

# The True Purpose Of Nutrition

# Robert H. Lustig, MD, MSL

LISPEN, Plainview, NY, Oct 24, 2023



### **Disclosures**



Chief Medical Officer: Kalin Health BioLumen Foogal Perfact Paid Advisor: Myka Bio Journeys Metabolic Simplex Health Levels Health Unpaid Advisor: Kuwaiti Danish Dairy

## **Learning Objectives**

- To explain the subcellular pathologies that drive chronic disease, and how food can make each one worse or better
- To explain how exercise does not mitigate these pathologies
- To discern the associations between ultraprocessed food and both metabolic health and mental health
- To explain the precepts of good nutrition
  - feed the gut
  - protect the liver
  - support the brain



Zimmet et al. Nature 414: 782, 2001 **Projected annualized inflation rate 3.88%** 



Zimmet et al. Nature 414: 782, 2001 Actual annualized inflation rate 6.55%



Zimmet et al. Nature 414: 782, 2001 Actual annualized inflation rate 10.30%



Zimmet et al. Nature 414: 782, 2001

### The money is not going to hospitals, physicians, or Big Pharma

#### Trends and Projections in U.S. Health Care Costs: 1970-2021 (in billions U.S. \$)



### The money is not going to hospitals, physicians, or Big Pharma It's going to chronic metabolic disease

Trends and Projections in U.S. Health Care Costs: 1970-2021 (in billions U.S. \$)



### Life expectancy vs. health expenditure over time (1970-2014) Our World



Health spending measures the consumption of health care goods and services, including personal health care (curative care, rehabilitative care, long-term care, ancillary services and medical goods) and collective services (prevention and public health services as well as health administration), but excluding spending on investments. Shown is total health expenditure (financed by public and private sources).



Data source: Health expenditure from the OECD; Life expectancy from the World Bank Licensed under CC-BY-SA by the author Max Roser. The interactive data visualization is available at OurWorldinData.org. There you find the raw data and more visualizations on this topic.

#### Life expectancy, 1970 to 2021



Our World in Data

Source: UN WPP (2022); Zijdeman et al. (2015); Riley (2005) OurWorldInData.org/life-expectancy • CC BY Note: Shown is the 'period life expectancy'. This is the average number of years a newborn would live if age-specific mortality rates in the current year were to stay the same throughout its life.



Only 7% of American Adults Have Good Cardiometabolic Health

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FOOD & NUTRITION

# Only 7% of American Adults Have Good Cardiometabolic Health

Tufts researchers find that most U.S. adults rate poorly across five components of heart and metabolic health, with clear racial disparities

#### Life expectancy, 1970 to 2021



Source: UN WPP (2022); Zijdeman et al. (2015); Riley (2005) OurWorldInData.org/life-expectancy • CC BY Note: Shown is the 'period life expectancy'. This is the average number of years a newborn would live if age-specific mortality rates in the current year were to stay the same throughout its life.

#### Life expectancy vs. health expenditure, 1970 to 2015

Our World in Data

Health financing is reported as the annual per capita health expenditure and is adjusted for inflation and price level differences between countries (measured in 2010 international dollars).

Our World in Data



Source: Data compiled from multiple sources by World Bank; Health Expenditure and Financing - OECDstat (2017) OurWorldInData.org/the-link-between-life-expectancy-and-health-spending-us-focus • CC BY



Hospitals Payer Health IT Government Finances Medical Groups

**DIVE BRIEF** 

# Medicare insolvency still expected by 2026, unchanged by COVID-19, trustees say

Published Sept. 1, 2021



<u>Rebecca Pifer</u>

Senior Reporter

in 🖬 🎔 👼 🖬







## **Definitions**

- Food Science: What happens between the ground and the mouth
- Nutrition: What happens between the mouth and the cell
- Metabolic Health: What happens inside the cell

## **Definitions**

- Food Science: What happens between the ground and the mouth
- Nutrition: What happens between the mouth and the cell
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IT'S ONLY WHAT HAPPENS INSIDE THE CELL THAT LEADS TO DISEASE



### **Consultative Brief – March 2023**

### **New Frontiers of Nutrition**

Evolved science-based insights from global nutrition experts to inform food system/transformation.



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### **New Frontiers of Nutrition**

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## The True Purpose Of Nutrition: METABOLIC HEALTH



### **Consultative Brief – March 2023**

### **New Frontiers of Nutrition**

Evolved science-based insights from global nutrition experts to inform food system/transformation.

