MHIF Research Highlights: NOVEMBER 2019

WAY TO GO TEAM!
MHIF was well represented at TCT 2019

• 37 MHI/MHIF physician & staff
• 58 total presentations
• 36 posters
• 11 podium presentations
• 9 moderators/panelists
• 2 lives cases

SAVING LIVES, “HEART IN A BOX” CLINICAL TRIAL
MHIF is at the forefront of new clinical research, completing 3 successful heart transplants with use of the investigational TransMedics Organ Care System (OCS™).

The system preserves donor hearts, keeping them beating instead of simply storing them on ice in a cooler during transport.

FEATURED MHIF STUDIES
Open for Enrollment and Referrals!

OPTION comparison of anticoagulation with left atrial appendage closure after AF ablation
CONTACT: Jacob Cohen, 612-863-4022

SPYRAL-HTN renal denervation for patients with uncontrolled hypertension
CONTACT: Carina Benson, 612-863-6288

Heart EXPAND CAP extended criteria donor hearts for transplantation
CONTACTS: Kari Thomas, 612-863-7493 or
Kari Williams, 612-863-0027

MARK YOUR CALENDARS

2018 MHIF Annual Report
We’re proud to share highlights from 2018. Please find the report online mplsheart.org/2018annualreport
2019 Kevin Graham Prevention Lecture
Food is Medicine: Dietary and Policy Priorities for Cardiometabolic Health

Speaker: Dariush Mozaffarian, MD, DrPH
Dean, Friedman School of Nutrition Science & Policy
Tufts University
Boston, MA

Learning Objectives
At the completion of this activity, the participants should be able to:
• Be familiar with the current dietary priorities to improve cardiometabolic health
• Gain an appreciation for new "Food is Medicine" approaches to integrate food and nutrition into the healthcare system
• Understand the potential economic cost-benefit and policy implications of such interventions

Minneapolis Heart Institute Foundation Cardiovascular Grand Rounds
Date: October 28, 2019 | Time: 7 - 8 A.M. | Location: Abbott Northwestern Hospital Education Building, Auditorium A/B

Seating is limited. Please register here: https://mhifgrandrounds-mozaffarian.eventbrite.com

Webinar: If you cannot attend grand rounds in person, attend via webcast (you can join the webinar up to 15 minutes before the presentation starts at 7:00 a.m.). Connect to the webinar at mplsheart.org/gr

About: Dr. Kevin Graham
Dr. Kevin J. Graham has been a tireless and innovative thought leader in cardiology. His bold vision spearheaded Hearts Beat Back: The Heart of New Ulm Project — an initiative to reduce heart attacks and improve modifiable cardiovascular disease risk factors in a southwestern Minnesota community. This award-winning heart disease prevention initiative, offered in partnership with the Minneapolis Heart Institute Foundation®, Allina Health and the city of New Ulm, moved beyond the walls of health care establishments and into the community to make health and well-being the easy choice where people live, learn, work, worship and play.

He has been actively involved in the development of cardiology practice guidelines and computerized interfaces for cardiovascular disease management in both specialty and primary care settings. He has authored numerous articles in both preventive cardiology and managed care, especially with regard to quality measures.

Dr. Graham served as the President of the Minneapolis Heart Institute® and the Cardiovascular Services Division of Abbott Northwestern Hospital from 2007 to 2012. He established and led the Preventive Cardiology practice and was Director of Outpatient Clinical Laboratory at the Minneapolis Heart Institute®. Dr. Graham was also an Assistant Professor of Clinical Medicine at the University of Minnesota Medical School. He completed his residency in Internal Medicine at Hennepin County Medical Center and his fellowship in cardiovascular disease at the University of Minnesota.
ACCREDITATION

Physician: Allina Health is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. Allina Health designates this live activity for a maximum of 1.0 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Nurse: This activity has been designed to meet the Minnesota Board of Nursing continuing education requirements for 1.0 hours of credit. However, the nurse is responsible for determining whether this activity meets the requirements for acceptable continuing education.

DISCLOSURE POLICY AND STATEMENTS

Allina Health, Learning & Development intends to provide balance, independence, objectivity and scientific rigor in all of its sponsored educational activities. All speakers and planning committee members participating in sponsored activities and their spouse/partner are required to disclose to the activity audience any real or apparent conflict(s) of interest related to the content of this conference.

The ACCME defines a commercial interest as “any entity” producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients. The ACCME does not consider providers of clinical service directly to patients to be commercial interests - unless the provider of clinical service is owned, or controlled by, an ACCME-defined commercial interest.

