



## Conference on 'Translating nutrition: integrating research, practice and policy' Plenary Lecture II

### Food synergy: the key to a healthy diet\*

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Food synergy is the concept that the non-random mixture of food constituents operates in concert for the life of the organism eaten and presumably for the life of the eater. Isolated nutrients have been extensively studied in well-designed, long-term, large randomised clinical trials, typically with null and sometimes with harmful effects. Therefore, although nutrient deficiency is a known phenomenon, serious for the sufferer, and curable by taking the isolated nutrient, the effect of isolated nutrients or other chemicals derived from food on chronic disease, when that chemical is not deficient, may not have the same beneficial effect. It appears that the focus on nutrients rather than foods is in many ways counterproductive. This observation is the basis for the argument that nutrition research should focus more strongly on foods and on dietary patterns. Unlike many dietary phenomena in nutritional epidemiology, diet pattern appears to be highly correlated over time within person. A consistent and robust conclusion is that certain types of beneficial diet patterns, notably described with words such as 'Mediterranean' and 'prudent', or adverse patterns, often described by the word 'Western', predict chronic disease. Food is much more complex than drugs, but essentially uninvestigated as food or pattern. The concept of food synergy leads to new thinking in nutrition science and can help to forge rational nutrition policy-making and to determine future nutrition research strategies.

#### Diet pattern: Food: Research design

Food synergy is a concept linking foods and dietary patterns to health, defined as 'additive or more than additive influences of foods and food constituents on health'<sup>(1)</sup>. This is the idea of concerted action of food constituents on health. This concept has many implications for defining a healthy individual diet, for making dietary policy, and for the future direction of nutrition research. The purpose of the present paper is to define and consider the implications of this statement.

#### Why 'additive or more than additive'?

The term 'synergy' used regarding food is meant to imply the benefits of looking at whole foods and diet patterns. Even if there is not any mathematical synergy, the many constituents of individual foods and dietary patterns are composed in complex ways that would be hard to synthesise in a laboratory. 'Food synergy' implies that the food constituents act in concert on health; that is, in maintaining

**Abbreviations:** AMI, acute myocardial infarction; CARDIA, Coronary Artery Risk Development in Young Adults; SEAD, Southern European Atlantic Diet.

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a healthy body by promoting homeostasis. Thus the term 'more than additive' refers to mathematical synergy, while the term 'additive' refers to a 'complicated system acting in concert'.

There are several reasons to believe that food synergy is fundamentally a good model. Food consists of non-random complex mixtures of compounds, developed under evolutionary control. The composite nature of food, serving the life of the organism being eaten as well as the life of the eater, is central to the food synergy concept. The fact that foods are eaten in patterns has also arisen over millennia, perhaps partly under evolutionary control. Viability of the food synergy idea implies that there is balance in the biochemical constituents of the organism being eaten, that pieces of this orchestration survive digestion and that coordinated constituents mutually affect human biology. There is evidence in favour of these assumptions, as previously discussed<sup>(2)</sup>.

### How many compounds are in food?

Food is biologically complex. It consists of cells, other non-cellular material and their molecular constituents. Each food consists of many thousands of molecules, as is apparent from the many peaks seen in biochemical analysis of food with procedures such as MS. It is accentuated by the observation that tiny changes in a molecule can have huge physiological effects. An example striking in its simplicity is oleic acid, 18:1*n*-9, which has a bent configuration and is thought to be beneficial for health<sup>(3)</sup>. The *trans* version, which simply has the double bond on the other side of the molecule, is flat and has adverse health effects. As illustrated in this example, shape matters in biology. Furthermore, the molecules are arranged in specific ways for biological functionality, as illustrated on the March, 2009 cover of the journal *ChemMedChem* by the intricate relationship between cobalamin and the insulin receptor<sup>(4,5)</sup>. The beautiful colour image presented, derived from terahertz spectroscopy, depicts in great detail the part of the huge insulin receptor that is above the cell membrane, nestling a very complex transcobalamin molecule, which in turn is holding a much smaller (but still complex) cobalamin molecule, intended for delivery into the cell. This illustrates the complexity involved in maintaining a healthy organism. To the extent that arrangement of molecules influences or survives digestion, this aspect could be important to health. This complexity is found, operating in parallel and in a coordinated way at millions of receptors and other points of molecular interfaces on a moment-by-moment basis in every living organism. Keeping these interactions working right to maintain homeostasis is in part the job of food.