## The True Purpose Of Nutrition: METABOLIC HEALTH OK, what is that?



The Diseases That Aren't Diseases

**Subcellular Pathologies that Belie Aging** 



Lustig, METABOLICAL, Spring 2021



The Diseases That Aren't Diseases

**Subcellular Pathologies that Belie Aging** 



1. Glycation (carbon deposits)





The Diseases That Aren't Diseases



- 1. Glycation (carbon deposits)
- 2. Oxidative Stress (rusting)





The Diseases That Aren't Diseases



- 1. Glycation (carbon deposits)
- 2. Oxidative Stress (rusting)
- 3. Mitochondrial Dysfunction (transmission)





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- 5. Membrane Integrity (oil leak)





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- 4. Insulin Resistance (carburetor)
- 5. Membrane Integrity (oil leak)
- 6. Inflammation (rotted fuel lines)





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- 6. Inflammation (rotted fuel lines)
- 7. Methylation (spark plugs)





The Diseases That Aren't Diseases



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- 4. Insulin Resistance (carburetor)
- 5. Membrane Integrity (oil leak)
- 6. Inflammation (rotted fuel lines)
- 7. Methylation (spark plugs)
- 8. Autophagy (oil sludge)





The Diseases That Aren't Diseases

**Subcellular Pathologies that Belie Aging** 



- 1. Glycation ---- carbohydrate, fructose, lack of fiber
- 2. Oxidative Stress ---- glucose, fructose, trans-fats
- 3. Mitochondrial Dysfunction --- fructose, omega-6's, trans-fats, lack of micronutrients
- 4. Insulin Resistance --- fructose, branched chain amino acids
- 5. Membrane Integrity --- lack of omega-3's
- 6. Inflammation ---- carbohydrate/gluten (in some), omega-6s, fructose, lack of fiber
- 7. Methylation --- lack of folic acid, B<sub>6</sub>, B<sub>12</sub>
- 8. Autophagy --- frequent feeding, lack of fiber

None of these are "druggable" But they are all "foodable"

Lustig, METABOLICAL, Spring 2021



The Diseases That Aren't Diseases

**Subcellular Pathologies that Belie Aging** 



- 1. Glycation ---- NOT amenable to exercise
- 2. Oxidative Stress ---- NOT amenable to exercise
- 3. Mitochondrial Dysfunction
- 4. Insulin Resistance
- 5. Membrane Integrity ---- NOT amenable to exercise
- 6. Inflammation
- 7. Methylation ---- NOT amenable to exercise
- 8. Autophagy

### "You can't outrun a bad diet"

Lustig, METABOLICAL, Spring 2021

### TIME



SHOPPING CART

**GETTY IMAGES—KUTAY TANIR** 

# Why Ultra-Processed Foods Are So Bad for You

Recent research finds that highly processed food may pose health risks.

## Is ultraprocessed food "food"?

## Is ultraprocessed food "food"?

Food: Substrate that contributes either to the burning or growth of an organism
## **Burning:**

### Ultraprocessed food inhibits mitochondria



bad for whole body metabolism." Dr. C. Ronald Kahn, CEO Joslin Diabetes Center

"The most important

takeaway of this study is

that high fructose in the diet

is bad," says Dr. Kahn. "It's

not bad because it's more

calories, but because it has

effects on liver metabolism

to make it worse at burning

fructose to the diet makes

the liver store more fat, and

this is bad for the liver and

fat. As a result, adding

#### Softic et al. Cell Metab 30:735, 2019

## **Growth:** Ultraprocessed food inhibits bone growth





#### D. Mechanical properties



Tested parameter	Control	UPF+CSD
Stiffness (N/mm)	393.5 ± 58.9	103.5 ± 40.6 <sup>*</sup>
Yield (N)	57.7 ± 6.4	27.0 ± 4.0 <sup>*</sup>
Fracture load (N)	94.7 ± 10.5	24.7 ± 4.5*
Max load (N)	110.9 ± 10.1	37.8 ± 6.4 <sup>*</sup>

UPF: Ultraprocessed food CSD: Caloric soft drink

B. Cortical analysis



A. Trabecular analysis





Zarestsky et al. Bone Res 9:14, 2021



Contents lists available at ScienceDirect

#### **Clinical Nutrition**

journal homepage: http://www.elsevier.com/locate/clnu

Original article

#### Consumption of <u>ultra-processed foods</u> associated with weight gain and <u>obesity</u> in adults: A multi-national cohort study