Moderator(s)/Speaker(s):

Dean Mozaffarian has declared the following relationships: Research funding – National Institutes of Health, Gates Foundation; Consultant fees – GOED Omega-3 (Global Organization for EPA and DHA Omega-3), Nutrition Impact, Pollock Communications, Bunge, Indigo Agriculture, Amarin, Acasti Pharma, Cleveland Clinic Foundation, America’s Test Kitchen, Danone; Scientific advisory board – Elysium Health (with stock options), Omada Health, Day Two; Royalties – UpToDate (all outside the submitted work).

Planning Committee: Dr. Alex Campbell, Jake Cohen, Jane Fox, Dr. Mario Goessl, Dr. Kevin Harris, Dr. Kasia Hryniewicz, Rebecca Lindberg, Amy McMeans, Dr. Michael Miedema, Dr. JoEllyn Moore, Pamela Morley, Dr. Scott Sharkey, and Jolene Bell Makowesky have declared that they do not have any conflicts of interest associated with the planning of this event. Dr. David Hurrell discloses the following relationship- Boston Scientific: Chair, Clinical Event Committee

PLEASE SAVE YOUR SERIES FLIER

When you request a transcript this serves as your personal tracking of activities attended. Most professional healthcare licensing/certification boards will not accept a Learning Management System (LMS) transcript as proof of credit; there are too many LMS’s across the country and their validity/reliability are always in question.

If audited by a licensing board or submitting for license renewal or certification renewal, boards will ask you not the entity providing the education for specific information on each activity you are using for credit. You will need to demonstrate that you attended the activity with a copy of your certificate/evidence of attendance, a brochure/flier and/or the conference handout.

Each attendee at an activity is responsible for determining whether an activity meets their requirements for acceptable continuing education and should only claim those credits that he/she actually spent in the activity.

Maintaining these details are the responsibility of the individual.

PLEASE SAVE A COPY OF THIS FLIER AS YOUR CERTIFICATE OF ATTENDANCE.

Signature:

My signature verifies that I have attended the above stated number of hours of the CME activity.

Allina Health - Learning & Development
2925 Chicago Ave - MR 10701 - Minneapolis MN 55407

NON-ENDORSEMENT OF COMMERCIAL PRODUCTS AND/OR SERVICES

We would like to thank the following companies for exhibiting at our activity:

Amgen

Janssen Pharmaceutical Companies of Johnson & Johnson

Accreditation of this educational activity by Allina Health does not imply endorsement by Allina Learning & Development of any commercial products displayed in conjunction with an activity.

A reminder for Allina employees and staff: The Allina Policy on Ethical Relationship with Industry prohibits taking back to your place of work, any items received at this activity with branded and or product information from our exhibitors.

Together, we can create a world without heart and vascular disease.
Food is Medicine: Dietary and Policy Priorities For Cardiometabolic Health

Dariush Mozaffarian, MD, DrPH
Dean
Jean Mayer Professor of Nutrition & Medicine

Kevin Graham Lecture
Minneapolis Heart Institute
October 28, 2019

Disclosures

- **Research funding:** National Institutes of Health, Gates Foundation

- **Honoraria:** GOED, Nutrition Impact, Pollock Communications, Bunge, Indigo Agriculture, Amarin, Acasti Pharma, Cleveland Clinic Foundation, America's Test Kitchen, Danone

- **Scientific advisory boards:** Elysium Health, DayTwo, Filtricine

- **Online chapters:** UpToDate
• Preventive Cardiology champion

• Community prevention in the New Ulm Project, southwestern Minnesota

• President, Minneapolis Heart Institute

• Founded Preventive Cardiology at the Minneapolis Heart Institute

Dr. Kevin Graham

The Global Nutrition Crisis

Health and wellbeing
Hunger, disparities
Health care costs and access
Government budgets
Private business, economic growth
Sustainability and climate change
National security
Our Food: The #1 Cause of Poor Health

Risk Factors
- Dietary risks
- Tobacco smoking
- High blood pressure
- High body mass index
- Physical inactivity and low physical activity
- High fasting plasma glucose
- High total cholesterol
- Ambient particulate matter pollution
- Alcohol use
- Drug use
- Lead exposure
- Occupational risks
- Low bone mineral density
- Residential radon
- Ambient ozone pollution
- Intimate partner violence
- Childhood sexual abuse

US Burden of Disease Collaborators, JAMA 2013

Americans Are Sick – Really Sick

- 100+ million Americans – nearly half of all U.S. adults – have prediabetes or diabetes.

- 122 million have cardiovascular disease, which causes 841,000 deaths per year – about 2,300 deaths each day.