This is sharply distinguished from the job of drugs, which are typically designed to alter a single pathway that governs signs, symptoms or pathology of a known disease process. It is recognised that drugs, in interrupting such an otherwise normal pathway, might in the long term have adverse effects, either by preventing normal function or by unintentionally affecting other pathways and causing side effects. The benefit of interrupting a disease pathway is

valued, despite otherwise adverse effects (for example, beta-blockers lowering blood pressure and heart rate in the near term despite slowly increasing insulin resistance in the long term).

In summary, the term synergy is used in this model of the health effects of food or diet pattern constituents whether there is mathematical synergy or not. With so many constituents, it does seem likely that there are formal mathematical interactions; this is the phrase in the definition, 'more than additive', meaning the whole is more than the sum of the parts. However, such complex, multi-way interaction is difficult to establish experimentally and need not be established for food to be important. Thus food synergy includes purely additive effects, because the combination of thousands of constituents in a particular arrangement working in concert is special. It would be extremely difficult to put this together synthetically to meet the dynamic needs of a living organism responding to an ever-changing environment.

### Single nutrients

The importance of the discovery of conditions that were caused by deficiency of single nutrients and which could be cured by providing the deficient nutrient in isolation cannot be overstated. Best known examples would include scurvy and ascorbic acid, pellagra and niacin, beriberi and thiamin, rickets and vitamin D and neural tube defects and folic acid. The last is particularly interesting because the deficiency is in the fetus, even if the mother is not herself deficient, and has led to a food fortification programme in which neural tube defects have decreased considerably<sup>(6,7)</sup>. Vitamin B<sub>12</sub> or cobalamin deficiency occurs frequently (>20 %) among elderly people and is medically treated<sup>(8)</sup>. It is often unrecognised, because its clinical manifestations (peripheral neuropathy, memory loss and other cognitive deficits) are often subtle. It is potentially serious, particularly from a neuropsychiatric and haematological perspective. The causes of the deficiency include food-cobalamin malabsorption syndrome (>60 % of all cases), pernicious anaemia (15–20 % of all cases), and insufficient dietary intake and malabsorption. Therefore, vitamin B<sub>12</sub> is a medical problem.

Based on a nutritional epidemiological model that a nutrient approach would explain disease incidence, Shekelle<sup>(9)</sup> collapsed foods into their nutrients and found that 'intake of dietary provitamin A (carotene) was inversely related to the 19-year incidence of lung cancer in a prospective epidemiological study of 1954 middle-aged men', while 'intake of preformed vitamin A (retinol) and intake of other nutrients were not significantly related to the risk of lung cancer'. The risk for lung cancer was graded across the carotene index and was specific to lung cancer ('unrelated to the risk of other carcinomas grouped together'). It is informative to view this article from the perspective of the theory of using observational data to make causal inference. Many aspects of the classical criteria<sup>(10)</sup> were fulfilled (strength of relationship, specificity, temporality, biological gradient, plausibility and coherence with natural history), while others were weaker or at least

were not addressed (consistency with other observations, experiment and analogy). The concept of food synergy was not considered. This kind of evidence was considered sufficient to establish a series of randomised clinical trials testing the effects of long-term supplemental vitamins (especially E, C,  $\beta$ -carotene and B vitamins), in excess of intakes that would be obtained by diet, on mortality and other outcomes such as cancer occurrence. In this sense, a systematic review and meta-analysis of primary and secondary prevention trials has shown that some supplements are well studied and ineffective or worse<sup>(11,12)</sup>. Bjelakovic<sup>(11)</sup> found significant adverse effects on total mortality in randomised clinical trials; low risk of bias of  $\beta$ -carotene had relative risk 1.07 (95 % CI 1.02, 1.11), vitamin A had relative risk 1.16 (95 % CI 1.10, 1.24), and vitamin E had relative risk 1.04 (95 % CI 1.01, 1.07), singly or combined. In the same meta-analysis, 'Vitamin C and selenium had no significant effect on mortality'. B vitamins, especially folate that promotes growth and might in this way be detrimental for people prone to cancer, have been questioned<sup>(7,13)</sup>, despite clear success in preventing neural tube defects<sup>(6)</sup>. A popular view of this situation was expressed by Mulholland and Benford<sup>(14)</sup>, in which intake of a nutrient has a U-shaped relationship with risk. Risk is seen as high in deficiency, flat over a broad range and high again in excess. An obvious conclusion is that isolated nutrients are drugs, but not studied or regulated as drugs, and perhaps they should be. Food, on the other hand, needs to be treated in a different way, cognisant of the food synergy concept.

