From challenges of the past to opportunities of the future: Evolution of the field of nutrition

Andrew Shao, Ph.D.

Outline

- Early days of nutrition
- Contemporary challenges
- Scientific advancements
- Fatal flaws of the reductionist approach
- Transition to a holistic approach
- Closing thoughts

The early days of nutrition

Casimir Funk

- Public health challenges
  - Communicable disease, short life-span
  - Overt nutrient deficiency
- Scientific focus
  - Discovery of vitamins and essential minerals, hunger and malnutrition

Early nutrition science: The single nutrient model

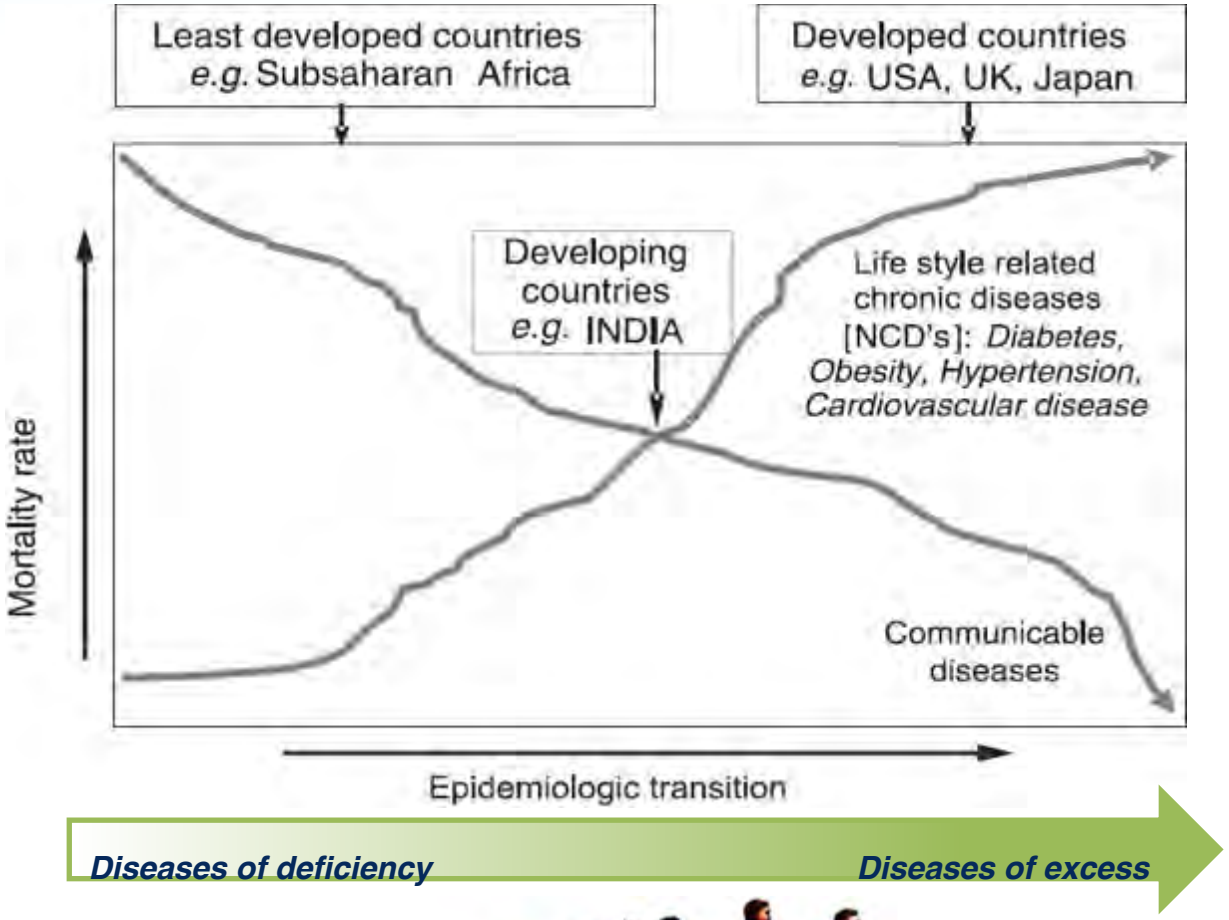
Successful model was based on three main premises

1. Simple cause-effect relationship exists between a specific disease and a particular nutrient
2. Each nutrient deficiency disease can be explained physiologically in terms of the role played by the respective nutrient
3. Providing the nutrient in the diet can prevent, and in many cases reverse, the disease

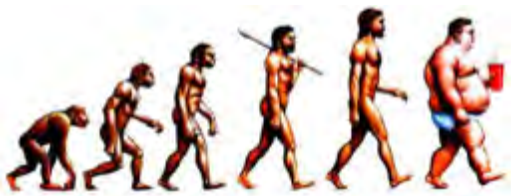
Raubenheimer and Simpson. *Annu. Rev. Nutr.* 2016. 36:603–26