- 3 in 4 U.S. adults are overweight or obese.

- More Americans are sick, in other words, than are healthy.

American Heart Association, Heart Disease and Stroke Statistics, 2018
Unsustainable Rise in Healthcare Costs

Federal Healthcare Spending

U.S. Healthcare Costs

- 28% of the total federal budget
- 30% of total state budgets
- Top concern for U.S. businesses

Diabetes: $335 billion per year
CVD: $351 billion per year
Obesity: $1.72 trillion per year

Centers for Medicare & Medicaid Services, 2018
American Heart Association, Heart Disease and Stroke Statistics, 2018
The Milken Institute, America’s Obesity Crisis, 2018

Nutrition: Passion and Confusion

Source: Google images
What is Driving Policy and Public Choices?

**Policy Makers:**
- Total fat
- Saturated fat
- Cholesterol
- Total calories
- Added sugar

**The Public:**
- Clean labels
- Natural
- Gluten-free
- Organic
- Local
- Paleo
- Low-carb
- Plant-based
- Vegetarian

Modern Nutrition Science – A Rapid Evolution

- **Era of vitamin discovery**
  - 1920: Isolation and synthesis of all known vitamins
    - A
    - B1
    - B12
    - C
    - D
    - E
    - K
  - 1940: Single nutrient is born
    - Pellagra: B3
    - Scurvy: C
    - Rickets: D
  - 1950: Recommended daily allowances
    - Protein
    - Calcium
    - Phosphorus
    - Iron
    - Vitamins

- **Commodity crops, fortification**
  - Food as a delivery system
  - Fat v sugar

Mozaffarian et al., BMJ 2018
Reductionist Focus Permeates U.S. Nutrition Policy

National School Lunch Program

New Nutrition Facts Panel

Restaurant Menu Calorie Labeling

Reductionist Focus Dominates International Policy

U.K. front-of-pack “traffic light” label

Chile “black box” warning labels
**Explosion of Nutrition Science**

Number of Scientific Publications

- **Diet and Cardiovascular**
- **Diet and Diabetes**
- **Diet and Obesity**

Source: Pubmed/Medline (through Feb 2019)

Tufts: Gerald J. and Dorothy R. Friedman School of Nutrition Science and Policy

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**WHI**

Usual care

Low-fat diet
- 8.2% total fat
- 2.9% saturated fat

HR: 0.97 (95% CI: 0.90, 1.06)

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**PREDIMED**

Control diet

Med. Diet, nuts

Med. Diet, EVOO

HR: 0.70 (95% CI: 0.55, 0.89)

+ 4.4% total fat (no change in sat. fat)
Lesson #1: Nutrition & Obesity – More Than Calories

- Hunger, fullness
- Glucose, insulin, other hormonal responses
- Liver *de novo* fat synthesis (conversion of starch and sugar to fat)
- Brain reward, craving
- Gut microbiome (bacteria) responses
- Body’s metabolic rate (energy *out*)

*Cannot judge a food by its calorie count alone*

e.g., Browning AJCN 2011; Ebbeling JAMA 2012; Poutahidis Plos ONE 2013; Lennerz AJCN 2013; Ludwig JAMA 2014; Bazzano Ann Intern Med 2014; Hallberg Diabetes Therapy 2018; Gardner JAMA 2018; Ebbeling BMJ 2018, etc.

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Short-Term Weight Loss (*secondary prevention*)

*High-Fat Diets Similar or Better Than Low-Fat Diets*

P<0.001 for both comparisons with the low-fat diet

Shai et al NEJM 2008
### Weight Change Each Four Years (lbs)

For Each Increased Daily Serving of:

- **Foods**
  - Potato chips
  - Potatoes/fries
  - Processed meats
  - Unprocessed red meats
  - Butter
  - Sweets and desserts
  - Refined grains

- **Cheese**
- **Vegetables**
- **Nuts**
- **Whole grains**
- **Fruits**
- **Yogurt**

- **Beverages**
  - Sugar-sweetened beverages
  - Alcohol
  - 100% fruit juice
  - Low fat or skim milk
  - Whole fat milk
  - Diet (zero calorie) soda

Time-varying multivariable adjustment for age, sex, baseline BMI, sleep duration, smoking, physical activity, television watching, and all dietary factors jointly.

120,877 US adults in 3 separate cohorts followed for 24 years.

