with the scientific and regulatory principles described earlier?[3–5] Table 4 provides a tentative analysis of who benefits from poor-quality nutritional research and why.[5] Table 5

reveals a similar tentative analysis of who is harmed and how.[5]

As I described earlier, unless proper studies are done (randomized, single variable, hypothesis-driven, with validated instruments and proper statistical analyses), the literature is doomed to potential, often-unknown bias and confounding.[4] Although it is difficult and expensive to do long-term adequate nutritional studies, it is possible, and scientific studies have been done with megavitamins (e.g., E, C, folate, carotene), certain diets, and supplements[9] with definitive results (Tables 1, 3).

In view of the nutritional chaos I have described, it is a sad commentary on American regulatory authority that the FDA does not have the authority to regulate nutraceutical content and claims except when egregious safety concerns become apparent.[9] Thus, the public is at the mercy of the media, journals, and company advertising (Tables 4, 5), which is often misleading—from the subtle to the outrageous. This unfortunate state of affairs has recently been expertly reviewed.[9]

Table 5. Who or What is Harmed by Current Publication Policies and How[5, 9]

Category	How?
1. Consumers and patients	They receive incorrect nutritional advice (e.g., concerning diet, vitamins) and fail to benefit from obtaining better therapy.
2. Physicians and nutritionists	Time is wasted sorting nutritional wheat from chaff in the literature.
3. Nutrition scientists	Incorrect research in the literature is misleading.
4. Societal resources	Money is wasted on research that cannot yield a definitive answer and on unnecessary or harmful advice.
5. Media	Reporting advice that ultimately requires revision or repudiation makes them appear foolish.
6. Ethical behavior	Scientists, journal editors, and funding authorities that support and/or perform and publish inadequate or incorrect research (because of employing inadequate methods) that affects behavior/nutritional practice are diminished by this practice, thereby setting poor examples for students/fellows.

Finally, untrue claims that certain nutrients and nutraceuticals reduce cardiovascular risk and prevent cognitive decline or cancer (Table 3) steer patients away from safe, proven treatments that are often cheap and generic.[3–5] For example, generic aspirin, ACE inhibitors, and statins have been unequivocally proven to decrease cardiovascular risk and death in selected populations.[3–5]

The issue of why there is such persistence of contradicted nutritional claims is discussed at length by J.P.A. Ioannidis's group using megavitamin E as an example.[7] They focus on "wish bias."[7] But the unwillingness of investigators who perform pseudoscientific studies to concede error and the role of commercial profit-driven interests cannot be underestimated.[3–5, 9] It is worth noting that Walter Willet of the Harvard School of Public Health was still recommending megavitamin E in 2005 (at ten times the RDA),[6] notwithstanding the overwhelming evidence that, if anything, megavitamin E is harmful.[9, 14]

In summary, the critics of nutritional research and practice suggest that much nutritional research and practice is, to paraphrase Thomas Hardy, science's laughingstock, for two reasons: much of the research, especially EOS, is pseudoscientific for the reasons I have discussed and second, many practitioners and commercial interests do not readily acknowledge the truth.[1–5, 7–9]

Conclusions and Recommendations

The value of following the scientific principles noted above is well established.[1–5; 7–9]

1. Readers of medical reports and journals should focus on studies that employ methods that test a hypothesis definitively. Readers should be skeptical of the results of EOS that test a contributory causal hypothesis and draw causal conclusions unless they satisfy the Hill criteria.[3–5] Such studies must be considered at best hypothesis-generating. Moreover, unless such studies have a clear "upfront" hypothesis and prespecified data analysis plan *and* are not the result of "data-dredging," they merit even less credence.[3–5]

The editors did not blame themselves (and other editors) for publishing low-quality or uninterpretable papers. Instead, the editors blamed the media, which should "improve the way they interpret science."

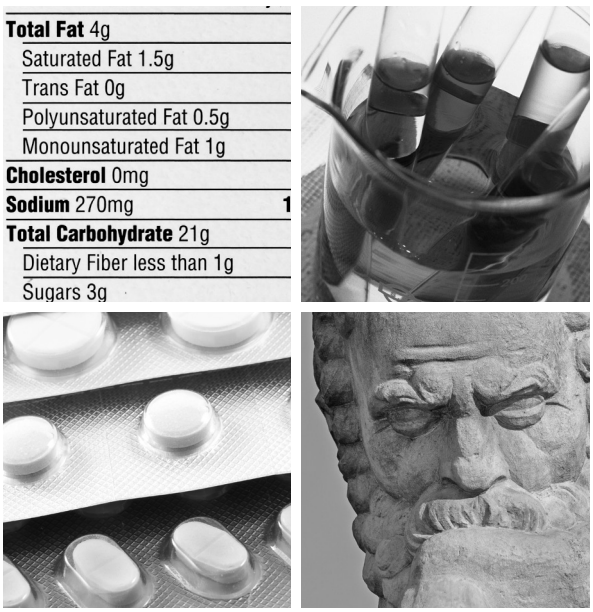
2. Readers and viewers should encourage journals and the media to reform their publication and reporting standards. Journals should publish only scientifically sound studies and label most EOS as, at best, hypothesis-generating. Journals should have a section where authors who have published incorrect studies or nutritional advice can correct their views—analyze where they erred and discontinue defending erroneous and misleading publications.[7] Journals should carefully edit opinions on nutritional and therapeutic advice, rather than leaving such advice mainly to authors. The criteria for recommendations should include "substantial evidence" for efficacy and safety (as per the FDA) as well as chemically defined ingredients to avoid disasters like the tryptophan recall described earlier.[9]

3. Readers should encourage journal editors, academicians, and funding agencies to support quality studies (e.g., randomized controlled studies) rather than those unlikely to answer questions definitively (e.g., EOS, case-control studies, or cohort studies). Special recognition should be accorded investigators who do difficult but definitive studies.

In the end, as Socrates pointed out, the big question is: How should one live one's life? To decide, one needs good data! In terms of nutritional advice:

1. Demand scientific studies.
2. Follow the FDA criterion: only follow nutritional advice if *proven* to be safe and effective.
3. View the nutritional advice of "experts," like those who prepared the agriculture department's original food pyramid[1] and the newer food pyramids,[6] with a hypercritical eye. Their track record is poor.[1–5, 7, 9, 10]
4. Unless there is sound evidence, follow Aristotle's principles:

- Aim for a sound mind in a sound, stable body with a BMI between 20–25.
- Practice moderation in nutritional matters.
- Observe Table 1—especially elderly people and those on certain drugs (e.g., diuretics that can deplete the body of essential substances) or others (e.g., proton pump inhibitors that can interfere with nutrient absorption).
- Eat what works for you—especially as you age. For example, the elderly should often avoid lactose in milk products and should be careful to ingest enough vitamins and minerals, especially vitamins B-12 and D.
- In life, there are often special situations, such as early pregnancy, where special nutritional needs arise (e.g., folate). □



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