Evolution to contemporary challenges

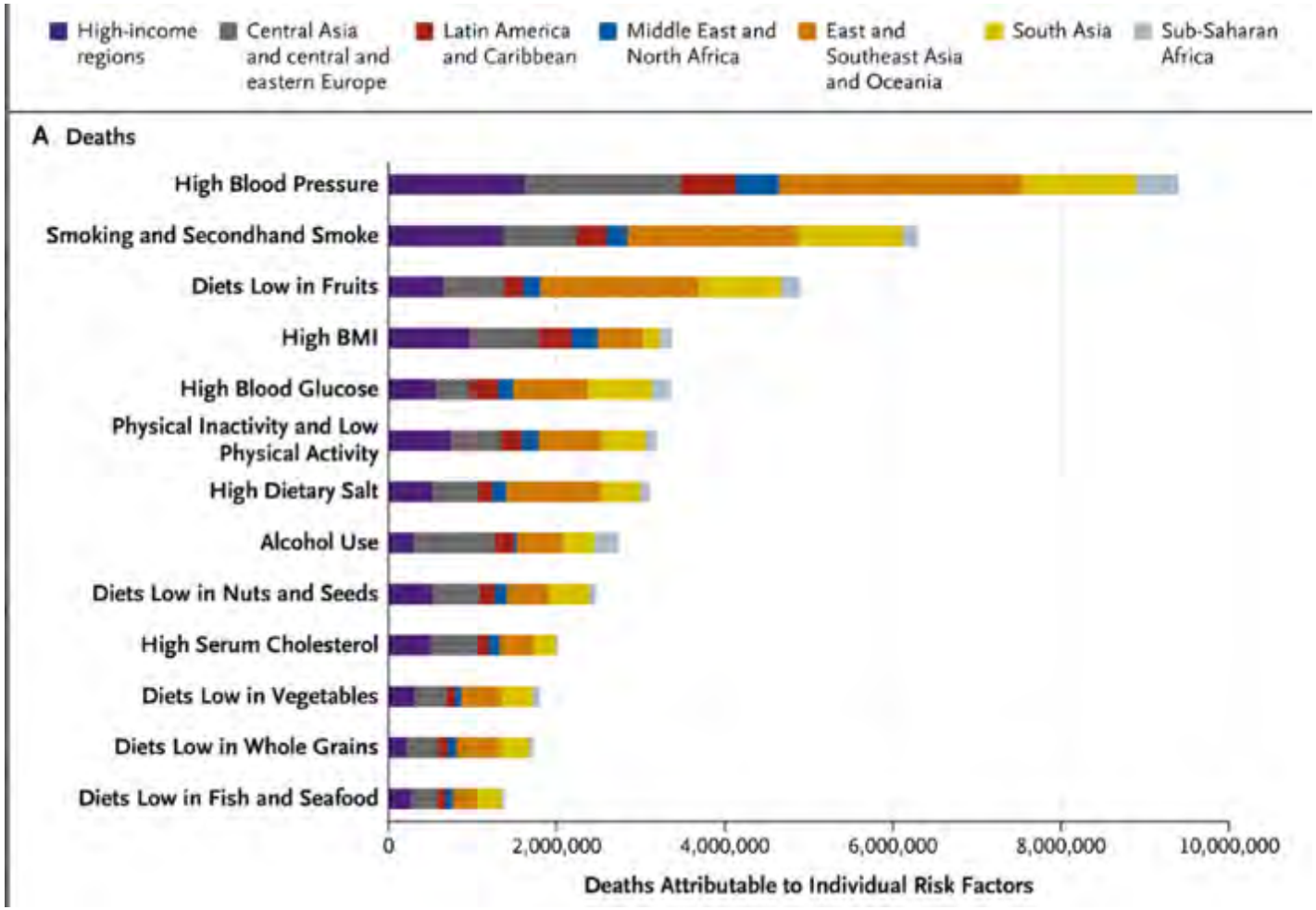
- Rapidly aging population
- Rapidly expanding population
- Physical inactivity
- Dietary imbalance
- Climate change and nutrition sustainability



Anjana, RM et al. *Indian J Med Res* 133, April 2011, pp 369-380



Diet and lifestyle have become major contributors to death



Ezzati, M. *N Engl J Med* 2013;369:954-64.

Research trends

» Evolution of the scientific focus to diet and nutrition's role in etiology of chronic disease

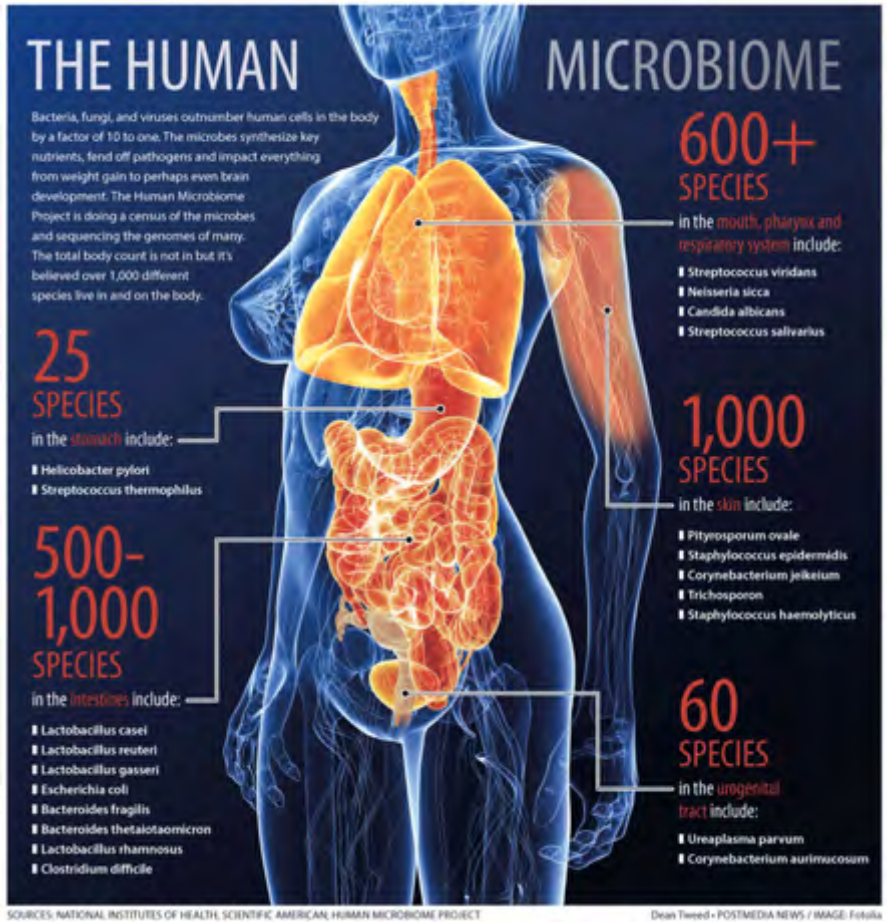
"Nutrition" OR "Diet" AND "Chronic disease" = 11572 citations

1946 = 2

PubMed

2015 = 634

"Microbiome"