#### Saturated fat from different food sources

A true nutrient effect should be observed independent of the food that it occurs in<sup>(15,16)</sup>. Saturated fat by food source was studied in relation to incident CVD in the Multi-Ethnic Study of Atherosclerosis<sup>(17)</sup>. This is a population-based sample initially aged 45–84 years, free of clinical CVD and diabetes. Median SFA intake was 18 g/d: dairy other than butter 39 %, meat 21 %, butter 4 %, plant 6 % and mixed sources 30 %. The majority was palmitic acid, 16:0. We studied 5209 men and women over 7 years and observed 316 cases of incident CVD. The amount of saturated fat from dairy foods, despite exceeding the intake from meat, was inversely related to disease incidence, while the saturated fat from meat was positively associated. The intake from plant food and from butter was much lower and no trends of CVD risk were seen (it cannot be excluded that a different effect would be seen with greater intake). It is recognised that the confounders associated with saturated fat from one source may not be the same as those with saturated fat from another, so it is possible that the nutritional epidemiological analysis introduced confounding. However, food synergy should be considered, namely that food, in all its complexity, is a more fundamental unit than any individual nutrient. There are very convincing studies that show that saturated fat intake increases total cholesterol<sup>(18)</sup>, although there is also evidence that HDL-cholesterol increases, which are thought to be beneficial, occur with increased saturated fat intake. It is

important to note that saturated fat is not the only constituent in saturated-fat-containing food. In this light, the nutrient-based recommendation to reduce saturated or total fat is not completely coherent.

Kromhout *et al.*<sup>(19)</sup> concluded that fat-intake recommendations must be within a food-based approach to CHD prevention in the whole diet context. People should consume nutritionally adequate diets that are low in saturated fat and as low as possible in *trans*-fat. Nutritionally adequate diets should fulfil the requirements for the intake of *n*-6, *n*-3 and *cis*-MUFA. A diet pattern approach was supported, citing that natural experiments showed that both traditional Mediterranean and Japanese diets were associated with a low risk of CHD. However, a frequent reaction encountered by us in people without nutrition training to this type of statement is that it is permission to eat unrestricted amounts of fat, which some people equate with eating a lot of red meat. A counter-example comes from Northern Portugal and the Southern European Atlantic Diet (SEAD) in relation to non-fatal acute myocardial infarction (AMI)<sup>(20)</sup>. This was a population-based case-control study in Porto, Portugal, among 820 hospitalised incidents of AMI and 2196 randomly selected control participants aged  $\geq 18$  years. The SEAD adherence score ranged from zero to nine points following a similar principle to that used in the Mediterranean diet score (one point for above control group median intake). Food groups were cod (fresh, dried or salted), fresh fish excluding cod and canned fish, red meat and pork products (including processed meats), dairy products (milk, yoghurt and cheese), legumes and vegetables, vegetable soup (including some olive oil), potatoes, whole-grain bread and wine. The OR for AMI risk in the highest SEAD quartile (best adherence to traditional pattern) *v.* the lowest quartile was 0.67; 95 % CI 0.51, 0.88; *P* for trend = 0.003. Consonant with the pastoral culture in the area, this diet score awarded a point for higher meat intake. However, an alternate SEAD index calculated by reverse scoring for red meat and pork products led to an even stronger inverse association (upper *v.* lower quartile: OR: 0.45; 95 % CI 0.34, 0.60; *P* for trend <0.001). Therefore, this study does not support unlimited meat eating. It is recognised that changing meat consumption would be a large cultural change in this instance and it is noteworthy that the overall pattern does well, even encouraging consumption of local meats. Thus a dietary pattern that works in a given cultural context will include a mix of foods, some of which might be less desirable in another context.