Mozaffarian et al., NEJM 2011

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### Probiotics and Weight: Randomized Trials

~1000 total subjects, duration 3-12 wks

**BMI:**
- \(-0.27 \text{ kg/m}^2\)
- \([-0.45, -0.08]\)

**Weight:**
- \(-0.60 \text{ kg}\)
- \([-1.19, -0.01]\)

Borgeraas et al. Obesity Rev 2018
Food processing alters energy consumption

Changes in leptin, PYY, adiponectin, insulin, C-peptide

Lesson #2: Diet & Health – Beyond Obesity

Mozaffarian D, Circulation 2016
### Dairy Foods and Risk of Diabetes

Sluijs et al., AJCN 2012

340,234 Europeans, 8 countries, 12,403 cases

- **Milk**: P-trend = 0.50
- **Yogurt**: P-trend = 0.06
- **Cheese**: P-trend = 0.01

Relative Risk of Diabetes vs Quintiles of Consumption

#### Dairy & Cardiometabolic Health: Pleotropic Mechanisms

Mozaffarian & Wu, Circulation Res 2018

- Cultivation/Selection of Bacteria and Yeast
- Probiotics
- Modulate Gut Microbiota
- Bioactive Peptides
- Calcium
- GLP-1 Signaling
- Sphingolipids
- Phospholipids
- ΔGene Expression
- MFGM
- Animal Breeding and Feeding Practice
- Homogenization

Dairy Protein

Fermentation

Vitamin K2

MCSFA

OSFA

Trans-16:1 n-7

IC50

Vitamin D

Dairy Fat
Lesson #3: Protective Foods

**Benefit**
- Fruits, Nuts, Fish
- Vegetables, Plant Oils
- Whole Grains, Beans, Yogurt
- Cheese
- Poultry, Milk
- Eggs, Butter
- Unprocessed Red Meats
- Refined Grains, Starches, Sugars
- Processed Meats, High Sodium Foods
- Industrial Trans Fat

Emerging Priorities:
- Gut Microbiome
- Phenolics/Bioactives
- Healthy Fats
- Food Processing
- Additives
- Personalization
- Allergies, Autoimmunity,
- Cancer, Brain Health

“Foods that give rise to life.”

Single Nutrients, Fat, Calories: Misleading

- Low calorie = “Less weight gain”
- Fat free = “Healthy”
- Low saturated fat = "Healthy“
- Vitamin fortified = “Good for you”
### Lesson #4: Systems Changes

#### Individual
- Age, gender, personal norms, education, income, taste preferences, nutritional knowledge and skills, health status, eating behaviors, attitudes, motivation, sleep, screen time, alcohol use

#### Sociocultural
- Social and cultural norms
- Social support
- Social class
- Race/ethnicity
- Neighbourhood socioeconomic status

#### Community environment
- Access to transport
- Accessibility to restaurants and fast food
- Accessibility to supermarkets and grocery stores

#### Workplace environment
- Food availability at local stores
- Food availability at restaurants

#### Academic environment
- School food environment
- School meal standards

#### Governmental
- Government priorities
- Government food policies

#### Agricultural, industry and market
- Land use and transportation
- Food production and distribution systems

#### Health and economic systems
- Food and agricultural policies
- Food assistance programmes

#### Climate and season
- Agriculture and food industry incentives
- Food marketing and media

#### International agreements
- International commodity pricing
- International food distribution and shipping

#### Multinational corporate lobbying
- Trade
- Corporate

#### Dietary research and science
- Research
- Scientific

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### Lesson #4: “Best Buy” Systems Changes

<table>
<thead>
<tr>
<th>Research &amp; Innovation</th>
<th>Healthcare Systems</th>
<th>Economic Incentives</th>
<th>Schools</th>
<th>Worksite Wellness</th>
<th>Standards and Labeling</th>
</tr>
</thead>
<tbody>
<tr>
<td>• National Institute of Nutrition</td>
<td>• Electronic health record</td>
<td>• Govt feeding programs (SNAP, WIC)</td>
<td>• School meal standards</td>
<td>• Procurement standards</td>
<td>• Additives (trans fat, salt, sugar)</td>
</tr>
<tr>
<td>• Public-private partnerships</td>
<td>• Healthy food prescriptions</td>
<td>• Tax policy (marketing, R&amp;D, etc.)</td>
<td>• Competitive food standards</td>
<td>• Behavioral economics</td>
<td>• Qualified health claims</td>
</tr>
<tr>
<td>• Fundamental discovery</td>
<td>• Medically tailored meals</td>
<td>• B Corps</td>
<td>• Breakfast in the classroom, summer meals</td>
<td>• Technology wellness platforms</td>
<td>• Marketing to children</td>
</tr>
<tr>
<td>• Big data, technology</td>
<td>• Medical education</td>
<td>• Investor vehicles</td>
<td>• Fresh F&amp;V programs</td>
<td>• Wellness incentives for healthy food</td>
<td>• Menu, FOP, and warning labels</td>
</tr>
<tr>
<td>• VA, DOD</td>
<td>• VA, DOD</td>
<td>• Taxes on SSBs, sugar, salt</td>
<td>• School gardens</td>
<td>• Retail incentives</td>
<td><a href="http://www.food-price.org">www.food-price.org</a>: Mozaffarian, Angell, Lang, Rivera, BMJ 2018</td>
</tr>
<tr>
<td>• Billing &amp; quality metrics</td>
<td>• Billing &amp; quality metrics</td>
<td>• Retail incentives</td>
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</tbody>
</table>
**Medically Tailored Meals**