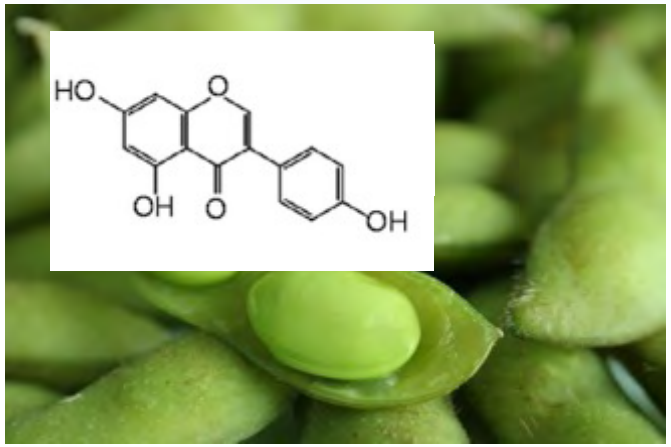
1981 = 9

PubMed

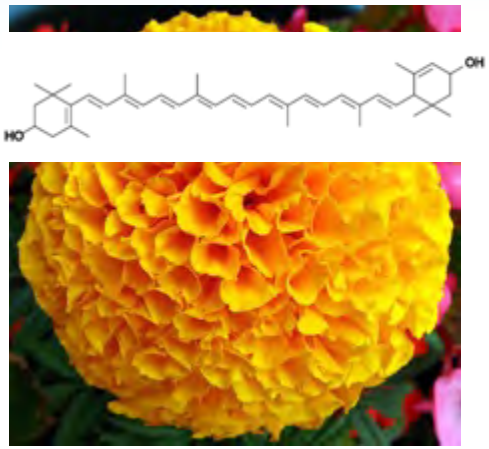
2017 YTD = 6913

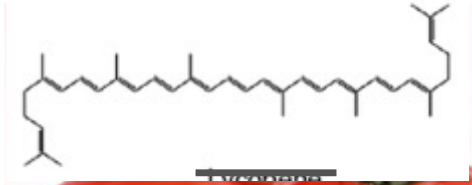
- Number of bacterial cells in (oral, gut) or on (skin) the body exceed our own by 10-fold (100 trillion vs. 10 trillion)
- The composition, nature and metabolism of these cells is influenced by diet and lifestyle and in turn influences health and well being

Beyond essential nutrients

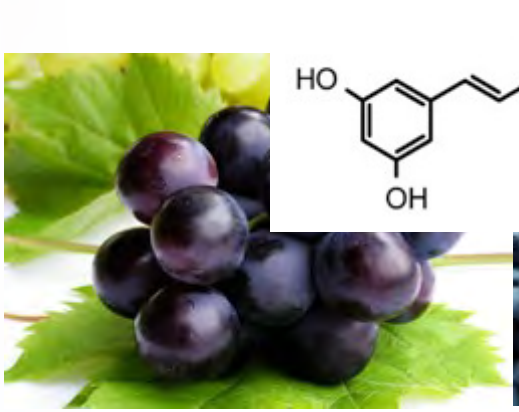


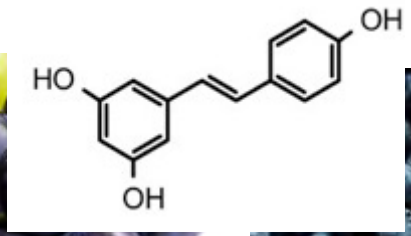
Isoflavones





Carotenoids





Anthocyanins

Catechins

Evolution of dietary reference intakes

Options for basing Dietary Reference Intakes (DRIs) on chronic disease endpoints: report from a joint US-/Canadian-sponsored working group[1–3]

Elizabeth A Yetley,[4] Amanda J MacFarlane,[5] Linda S Greene-Finestone,[5] Cutberto Garza,[6–8] Jamy D Ard,[9] Stephanie A Atkinson,[10] Dennis M Bier,[11] Alicia L Carriquiry,[12] William R Harlan,[13] Dale Hattis,[14] Janet C King,[15–17] Daniel Krewski,[18] Deborah L O'Connor,[19,20] Ross L Prentice,[21,22] Joseph V Rodricks,[23] and George A Wells[24]*

TABLE 4
Traditional and chronic disease endpoints for DRIs[1]

Issue	Eligibility for consideration	Focus	Characteristics	Expression of risk
Traditional endpoints	Food substan… are essenti… conditiona… essential o… componen… energy nut… fats, proteins, and carbohydrates).		…essential …reating …above …y pose the risk of adverse health effects.	Average inflection point between adequate and inadequate intakes (EAR) of a group and its associated population variance (RDA). Highest intake of a group that is unlikely to pose a risk of adverse effects and above which the risk of adverse effects increases (UL).
Chronic-disease endpoints	Naturally occurring food substances, including nutrients, for which changes in intake have been demonstrat… a causal re… to the risk … more chro… diseases.	↑ … ↓Intakes of	With ↑ intakes, the relative risk ↓ compared with baseline intakes. With ↓ intakes, the relative …red with baseline	Relative risk (ratio of the probability of an event occurring in a group with higher intakes to the probability of an event in a comparison group with lower intakes). Relative risk (ratio of the probability of an event occurring in a group with lower intakes to the probability of an event in a comparison group with higher intakes).

[1] DRI, Dietary Reference Intake; … …mended Dietary Allowance; UL, Tolerable Upper Intake Level; ↑, increased or increases; ↓, decreased or decreases.

"…substances that are essential or conditionally essential…"

"…Naturally occurring food substances, including nutrients…"

Yetley et al. *Am J Clin Nutr* 2017;105(Suppl):249S–85S.