CLINICAL

Reynalda Cordova <sup>a, b</sup>, Nathalie Kliemann <sup>a</sup>, Inge Huybrechts <sup>a</sup>, Fernanda Rauber <sup>c, d</sup>, Eszter P. Vamos <sup>e</sup>, Renata Bertazzi Levy <sup>c, d</sup>, Karl-Heinz Wagner <sup>b</sup>, Vivian Viallon <sup>a</sup>, Corinne Casagrande <sup>a</sup>, Geneviève Nicolas <sup>a</sup>, Christina C. Dahm <sup>f</sup>, Jie Zhang <sup>f</sup>, Jytte Halkjær <sup>g</sup>, Anne Tjønneland <sup>g, h</sup>, Marie-Christine Boutron-Ruault <sup>i, j</sup>, Francesca Romana Mancini <sup>i, j</sup>, Nasser Laouali <sup>i, j</sup>, Verena Katzke <sup>k</sup>, Bernard Srour <sup>k</sup>, Franziska Jannasch <sup>1, m, n</sup>, Matthias B. Schulze <sup>1, o</sup>, Giovanna Masala <sup>p</sup>, Sara Grioni <sup>q</sup>, Salvatore Panico <sup>r</sup>, Yvonne T. van der Schouw <sup>s</sup>, Jeroen W.G. Derksen <sup>s</sup>, Charlotta Rylander <sup>t</sup>, Guri Skeie <sup>t</sup>, Paula Jakszyn <sup>u, v</sup>, Miguel Rodriguez-Barranco <sup>w, x, y</sup>, José María Huerta <sup>z, aa</sup>, Aurelio Barricarte <sup>y, ab, ac</sup>, Lousie Brunkwall <sup>ad</sup>, Stina Ramne <sup>ad</sup>, Stina Bodén <sup>ae</sup>, Aurora Perez-Cornago <sup>af</sup>, Alicia K. Heath <sup>e</sup>, Paolo Vineis <sup>e</sup>, Elisabete Weiderpass <sup>a</sup>, Carlos Augusto Monteiro <sup>c, d</sup>, Marc J. Gunter <sup>a</sup>, Christopher Millett <sup>e</sup>, Heinz Freisling <sup>a, \*</sup>





#### Article

### Ultra-Processed Food Consumption Associated with Incident Hypertension among Chinese Adults—Results from China Health and Nutrition Survey 1997–2015

Ming Li<sup>1,\*</sup> and Zumin Shi<sup>2</sup>

Research

#### JAMA Internal Medicine | Original Investigation

## Ultraprocessed Food Consumption and Risk of Type 2 Diabetes Among Participants of the NutriNet-Santé Prospective Cohort

Bernard Srour, PharmD, MPH, PhD; Léopold K. Fezeu, MD, PhD; Emmanuelle Kesse-Guyot, MSc, PhD; Benjamin Allès, PhD; Charlotte Debras, MSc; Nathalie Druesne-Pecollo, PhD; Eloi Chazelas, MSc; Mélanie Deschasaux, MSc, PhD; Serge Hercberg, MD, PhD; Pilar Galan, MD, PhD; Carlos A. Monteiro, MD, PhD; Chantal Julia, MD, MPH, PhD; Mathilde Touvier, PhD, MSc, MPH European Journal of Public Health, Vol. 32, No. 5, 779-785

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## Associations of <u>ultra-processed food</u> consumption with <u>cardiovascular disease</u> and all-cause mortality: UK Biobank

Xuanli Chen (), Jiadong Chu, Wei Hu, Na Sun, Qida He, Siyuan Liu, Zhaolong Feng, Tongxing Li, Qiang Han, Yueping Shen

British Journal of Nutrition, page 1 of 9 © Department of Gastroenterology, the First Affiliated Hospital, Zhejiang University School of Medicine, 2022. Published by Cambridge University Press on behalf of The Nutrition Society

# Association between <u>ultra-processed foods</u> consumption and risk of <u>non-alcoholic fatty liver disease</u>: a population-based analysis of NHANES 2011–2018

Zhening Liu, Hangkai Huang, Yan Zeng, Yishu Chen and Chengfu Xu\* Department of Gastroenterology, The First Affiliated Hospital, Zhejiang University School of Medicine, 79 Qingchun Road, Hangzhou 310003, People's Republic of China

#### RESEARCH

#### **Open Access**



Lídia Bezerra Barbosa<sup>1,2</sup>, Nancy Borges Rodrigues Vasconcelos<sup>1</sup>, Ewerton Amorim dos Santos<sup>3</sup>, Tamara Rodrigues dos Santos<sup>1</sup>, Thays Ataide-Silva<sup>2</sup> and Haroldo da Silva Ferreira<sup>2\*</sup>