#### Diet patterns

Many dietary patterns have been studied in the last decade, derived largely from FFQ in which participants self-report intake over a recent period, such as a month or a year. Patterns loosely grouped as Western (adverse) or prudent/Mediterranean (beneficial) have been identified repeatedly. SEAD is intermediate in its advocacy of meat, but is otherwise similar to Mediterranean (and successful in its inverse association with AMI<sup>(20)</sup>). Mente *et al.*<sup>(21)</sup> concluded that diet pattern associations with risk in

**Table 1.** *A priori* Diet Quality Score: food groups and point values as implemented in Coronary Artery Risk Development in Young Adults<sup>(23)</sup>

Diet category	Food groups*					
	Positive foods (preferred)	Available points (low–high intake)	Neutral (any intake)	Available points	Negative (limited)	Available points (low–high intake)
<i>Staple foods</i>						
Vegetables and fruit	Avocado; beans, legumes; green vegetables; yellow vegetables; tomato; other vegetables; fruit	0–28	Potato	0	Fried potato	4–0
Fish, meat, and poultry	Fatty fish; lean fish; poultry	0–12	Lean meat; shellfish	0	High-fat meat; processed meat; organ meat; fried fish, poultry	16–0
Nuts, seeds	Nuts and seeds; soya products	0–8				
Grains, desserts, snacks	Whole grain	0–4	Refined grain	0	Grain dessert; salty snacks; pastries; sweets	16–0
Dairy foods and fats	Low fat milk, cheese, yoghurt; vegetable oil	0–8	Eggs; margarine; chocolate	0	Full fat milk, cheese, yoghurt; butter	4–0
<i>Beverages and other</i>						
Beverages	Coffee; tea	0–8	Diet drinks; fruit juice	0	Soft drink	8–0
Alcohol	Moderate amounts of beer; wine; liquor	0–12				
Other			Soups; meal replacements; pickled food; sugar substitutes	0	Sauces	4–0

\*Food groups are separated by semicolons. Magnitudes are United States Department of Agriculture servings/day, which are placed in quintiles (or 0 and quartiles for consumers). The score was formed for research purposes, but since it is based on all foods that people tend to eat, it could be adapted for individual use, to 'swing' intake in a generally good direction. Specific implementation details are available to researchers from the authors.

prospective epidemiological studies were among the most consistent findings in nutritional epidemiology. Lockheart *et al.*<sup>(22)</sup> defined a particular pattern, the *A Priori* Diet Quality Score in a case–control study of AMI. The *a priori* score is constructed using specific principles specifically for each study, depending on the questionnaire used and which specific foods it asks about. It is formed entirely from thirty-five to fifty food groups placed in categories (e.g. quintiles or else one group for non-eaters and quartiles among eaters). In the Coronary Artery Risk Development in Young Adults (CARDIA) study, we used absolute cut-points (based on the categories at the baseline examination), so that the score would be comparable across time<sup>(23)</sup>. The food groups are rated by experts with knowledge of nutrition and the literature; a list of justifications was provided with the original publication of this score<sup>(22)</sup>. In CARDIA forty-six food groups were used with twenty rated positively and thirteen rated negatively, the remaining being rated neutral. Groups rated positively get zero to four points for increasing category, while those rated negatively are scored in reverse, getting four points for the lowest intake and zero for the highest. Neutral foods get zero points regardless of intake. This formulation is substantially more nuanced than other formulations such as the Alternative Healthy Eating Index<sup>(24,25)</sup>, the Mediterranean diet score<sup>(26)</sup>, or the SEAD<sup>(20)</sup>. It makes many distinctions among foods, such as types of vegetables, of dairy products and beverages and gives partial credit for intermediate intake levels. A higher *A Priori* Diet Quality

Score has been shown, in several papers, to be associated with positive health effects<sup>(22,27–29)</sup>.

Although the *a priori* score was set up for research purposes, it is comprehensive and includes all foods that people commonly eat; therefore, a person could use the *a priori* score to formulate a diet by preferentially selecting from positively rated food groups and preferentially avoiding negatively rated food groups. The score is well described in an online supplement, the history of the different expert opinions and of different food group formulations<sup>(23)</sup>. Specifically, as used in CARDIA, the food choices and points are given in Table 1. The score emphasises high phytochemical plant food intake, but does not 'forbid' any food. The food weightings are drawn from population distributions of consumption and so do not fully consider excesses. For example, for alcohol intake, most people in CARDIA did not drink beer, wine and liquor, and maximum points were achieved for a little more than one drink per d among all alcoholic beverages. Neutrally rated food groups play a role because energy intake is limited by energy expenditure in a person in energy balance. Therefore, while eating negatively rated foods substantially reduces the attainable score, eating a lot of neutrally rated foods also limits how high the *a priori* score can get. Although the score in CARDIA had theoretical maximum of 132 and minimum of zero, most people's diets were a mixture of many food groups, with mean score at year zero of 64.1 and only 2 % of people outside the range thirty-seven to ninety-four in 1985–86

(minimum twenty-four to maximum 107). With the improved scores 20 years later, the mean score was 71.1 and only 2 % of people were outside the range forty-two to ninety-eight (minimum thirty to maximum 107).