IUNS 21st ICN
International Congress of Nutrition

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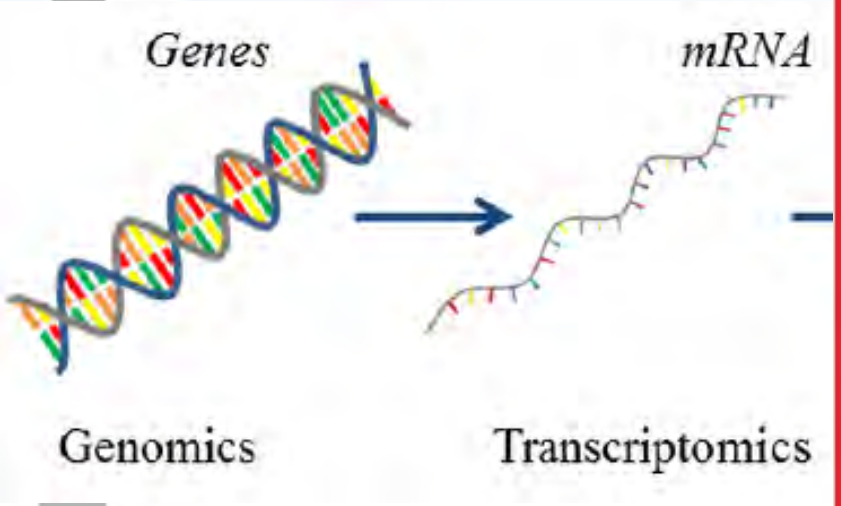
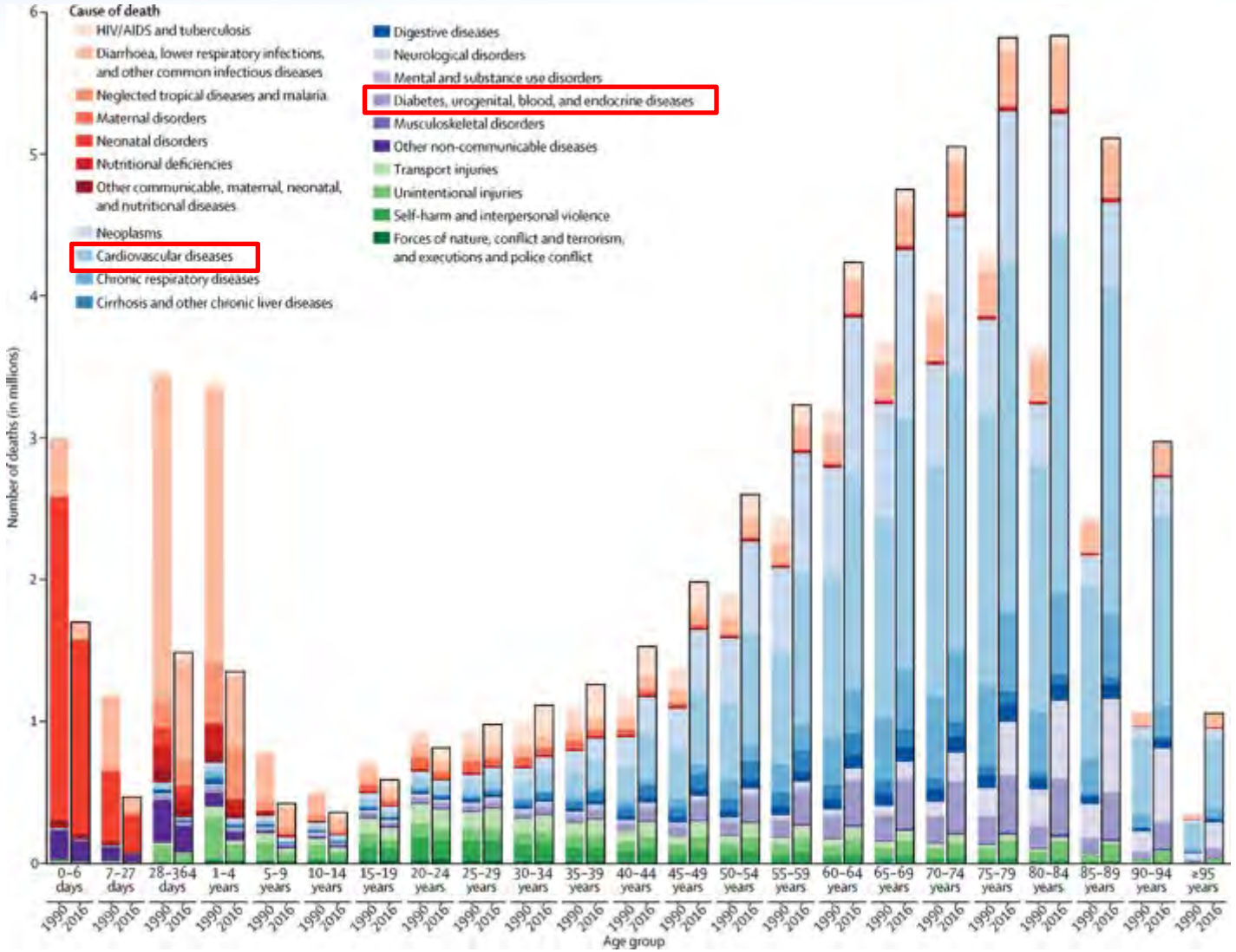
Buenos Ai
Sheraton B