Manuscript Doi: 10.1093/ecco-jcc/jjac167

Intake of ultra-processed foods is associated with an increased risk of Crohn's disease: a cross-sectional and prospective analysis of 187,154 participants in the UK Biobank

Jie Chen, <sup>a, b\*</sup> Judith Wellens, <sup>c, d\*</sup> Rahul Kalla, <sup>e</sup> Tian Fu,<sup>b</sup> Minzi Deng, <sup>b</sup> Han Zhang,<sup>a</sup> Shuai Yuan,<sup>f</sup> Xiaoyan Wang, <sup>b, #</sup> Evropi Theodoratou,<sup>g,h,†</sup> Xue Li,<sup>a,#</sup> Jack Satsangi,<sup>c,†</sup>

#### 

# Consumption of <u>ultra-processed foods</u> and <u>cancer</u> risk: results from NutriNet-Santé prospective cohort

Thibault Fiolet,<sup>1</sup> Bernard Srour,<sup>1</sup> Laury Sellem,<sup>1</sup> Emmanuelle Kesse-Guyot,<sup>1</sup> Benjamin Allès,<sup>1</sup> Caroline Méjean,<sup>2</sup> Mélanie Deschasaux,<sup>1</sup> Philippine Fassier,<sup>1</sup> Paule Latino-Martel,<sup>1</sup> Marie Beslay,<sup>1</sup> Serge Hercberg,<sup>1,4</sup> Céline Lavalette,<sup>1</sup> Carlos A Monteiro,<sup>3</sup> Chantal Julia,<sup>1,4</sup> Mathilde Touvier<sup>1</sup>

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<sup>E</sup> September 06, 2022; 99 (10) **RESEARCH ARTICLES** 

#### Association of <u>Ultraprocessed Food</u> Consumption With Risk of <u>Dementia</u> A Prospective Cohort Study

Huiping Li, Shu Li, Hongxi Yang, Yuan Zhang, Shunming Zhang, Yue Ma, Yabing Hou, Xinyu Zhang, Kaijun Niu, Yan Borné, Yaogang Wang First published July 27, 2022, DOI: https://doi.org/10.1212/WNL.000000000200871



Contents lists available at ScienceDirect

#### Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

High ultra-processed food consumption is associated with elevated psychological distress as an indicator of depression in adults from the Melbourne Collaborative Cohort Study

Melissa M. Lane<sup>a,\*</sup>, Mojtaba Lotfaliany<sup>a</sup>, Allison M. Hodge<sup>b,c</sup>, Adrienne O'Neil<sup>a</sup>, Nikolaj Travica<sup>a</sup>, Felice N. Jacka<sup>a,d,e,f</sup>, Tetyana Rocks<sup>a</sup>, Priscila Machado<sup>g,h</sup>, Malcolm Forbes<sup>a,i,j</sup>, Deborah N. Ashtree<sup>a</sup>, Wolfgang Marx<sup>a</sup>



## American Journal of Preventive Medicine

GLOBAL HEALTH PROMOTION AND PREVENTION

Premature Deaths Attributable to the Consumption of Ultraprocessed Foods in Brazil

Eduardo A.F. Nilson, ScD,<sup>1,2</sup> Gerson Ferrari, PhD,<sup>3</sup> Maria Laura C. Louzada, PhD,<sup>4</sup> Renata B. Levy, PhD,<sup>5</sup> Carlos A. Monteiro, PhD,<sup>1</sup> Leandro F.M. Rezende, ScD<sup>6</sup>



Ultra-processed food consumption and mental wellbeing outcomes

Rapid Report // September 2023

## Global Mind Project (n = 227,000)

#### Figure 3: Impact of ultra-processed food consumption for different levels of exercise and income

Relationship between MHQ scores and frequency of ultra-processed food consumptions for individuals who (i) exercise several times a week (blue line) or less than once a week to never (red line) for the global sample (left) and (ii) for those who are low income (<\$40,000 annually; red line) versus high income (>\$100,000 annually; blue line) for respondents in the United States (right)





#### NOVA I







#### NOVA II

#### NOVA I





#### NOVA II



NOVA III





#### NOVA III

#### NOVA I





#### NOVA II



NOVA III

NOVA IV

Only NOVA IV correlates with chronic disease 57% of US consumption 73% of US food supply

#### 🕲 wbcsd

#### Processed food and its role in nutritious and sustainable diets



#### VIEWPOINT

#### Robert H. Lustig, MD,

MSL Department of Pediatrics, University of California, San Francisco; and Philip R. Lee Institute for Health Policy Studies, University of California, San Francisco.