Given a long history in nutritional epidemiology in which within person variation of dietary elements is so large as to impede inference, we were pleasantly surprised to find that the diet pattern was highly repeatable<sup>(23)</sup>. The *a priori* score had a correlation of 0.6 over 20 years (average age increasing from 25 to 45 years) in the CARDIA study. This is comparable to tracking levels in other risk factors, such as serum cholesterol and blood pressure. Given this high correlation, we showed an interesting tendency in the CARDIA young to middle-aged adults to improvement in score with age, at the same time as the diet in the population at large worsened<sup>(23)</sup>. This is an interesting interpretation based on the food synergy concept that people are struggling to maintain better diet against a societal trend towards worse diet.

### Consequences of a nutrient focus

There are some positive, but, in our opinion, more negative consequences of a nutrient focus in considering the association of diet with chronic disease. On the positive side, a nutrient focus means deficiency conditions are avoided, which is perhaps most important in those with the least resources, such as those living in poverty or in less developed countries in which some nutrients are lacking. If a health effect of the nutrient exists independent of the rest of the food, science would uncover that effect by focusing on a nutrient or other biologically active compounds. Such might be the case occasionally, for example with saturated fat and serum cholesterol, with fluoride and dental caries, or with folate and neural tube defects, although even then the story seems far from clear-cut. Thus the primary positive is that it is relatively simple to make a policy that will 'assure adequacy'.

On the negative side, the many, conflicting findings about nutrients are difficult to interpret. While it is true that the maxim in science is to make hypotheses, test them and revise them, there is great diversity in nutrient findings in intact human subjects, and the failure to confirm a hypothesis is often confusing. Where science does find a reductionist solution that is valuable. Findings for nutrients *in vitro* are reasonable as significant scientific background, although it is not always obvious how to apply this knowledge to diets in people. The launching of major clinical trials of supplemental nutrients and confusion over their failure to reduce risk indicates that something is wrong with the single nutrient model. The lack of success may be in part due to the nutrient model missing food synergy. At least, it may be concluded that assuring diet adequacy to avoid chronic disease is not as simple as avoiding single nutrient deficiency.

Furthermore, the public is definitely confused. For example, the policy to eat low-fat foods would say to avoid the fatty olive, without thinking of whether olives might be a valuable food. Regulators' rules, established to be 'objective', can be internally inconsistent and difficult for

industry, which is the source of virtually all food. Industry, with a focus on profit (needed to keep them in business to supply food to the world), thinks of ways to increase nutrients, rather than focusing on foods. Some breeders (animal and plant husbandry) make changes, including genetic engineering, focusing on nutrients. Recent increases in coeliac disease<sup>(30)</sup> may be related to wheat bred to increase protein in response to both regulation and a desire for certain properties of flour (e.g. to make light cakes).

We observe that the media does not seem to have much room for reporting of in-process findings and loves short sound bites. In many articles, the result is: reporting on every new study as if it were definitive, complete with comments from detractors or other scientists who recite well-known and well-accepted caveats. This practice treats science as if it were politics and adds to public confusion.

The food industry naturally and appropriately tries to make money; to do this, food purveyors try to form a 'market wedge'; it therefore apparently makes sense to advertise in all possible ways. It is common to see on breakfast cereal packaging pictures of food (e.g. whole grain, nuts and berries), words such as 'less processed', and nutrient references such as 'fibre', 'antioxidants' (which may be equated with vitamins C and E) and implication of low fat ('3 g total fat'). By appealing to more than the food in the box, the nutrient message is furthered, despite questionable science (e.g. isolated antioxidants have not been shown to be beneficial and low fat is much too general and has led to industrial innovations that do not appear to be healthful).

Food is many times more complex than drugs, but is investigated as if it were simpler and less important. It has been stated that a functional food goes beyond basic nutrition, but this statement ignores the complexity in all food: basic nutrition is what keeps the multi-faceted organism working well. In the United States, the Dietary Supplement Health and Education Act, signed into law in 1994, allows untested substances which are actually drugs on the market with very little regulation or oversight, despite clinical trials suggesting null or even adverse outcomes<sup>(31)</sup>. The focus of food regulation is on food safety, which is appropriate, but there is little emphasis on healthfulness of food. One purpose of agriculture should be to keep the population healthy, not just to prevent starvation and make money.