Researchgate.net

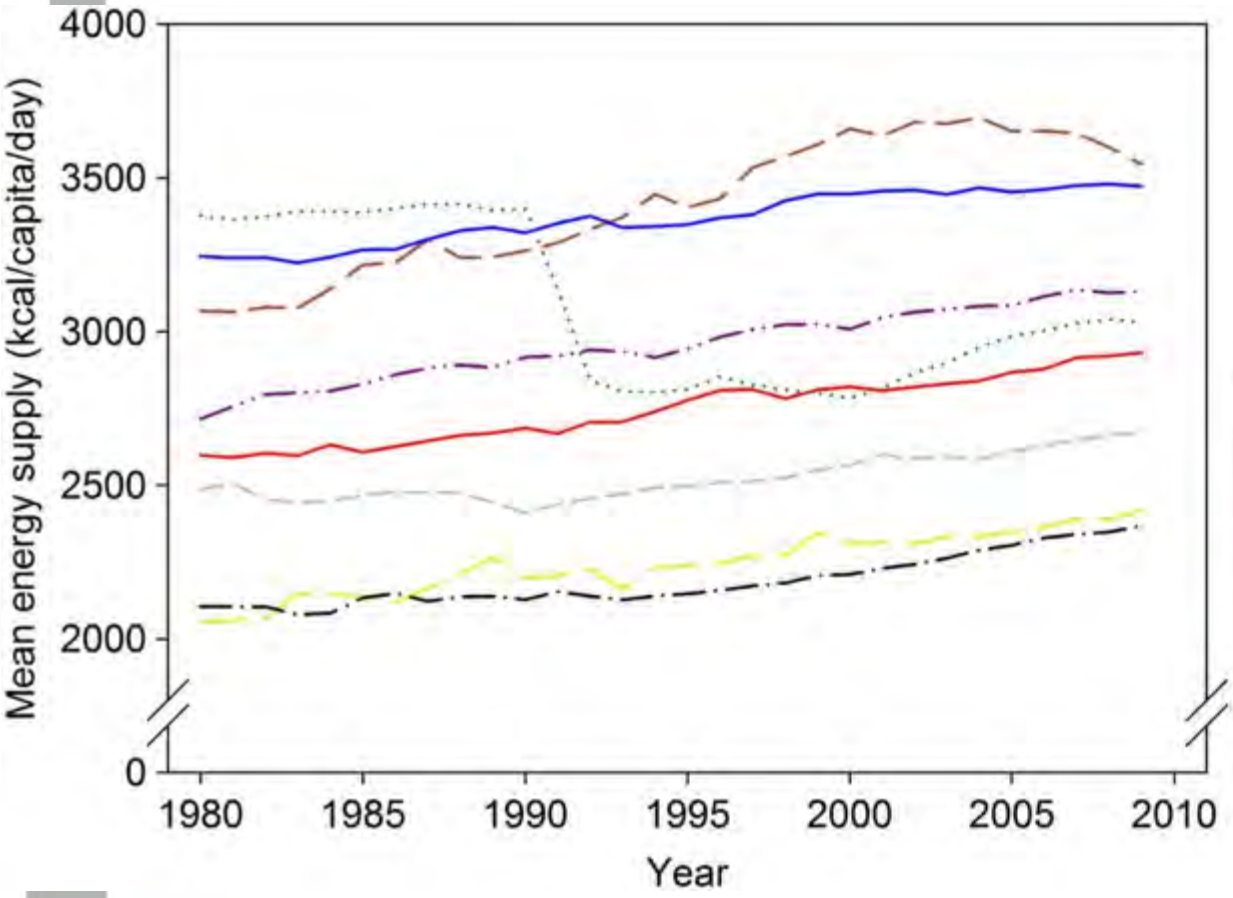
SMOKE FREE EVENT

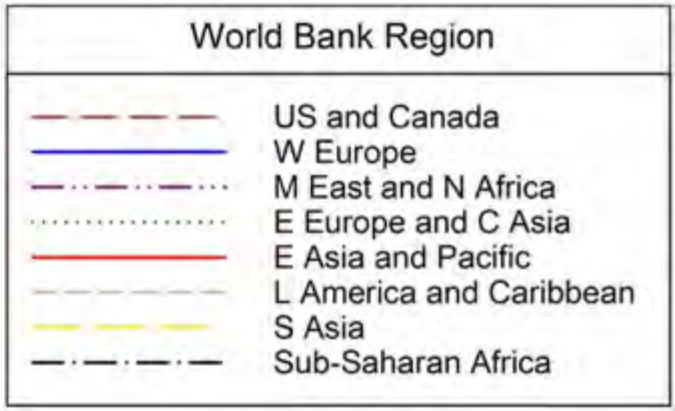
Yet chronic disease remains a leading cause of death



The Lancet 2017 390, 1151-1210DOI: (10.1016/S0140-6736(17)32152-9)

Diets have become energy rich…

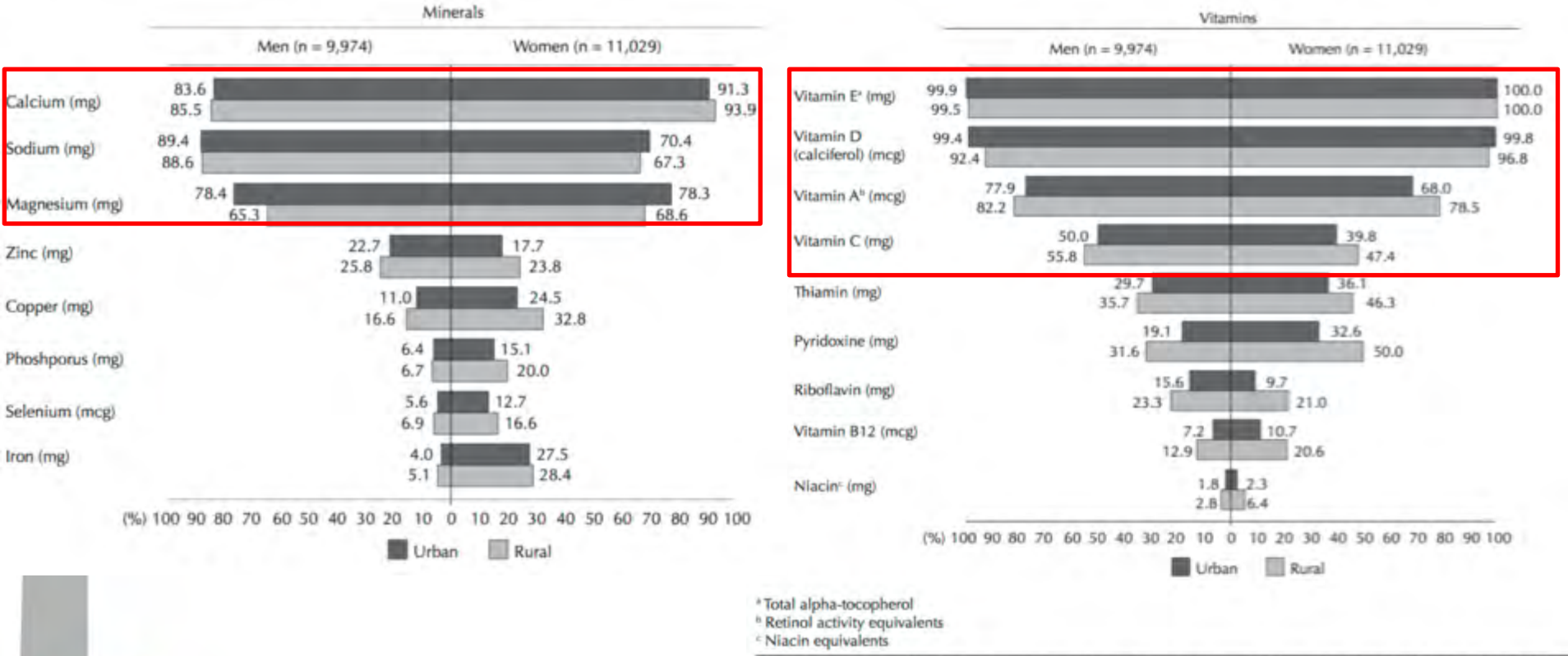




Green R, et al. *BMJ Open* 2016;5: e009331

…But nutrient poor

- Large % of Brazilian population fail to achieve recommended intake levels
- Situation is mirrored in many other developed countries