Corresponding Author: Robert H. Lustig, MD, MSL, Division of Pediatric Endocrinology, University of California, San Francisco, 550 16th St, PO Box 0434, San Francisco, CA 94143 (rlustig@ucsf.edu). Those of us who have participated in science know that 9 of every 10 experiments are failures. Now imagine that the last 50 years has been a grand clinical research experiment, with the American population as unwitting participants, conducted by 10 principal investigators—Coca-Cola, Pepsico, Kraft, Unilever, General Mills, Nestlé, Mars, Kellogg, Proctor & Gamble, and Johnson & Johnson. In 1965, these corporations posed the hypothesis that processed food is better than real food. To determine if the experiment was a success or a failure, we have to examine the outcome variables. In this case, there are 4: food consumption, health/disease, environment, and cash flow, divided into companies, consumers, and society.

Processed Food—An Experiment That Failed

Processed food is defined by 7 food engineering criteria; it is mass produced, is consistent batch to batch, is consistent country to country, uses specialized ingredients from specialized companies, consists of prefrozen macronutrients, stays emulsified, and has long shelf life or freezer life.<sup>1</sup>

JAMA Pediatrics March 2017 Volume 171, Number 3

Furthermore, 11 nutritional properties distinguish processed food.<sup>2</sup> (1) Too little fiber. When fiber (soluble and insoluble) is consumed within food, it forms a gelatinous barrier along the intestinal wall. This delays the intestine's ability to absorb nutrients, instead feeding the gut microbiome. Attenuation of the glucose rise results in insulin reduction. Attenuation of fructose absorption reduces liver fat accumulation. (2) and (3) Too few  $\omega$ -3 and too many  $\omega$ -6 fatty acids. ω-3s are precursors to docahexaenoic and eicosapentanoic acids (anti-inflammatory). Conversely, ω-6s are precursors of arachidonic acid (proinflammatory). Our ratio of  $\omega$ -6 to  $\omega$ -3 fatty acids should be approximately 1:1. Currently, our ratio is about 25:1, favoring a proinflammatory state, which can drive oxidative stress and cell damage. (4) Too few micronutrients. Antioxidants, such as vitamins C and E, quench oxygen radicals in peroxisomes to prevent cellular damage, while others, such as carotenoids and a-lipoic acid, prevent lipid peroxidation. (5) Too many

jamapediatrics.com

## FOODAS MEDICINE HOW FOOD AND

**DIET IMPACT** THE TREATMENT OF DISEASE AND DISEASE MANAGEMENT





Inside the Fauci Wuhan Controversy

## Newsweek XIC

Ultra-processed Food Raises the Risk WARNING: Ultra-processed rood kaises the kisk of Diabetes, Cancer, Heart Disease, Obesity, and Dying of COVID-19.

# O(1)D

YOUR MEAL SHOULD COME WITH A WARNING LABEL. HERE'S WHY.

#### U.S. Government's Top 10 "Greatest Hits" Still in Place Today

- 1. 1790 Sugar tariff
- 2. 1933 Dust Bowl, Farm Bill, first food subsidies
- 3. 1959 Fall of Bautista and rise of Castro in Cuba, altered sugar imports, Fanjul Bros.
- 4. 1971 Richard Nixon and USDA Secretary Earl Butz, make food cheap, monoculture
- 5. 1977 McGovern Commission, first Dietary Guidelines for Americans, fat is the enemy
- 6. 1980 Hurricane Allen destroyed Caribbean sugar crop, HFCS given green light
- 7. 1986 FDA reviews data on sugar, results "inconclusive"
- 8. 1990 Nutrition Labeling and Education Act (NLEA), Nutrition Facts
- 9. 1994 Dietary Supplement Health and Education Act (DSHEA), nutriceuticals

10. 1997 — Food Safety Modernization Act, Generally Recognized as Safe (GRAS) Loophole

## Prospects for the true cost accounting of food systems

Evaluating food systems in a holistic way is paramount to their transformation. Recent initiatives show how true cost accounting can help achieve that transformation at policy, product, organizational, farm, and investment levels.

Lauren Baker, Guillermo Castilleja, Adrian De Groot Ruiz and Adele Jones

Ultraprocessed foods are only "cheap" when the costs of their negative metabolic impact are externalized to health care and public health budgets.





#### Scientific Group of UN Food Systems Summit 2021

The goal: Metabolic Health

The Strategies:

Promote Metabolism

Inhibit Inflammation

#### What is the definition of "healthy"?

- Michael Pollan said, "Eat Food. Not Too Much. Mostly Plants."
- Eat food: Some need a low-fat diet, others need a high-fat diet.
- Not too much: Doesn't take into account mitochondrial dysfunction.
- *Mostly plants:* Coke, Doritos, and Oreos are plant-based.