### What research is needed?

The furtherance of nutrition research is made more complex by the differences between clinical trials in drugs *v.* food. The standard for causal reasoning set by the randomised clinical trial, so useful in drug studies, has very limited utility in nutrition research<sup>(32)</sup>. Randomisation, double blind and compliance are hard to maintain when a treatment is food. Food studies tend to be of limited duration and their outcomes tend to be intermediate, not clinical events. Foods are much more general research objects than are drugs, since food is an average of varieties, growing conditions and preparation over time. Perhaps most striking is the control or reference: the need to



maintain energy balance means that any energy-bearing food can be substituted in numerous different ways.

However, we do not believe that findings about nutrition and health have to be relegated to 'supported by B level evidence'. Nutrition scientists must seek strategies that reduce reliance on the randomised clinical trial to learn about diet and health. We propose that there should be many, repeated large cohort studies, over different ages, ethnicities and geographies. In our opinion, there should be strategically placed short-term randomised clinical trials and a few large ones of long duration with clinical outcomes. Nutrition science needs to work on design solutions to enhance interpretability of studies. Perhaps most importantly, the focus of studies should be on food and dietary patterns. The authors propose to regard a finding about a food or a dietary pattern as an end in itself, that is, as finished science. An interesting approach is working from 'complex to simple', that is, working backward from a successful diet pattern. This method was used by Oliveira *et al.*<sup>(20)</sup> with SEAD, where changing the sign of 'red meat and pork products' (effectively rating this food group as adverse, rather than positive) had a large effect on the disease association, and flipping the sign of 'potatoes' had a smaller effect. This method should be done thoughtfully, to avoid simply examining all possibilities without hypothesis. Studies of the *A Priori* Diet Quality Score with various nuances altered would be of interest, for example, weighting citrus and non-citrus fruits separately, both positively weighted, changing the weight of chocolate to 'positive' and of refined grain to 'neutral', or changing the weight of alcohol to 'negative' for high intake.

While we do think that reductionist studies of how foods work are of interest and enhance understanding, in our opinion, figuring out which components influence the health effects of foods, and how those components interact, should be secondary to understanding food itself. Food is both what people eat and also an object worthy of study in and of itself. Studies of nutrients should arise from observations about foods and patterns.

In these senses, the authors maintain that the infrastructure for food research is inadequate. 'Science' tends to be reductionist, looking for discrete causes and effects. It is hard to get food studies past peer grant reviewers unless they take the food apart, which seems to us to miss the point. The otherwise important value to understand mechanisms of biological action may be counter-productive, in that review panels appear often to assume that such deconstruction does not miss important synergies. Regulation often misses the point, encouraging simple solutions that are likely to be incorrect, at least from the perspective of food synergy. The situation could be ameliorated by government money, or even by industry setting aside money for food and pattern studies, administered by an independent agency, but there are very few such funds at the moment. It is certainly not rational to assume that the food industry would monitor itself. Although some branches of industry do good research, it is hard to imagine them continuing if their product starts to show harm. As is the case with pharmaceutical houses, the food purveyors might be inclined to suppress such research, or lacking fall back products, the most public health-interested companies

might go out of business. Thus, the authors feel that a solution is needed that serves the general community.

### Unifying principles: a new beginning for nutrition science and policy?

Since the inspiring work done in discovering the chemical composition of some nutrients and the existence of treatable deficiency diseases, the unifying principle for nutrition has been the nutrient. The belief was that nutrient studies would expose the simple action that describes how diet works on health. This strategy does work for deficiency conditions. However, it seems not to work well for chronic disease in the non-deficient state, e.g. in generally well-nourished populations. Food and diet pattern seem to be more enduring concepts relating to chronic disease development. In this regard consistently informative studies of dietary patterns and risk are encouraging the idea that nutrition science can go much further than it already has. The fact that dietary pattern tracks (has high within person correlation) allows it to be called a personal characteristic, and shows that it is suitable for discovery through epidemiological research. We propose that research into nutrients and bioactive food compounds should support research into food and not dominate it. New strategies for communicating about nutrients from a population, health and chronic disease avoidance perspective should be devised.

Food is synergistic in the sense that all the parts are probably needed, developed by evolution. Evolution is not necessarily optimal for all purposes, but works for life and its current circumstances, and is a good focus for answering the questions 'what should people eat' and 'how does that affect their health'.

We propose that this should be the new unifying principle for nutrition science.

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