[a] Total alpha-tocopherol
[b] Retinol activity equivalents
[c] Niacin equivalents

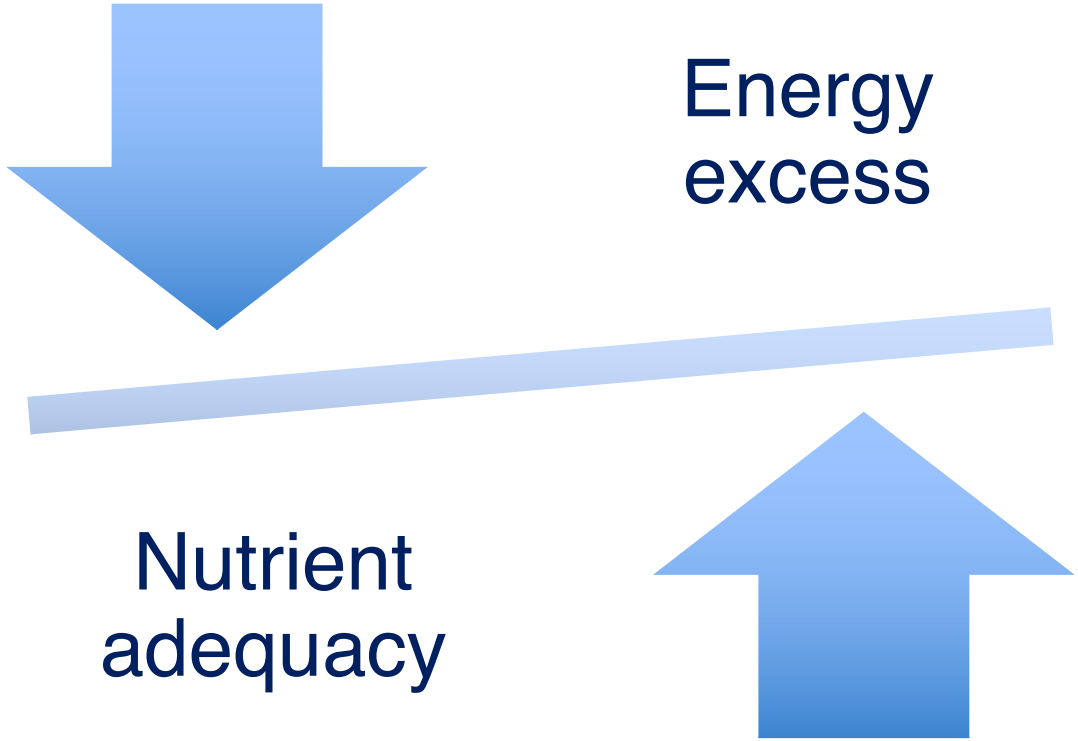
Figure 1. Prevalence of inadequate micronutrients intake according to sex and location of household. Brazil, 2008-2009.

Araujo MC, et al. *Rev Saúde Pública* 2013;47(1 Supl)

Obesity-nutrient inadequacy paradox

Diets have become energy rich, yet nutrient poor; populations are overfed, yet undernourished

Miller, et al. *J. Nutr*. 2009; 139: 1198–1202.



What went wrong?

- "Greedy reductionism":
- "*…in their eagerness for a bargain, in their zeal to explain too much too fast, scientists and philosophers . . . underestimate the complexities, trying to skip whole layers or levels of theory in their rush to fasten everything securely and neatly to the foundation*"

Dennett DC. 1995. Darwin's Dangerous Idea: Evolution and the Meanings of Life. New York: Simon & Schuster

Hierarchy of evidence

Misapplication of evidence-based medicine

- Designed to assess safety and efficacy of drug therapy
- Considers the randomized-controlled trial (RCT) to be the "gold standard" (or only standard) of evidence
  - In many cases, not designed to address unique complexities and challenges presented by nutrients and other food components
- In absence of similar guidelines for nutrition, has been applied to nutrition and bioactive research for the purpose of informing policy decisions

"By analogy, when keys are missing, it is common to look for them under the lamppost where there is light rather than in the murky location where the keys were more likely dropped."

JAMA. 2009;302(19):2152-2153

Looking for "the magic bullet"

- Studying nutrients as if they were drugs
- Can a nutrient reverse the effects of life-long smoking?

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ORIGINAL ARTICLE

Volume 330:1029-1035 April 14, 1994 Number 15 Next ▸

The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers

Beta Carotene Cancer Prevention Study Group The Alpha-Tocopherol

EDITORIAL

Editorials represent the opinions of the authors and *JAMA* and not those of the American Medical Association.

JAMA. 2009;301(1):102-103

Randomized Trials of Antioxidant Supplementation for Cancer Prevention

First Bias, Now Chance—Next, Cause

Peter H. Gann, MD, ScD

line serum levels, smoking status, and genetic factors that might have modified response. After that, like Voyager space probes,

"…nonpharmacological dietary prevention of prostate cancer is probably more complex and may involve certain inconvenient truths… If it requires whole foods, extracts, or dietary patterns, *it may be necessary to give up the reductionist need to know which molecule is most responsible* and perhaps give up the notion of placebo controls as well. If it requires starting exposure early in life and sustaining it for decades, it *may mean having to give up the idea of phase 3 trials altogether*. This does not mean that whole food or complex mixture studies cannot be sound and biologically based…it may be time to critically examine the methods used to vet hypotheses for some phase 3 trials…"