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- *Mostly plants:* Coke, Doritos, and Oreos are plant-based.
- It's not *what's in the food;*
- It's what's been done to the food; and really,
- It's what they did to the food that matters.
- And that's not listed on the food label.

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- It's what they did to the food that matters.
- And that's not listed on the food label.
- I suggest a different three principles:



Healthy essential fats Plant based, short chain, polyunsaturated fatty acids Omega 3s: pregnancy, lifespan, childhood, ADHD, depression Brain selective nutrients



## **The Metabolic Matrix**

## The Metabolic Matrix: Gut Health

- Digestion, Absorption, Metabolism
- Gut is an organ
- Unprocessed food feeds the gut
- Fiber
- Ultraprocessed food damages the gut
- Microbiome health



## If you don't feed your gut, your gut will feed on you



Desai et al. Cell 167:1339, 2016

## Higher dietary fiber content correlates with reduction in chronic disease

1.25

A All-cause mortality

## Soluble + Insoluble Fiber together protects the liver and feeds the gut:

- $\circ$  Acts as a barrier to sugar absorption
- Reduces insulin response
- o Feeds the intestinal microbiome
- Induces the satiety signal sooner
- Colonic bacteria make short chain fatty acids
- Removes cancer cells from colon

#### Soluble Fiber alone:

Feeds the intestinal microbiome Colonic bacteria make short chain fatty acids

#### Insoluble Fiber alone:

Induces the satiety signal sooner Removes cancer cells from colon



— Linear model — Spline model B Coronary heart disease incidence



(B) Total fibre and incidence of coronary heart disease. 6449 deaths over 2.5 million person-years. Assuming linearity a risk ratio of 0.81 (0.73-0.90) was observed for every 8 g more fibre consumed per day. (C) Total fibre and incidence of type 2 diabetes. 22 450 cases over 3.2 million person-years. Assuming linearity a risk ratio of 0.85 (0.82-0.89) was observed for every 8 g more fibre consumed per day. (C) Total fibre and incidence of type 2 diabetes. 22 450 cases over 3.2 million person-years. Assuming linearity a risk ratio of 0.85 (0.82-0.89) was observed for every 8 g more fibre consumed per day. (D) Total fibre and incidence of colorectal cancer. 20009 cases over 3.0 million person-years. Assuming linearity a risk ratio of 0.92 (0.89-0.95) was observed for every 8 g more fibre consumed per day.

Reynolds et al. Lancet 393: 434, 2019

## The Metabolic Matrix: Feed the Gut



#### **Fiber is critical**

- Supports healthy metabolism & regulates bowel movement through delayed gastric emptying
- Increases satiety
- Helps regulate blood glucose levels
- May help prevent certain cancers
- Lowers LDL (bad cholesterol)
- In Type 2 Diabetics, increasing fiber consumption may reduce fasting glucose and HbA1c

## The Metabolic Matrix: Liver Health

- Fat Fraction Maps
- Fructose reduction, metabolism, etc.
- Reduce total sugar, glycemic load
- Fiber
- Appropriate hydration
- Reduce environmental toxins
- Intestinal barrier



# PROTECT THE LIVER

## The Metabolic Matrix: Protect the Liver MRI Fat Fraction Maps



Fat, Metabolically Healthy Low Liver Fat = 2.6%

Fat, Metabolically III High Liver Fat = 24% Thin, Metabolically III High Liver Fat = 23%

#### Fructose is metabolized in the liver differently than glucose




Lustig et al. Obesity 2016 Gugliucci et al. Atherosclerosis 2016 Schwarz et al. Gastroenterology 2017 Olson et al. Nutrients 2022



Lustig et al. Obesity 2016 Gugliucci et al. Atherosclerosis 2016 Schwarz et al. Gastroenterology 2017 Olson et al. Nutrients 2022





## Tight junctions keep bad stuff out



Di Ciaula et al. J Clin Med 9:2648 2020

## **Tight junctions keep bad stuff out**

Gluten is a direct immunotoxin of zonulins, both in intestine AND brain- cause of Celiac Disease



Di Ciaula et al. J Clin Med 9:2648 2020

## Fructose also disrupts tight junctions, and lets bad stuff in



Cho et al. Hepatology 2019 Apr 8. doi: 10.1002/hep.30652.

## Sugar alters Th17 barrier in the intestine

### **Graphical abstract**



Kawano et al., Cell 185, 1, 2022





Article

## Dietary Intake of Free Sugars is Associated with Disease Activity and Dyslipidemia in Systemic Lupus Erythematosus Patients

María Correa-Rodríguez <sup>1,2</sup>, Gabriela Pocovi-Gerardino <sup>1,2,\*</sup>, José-Luis Callejas-Rubio <sup>3</sup>, Raquel Ríos Fernández <sup>3</sup>, María Martín-Amada <sup>4</sup>, María-Gracia Cruz-Caparros <sup>5</sup>, Irene Medina-Martínez <sup>1</sup>, Norberto Ortego-Centeno <sup>2,3,†</sup> and Blanca Rueda-Medina <sup>1,2,†</sup>

Higher consumption of free sugars in active vs. inactive SLE (8.60% ± 5.51 vs, 6.36% ± 4.82; p = 0.020)
Association between consumption of free sugars and number of complications of SLE

Correa-Rodriguez et al. Nutrients 12:1094, 2020

## Group A Streptococcus grow better with fructose than glucose



GAS responsible for psych disease:

1) Sydenham's chorea

2) PANDAS OCD tic disorders adult personality dis. mood disorder

Dmitriev et al. J Bacteriol 188:7230, 2006

Orlovska et al. JAMA Pediatr. 74:740, 2017

## **Fructose and Cancer/Dementia**

### CellPress

### **Cell Metabolism**

### Perspective

## "Sweet death": Fructose as a metabolic toxin that targets the gut-liver axis

Mark A. Febbraio<sup>1,\*</sup> and Michael Karin<sup>2,\*</sup> <sup>1</sup>Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC, Australia <sup>2</sup>Department of Pharmacology, School of Medicine, University of California, San Diego, San Diego, CA, USA \*Correspondence: mark.febbraio@monash.edu (M.A.F.), mkarin@health.ucsd.edu (M.K.) https://doi.org/10.1016/j.cmet.2021.09.004

### Febbraio et al. Cell Metab 33:2316, 2021



Review

## Fructose and fructose kinase in cancer and other pathologies

<u>Hongfei Jiang</u><sup>a</sup>, <u>Qian Lin</u><sup>a</sup>, <u>Leina Ma</u><sup>a</sup>, <u>Shudi Luo</u><sup>c</sup>, <u>Xiaoming Jiang</u><sup>c</sup>, <u>Jing Fang</u><sup>a</sup>  $\land$   $\boxtimes$ , <u>Zhimin Lu</u><sup>b c</sup>  $\land$   $\boxtimes$ 

### Jiang et al. J Genet Genom 48:531, 2021





Richard J. Johnson<sup>1</sup>\*, Fernando Gomez-Pinilla<sup>2</sup>, Maria Nagel<sup>3</sup>, Takahiko Nakagawa<sup>4</sup>, Bernardo Rodriguez-Iturbe<sup>5</sup>, Laura G. Sanchez-Lozada<sup>5</sup>, Dean R. Tolan<sup>6</sup> and Miguel A. Lanaspa<sup>1</sup>

### Johnson et al. Front Aging Neurosci 12:560865, 2020

Sugar is the marker for ultra-processed food 56% of the food sold in America is ultra-processed food Accounts for 62% of the sugar in the American diet



Fig 2 | Relative contribution (%) of each food group to consumption of ultra-processed food in diet

### Srour et al. BMJ 365:I1451, 2019

## The Metabolic Matrix: Brain Health

- What is your brain made of?
- Healthy & essential fats
- Plant based, short chain, polyunsaturated fatty acids
- Balance of omega 3 & 6 in the brain
- Omega 6
- Omega 3s: pregnancy, lifespan, childhood
- ADHD and depression
- Brain selective nutrients



# SUPPORT THE BRAIN

## What is your brain made of?





# Poor psychiatric health is persistently linked to low omega-3

Table 2. Fatty acid composition (%) of red blood cell data					
in adults with ADHD (n = 30)	ADHD				
	М	SD			
Omega 6					
c18: 2n-6 (LA)	13.95	1.62			
c18: 3n6	0.08	0.03			
c20: 2n6	0.30	0.05			
c20:3n6	1.55	0.36			
c20: 4n6 (AA)	13.71	1.35			
c22: 4n6	3.67	0.53			
c22: 5n6	0.53	0.10			
Total n6	33.87	2.25			
Omega 3					
c18: 3n3 (ALA)	0.19	0.04			
c20: 5n3 (EPA)	0.53	0.18			
c22: 5n3	2.05	0.24			
c22: 6n3 (DHA)	3.80	0.95			
Total n3	6.57	1.22			