Questioning the evidence-based paradigm

The Journal of Nutrition
2008 W. O. Atwater Memorial Lecture

Nutrients, Endpoints, and the Problem of Proof

Robert P. Heaney*

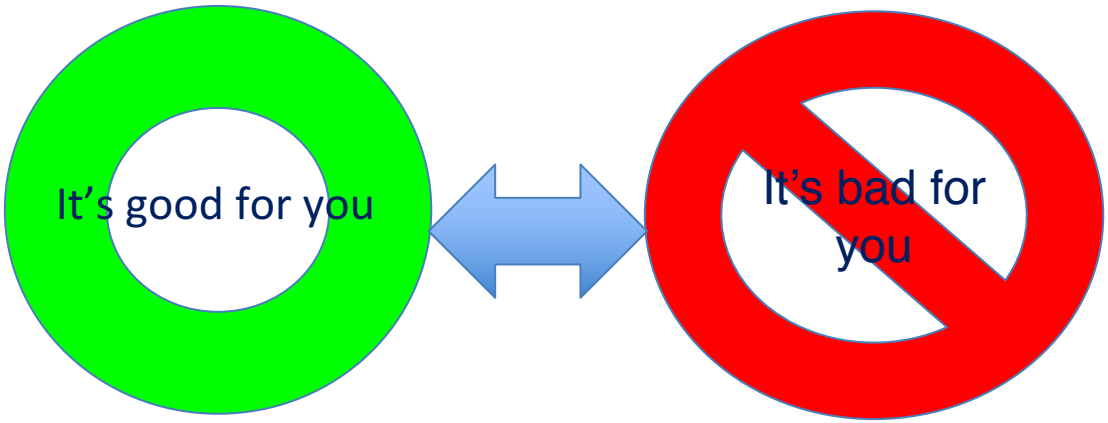
Creighton University, Omaha, NE 68131

J. Nutr. 2008;138 1591-1595

» Nutrients don't function in isolation and have beneficial effects on multiple tissues and organ systems; a focus on a single or "primary" outcome measure, which is favored by RCTs, is not practical.

Nutrition contradiction

- As nutrition science has evolved, public's perception of what is "good for you" vs. "bad for you" has "flip-flopped"
- Countless resources spent satisfying the demand for the nutrition "villain" and "hero"
- Perpetuated by reductionist approach on single macro & micronutrients



The nutrition "villain" and "hero"

- Antioxidants
- Fiber
- Protein
- Probiotics
- Organic
- All natural

- Saturated fat
- Refined carbs
- Trans fat
- Salt
- Sugar
- GMO?

The new science of nutrition

- Nutrition has rapidly evolved from a simple, nutrient and reductionist approach, to a complex systems approach
- ''Nutrition science is (now) defined as the study of food systems, foods and drinks, and their nutrients and other constituents; and of their interactions within and between all relevant biological, social and environmental systems''. *The Giessen Declaration*

Moving beyond the molecule: The "ecology" of nutrition

Goals in Nutrition Science 2015–2020

David B. Allison [1,2,3,4], Josep Bassaganya-Riera [5], Barbara Burlingame [6,7], Andrew W. Brown [1], Johannes le Coutre [8,9,10], Suzanne L. Dickson [11], Willem van Eden [12], Johan Garssen [13], Raquel Hontecillas [5], Chor San H. Khoo [14], Dietrich Knorr [15], Martin Kussmann [10,16], Pierre J. Magistretti [17,18], Tapan Mehta [19], Adrian Meule [20], Michael Rychlik [21] and Claus Vögele [22]*

Fontiers in Nutrition. Sept 2015, Vol 2(26)

» *"Nutrition is a field in which the need for interdisciplinarity is particularly pronounced, given the pervasive influence of nutrition on humans, from physiological to social, global, and planetary levels, and its extensive relationships with other domains including economics, politics, and environmental science"*

Evolving research agenda

- National Nutrition Research Roadmap 2016–2021: *Advancing Nutrition Research to Improve and Sustain Health*
- Interagency Committee on Human Nutrition Research, 2016

TABLE 2 The key research priorities for 2016–2021 put forth by the ICHNR in the National Nutrition Research Roadmap[1]

Question 1: How can we better understand and define eating patterns to improve and sustain health?
- Topic 1: How do we enhance our understanding of the role of nutrition in health promotion and disease prevention and treatment?
- Topic 2: How do we enhance our understanding of individual differences in nutritional status and variability in response to diet?
- Topic 3: How do we enhance population-level food- and nutrition-related health monitoring systems and their integration with other data systems to increase our ability to evaluate change in nutritional and health status, as well as in the food supply, composition, and consumption?

Question 2: What can be done to help people choose healthy eating patterns?
- Topic 1: How can we more effectively characterize the interactions among the demographic, behavioral, lifestyle, social, cultural, economic, occupational, and environmental factors that influence eating choices?
- Topic 2: How do we develop, enhance, and evaluate interventions at multiple levels to improve and sustain healthy eating patterns?
- Topic 3: How can simulation modeling that applies systems science in nutrition research be used to advance exploration of the impact of multiple interventions?
- Topic 4: How can interdisciplinary research identify effective approaches to enhance the environmental sustainability of healthy eating patterns?

Question 3: How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?
- Topic 1: How can we enhance innovations in measuring dietary exposure, including use of biomarkers?
- Topic 2: How can basic biobehavioral science be applied to better understand eating behaviors?
- Topic 3: How can we use behavioral economics theories and other social science innovations to improve eating patterns?
- Topic 4: How can we advance nutritional sciences through the use of research innovations involving Big Data?

[1] Data are from reference 2. ICHNR, US Interagency Committee on Human Nutrition Research.

Fleischhacker et al. *J Nutr* 2017;147:1833–8

A systems science perspective and transdisciplinary models for food and nutrition security

Ross A. Hammond[a,1] **and Laurette Dubé**[b]

[a]*Center on Social Dynamics and Policy, The Brookings Institution, Washington, DC 20036; and* [b]*McGill World Platform for Health and Economic Convergence, McGill University, Montreal, QC, Canada H3A 1G5*

Reduces complexity through revealing key interactions that influence the outcomes of interest…a systems approach can help to identify common causal factors underlying the otherwise seemingly opposite problems of malnutrition and obesity.

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"…the obesity epidemic is a systems problem, as opposed to a simple problem with a linear cause-and-effect relationship."

A systems approach to obesity

Bruce Y. Lee, Sarah M. Bartsch, Yeeli Mui, Leila A. Haidari, Marie L. Spiker, Joel Gittelsohn

Nutrition Reviews, Volume 75, Issue suppl_1, 1 January 2017, Pages 94–106,
https://doi.org/10.1093/nutrit/nuw049
Published: 03 January 2017

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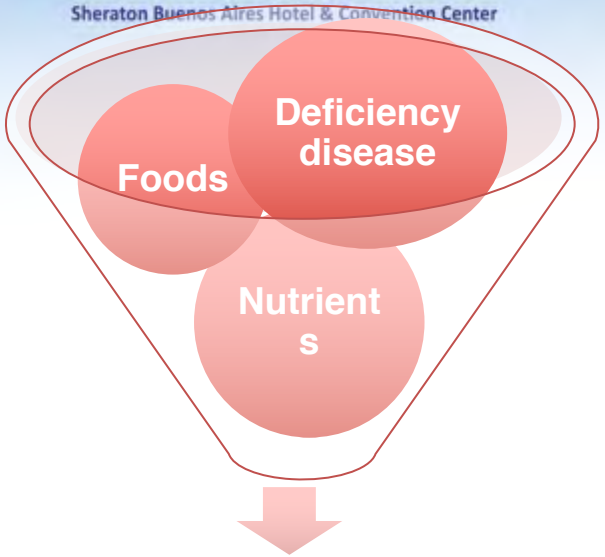
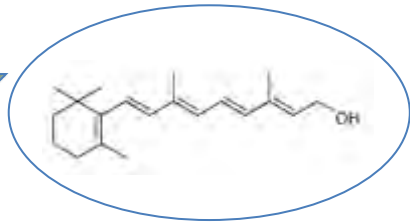
Obesity has become a truly global epidemic, affecting all age groups, all populations, and countries of all income levels. To date, existing policies and interventions have not reversed these trends, suggesting that innovative approaches are needed to transform obesity prevention and control. There are a number of indications that the obesity epidemic is a systems problem, as opposed to a simple problem with a linear cause-and-effect relationship. What may be needed to successfully address obesity is an approach that considers the entire system when making any important decision, observation, or change. A systems approach to obesity prevention and control has many benefits, including the potential to further understand indirect effects or to test policies virtually before implementing them in the real world. Discussed here are 5 key efforts to implement a systems approach for obesity prevention: 1) utilize more global approaches; 2) bring new experts from disciplines that do not traditionally work with obesity to share experiences and ideas with obesity experts; 3) utilize systems methods, such as systems mapping and modeling; 4) modify and combine traditional approaches to achieve a stronger systems orientation; and 5) bridge existing gaps between research, education, policy, and action. This article also provides an example of how a systems approach has been used to convene a multidisciplinary team and conduct systems mapping and modeling as part of an obesity prevention program in Baltimore, Maryland.

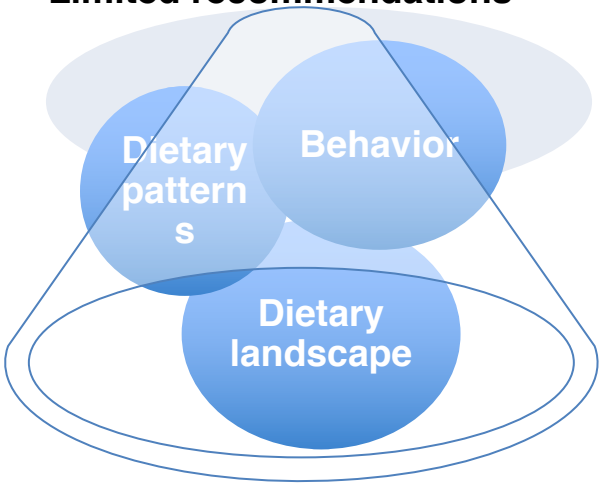
- Evolution from linking health benefits to specific nutrients at specific doses, to understanding the broader landscape that impacts health



Reductionism



Limited recommendations



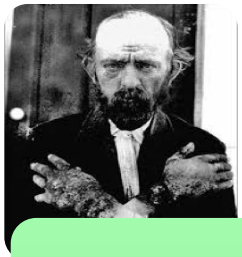
Holism

Comprehensive recommendations

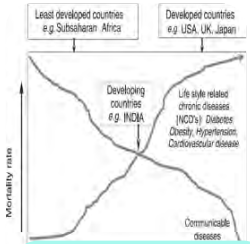
Understanding the "dietary landscape"

Evolving public health challenges

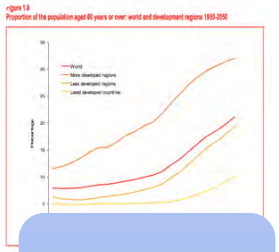
Communicable disease



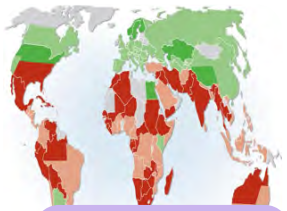
Overt nutrient deficiency



Rise of noncommunicable disease and obesity



Rising population, aging



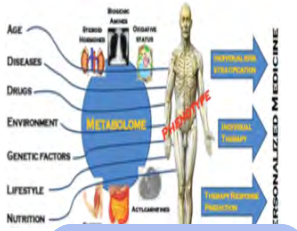
Food security, sustainability

Evolving nutrition research focus

Discovery of vitamins & minerals, eradicating overt nutrient deficiency

Diet & chronic disease

Bioactive substances



Personalized nutrition, microbiome

Behavior modification

Nutrition focus: Curing/preventing deficiency & chronic disease

Nutrition focus: Health maintenance & promotion

Nutrition continuum

Key learnings

- Nutrition science has evolved significantly over time (and will continue)
  - Scientific focus has narrowed (reductionism) and expanded (holism)
- Nutrition research has followed the trend of public health challenges in order to provide solutions
- Nutrition recommendations and policy must continue to evolve in parallel with advances in science and technology and public health challenges

Thank You!