PLEFA

People with schizophrenia and depression have a low omega-3 index

Natalie Parletta<sup>a,</sup> ▲ · <sup>≦</sup> , Dorota Zarnowiecki<sup>a,</sup> <sup>≦</sup> , Jihyun Cho<sup>a,</sup> <sup>≦</sup> , Amy Wilson<sup>b,</sup> <sup>≦</sup> , Nicholas Procter<sup>c, <sup>≦</sup></sup> , Andrea Gordon<sup>c,</sup> <sup>≦</sup> , Svetlana Bogomolova<sup>b,</sup> <sup>≦</sup> , Kerin O'Dea<sup>a,</sup> <sup>≦</sup> , John Strachan<sup>d,</sup> <sup>≦</sup> , Matt Ballestrin<sup>d,</sup> <sup>≦</sup> , Andrew Champion<sup>d,</sup> <sup>≦</sup> , Barbara J Meyer<sup>e,</sup> <sup>≦</sup>

Comparison of Means n-3: M = 5.63, SD = 1.25 n-6: M = 25.27, SD = 3.74The omega-3 index in Parletta et al (2016) study was **3.95%** in comparison to the omega-3 index in NORAA participants which was: **4.33%** 



ADHD and Depression

- Several meta-analyses have confirmed a small-modest effect size for reducing clinical symptoms of ADHD in children (see Hawkey & Niggs 2014, Clin Psychol Rev)
- Hallahan, Davis et al., Br J Psychiatry, 2016 confirmed an effect size of 0.61 (Cohens d) for reducing clinical depression in both cases EPA-rich formulations had the greatest efficacy







## The Metabolic Matrix Explains What Nutrition Needs To Do

### • The science is clear:

- more soluble and insoluble fiber (to feed the gut)
- less fructose (to protect the liver)
- more  $\alpha$ -linolenic acid, EPA, DHA (to support the brain)
- A Low Insulin Diet = A Real Food Diet
- The challenge is going from knowledge to transformation
  - We must "Debunk the Calorie", and promote metabolic health

### Impact: Walnut Creek Spotlight - 3rd Silver Level District



### Eat Real Featured Meal

### Housemade Baked Ziti

Served with 100% whole grain pasta & freshly prepared marinara sauce

Plain milk is nutrient rich and contains no added sugar.

#### Why this matters

Excess sugar negatively impacts your ability to learn.

Marinara sauce is made from scratch using minimally processed ingredients.

### Why this matters?

This sauce is filled with nutritious whole food ingredients & does not contain any added sugar or other harmful additives found in pre-made sauces.

### Served with 100% whole grain pasta.

### Why this matters?

Whole grain pasta contains fiber to support healthy digestion & is packed with micro nutrients to grow a healthy body.





Seasonal strawberries and kiwis are sourced locally from **Watsonville** and Gridley respectively.

Why this matters? Local sourcing of produce helps support businesses in our community and the planet's health.

The **salad bar** is stocked with a variety of fresh, local vegetables, including carrots from **Bakersfield** and romaine for Caesar salad from **Salinas**.

Why this matters Salad bars with fresh, local produce provide the opportunity to try a variety of fruits & vegetable

This meal showcases the values of our Eat Real Certification! Learn more at www.eatreal.org/walnut-creek-is-certified.





### WCSD Eat Real Certification Highlights

- ★ 66% of produce is sourced locally (34% increase from 2019)
- ★ Removed an average of 7 lbs of added sugar per student per year from breakfast grains alone
- Nothing on menu contains more than 3 tsp of added sugar
- Increased plant-based menu options
  - From 0 to 5 at K-5 and K-8 sites
  - From 1 to 7 at 6-8 sites
- Saw lunch participation increase by **73%** and breakfast by **2400%** from 2019 to 2023











### Nutrition

### 'Ultra-processed' products now half of all UK family food purchases

Exclusive: health experts warn increasing popularity of industriallymade food will lead to negative effects such as obesity and poor health



▲ Some of the UK's best-selling ultra-processed foods. Photograph: Jill Mead for the Guardian

Sarah Boseley Health editor

healthline	Health Condi	tions ~ D	Discover ~	Plan ~	Connect	~
NUTRITION Special Diets	Healthy Eating	Food Freedom	Conditions	Feel Good Food	Products	Vita

### Americans Are Eating More Ultra-Processed Foods: How to Cut Down on Them



Fast food such as hamburgers are among the ultra-processed foods that people are eating more often. Evrim Ertik/Getty Images

### 57% of US consumption 73% of the US food supply

## **Strategies for Advancing Metabolic Health**

Public Health Intervention (one population at a time)

Personal Intervention (one patient at a time)

Technological Innovation (one company at a time)