- Providing home MTMs to chronically ill, food insecure patients dramatically reduces hospitalizations, ER visits, nursing home admissions, and **costs**.
- Using the 2011-2015 Massachusetts All Payers Database, MTMs:
  - Reduced hospital admissions **by 49%**
  - Reduced nursing facility admissions **by 72%**
  - **Net savings:** $9,036 per patient per year
  - Number needed to treat (NNT): 2 per saved hospital admission, 1.1 per saved nursing facility admission

http://www.fimcoalition.org, Berkowitz et al., JAMA Int Med 2019,
Mozaffarian et al, JAMA Int Med 2019

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**Produce Prescriptions - “Fresh Food Farmacy”**

**Meals**
175,000 meals per year, $60 per meal, $2,400 per patient per year.

**Clinical Results** (over 18 months)
≥40% decrease in the risk of death or serious complications*

Meals: HbA1c levels dropped an average 2.1 percentage points with attendance of the Diabetes Self-Management Class

**Financial Results** (over 18 months)
80% drop in costs for our pilot patients

$240,000 per member to $48,000 per member per year

Percent Decrease from Baseline to Current by Measure

- A1c: 17.8% decrease
- Glucose: 26.9% decrease
- Cholesterol: 9.8% decrease
- LDL: 12.2% decrease
- Triglycerides: 16.4% decrease

https://www.geisinger.org/freshfoodfarmacy
https://catalyst.nejm.org/prescribing-fresh-food-farmacy/
**Produce Rx in Medicare/Medicaid: Cost-Effectiveness**

![Graph showing the cost-effectiveness of different incentive programs over time.](image)

- Overall
- Medicare
- Medicaid
- Dual-eligible

**ICER ($/QALY)**

- Cost-Effective: <$150,000/QALY
- Highly Cost-Effective: <$50,000/QALY

**Duration of Incentive Program**

- 5 yrs
- 10 yrs
- 20 yrs
- Lifetime

- Lee et al, Plos Med 2019
- www.food-price.org

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**Leveraging SNAP for Better Nutrition and Health**

<table>
<thead>
<tr>
<th>Incentive</th>
</tr>
</thead>
<tbody>
<tr>
<td>F&amp;V Incentive (30% subsidy)</td>
</tr>
<tr>
<td>F&amp;V Incentive (30% subsidy) + SSB Restriction</td>
</tr>
<tr>
<td>SNAP Plus Healthy foods (30% subsidy)</td>
</tr>
<tr>
<td>Unhealthy foods (30% disincentive)</td>
</tr>
</tbody>
</table>

**Prevent**

- 300,000 lifetime CVD events
- 800,000 lifetime CVD events
- 940,000 lifetime CVD events

**ICER:**

- $550k/QALY at 5 yrs
- $158k/QALY at 5 yrs
- Cost-savings: $10B at 5 yrs
- $66k/QALY lifetime
- $5k/QALY lifetime
- $63B lifetime

Liu et al, Plos Medicine 2018

www.food-price.org

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Business Innovation: Canaries in the Coal Mine

Kraft-Heinz / 3G

>70% decline in stock, $15B write-off

May 2 IPO, $33M annual sales, $0 profits, market cap: $6.1 billion

Beyond Meat

Lessons From Past Public Health Successes

FIGURE 1. Motor-vehicle–related deaths per million vehicle miles traveled (VMT) and annual VMT, by year — United States, 1925–1997

Deaths

Vehicle Miles Traveled

Year

Deaths Per Million VMT

VMT (Billions)

US Centers for Disease Control and Prevention, MMWR Morb Mortal Wkly Rep, 1999
Lessons From Past Public Health Successes

• Driver:
  – Education.
  – Licensing.
  – Limits on phone use, texting.

• Car:
  – Active: seat belts, child seats, motorcycle helmets.
  – Passive: padded interiors, collapsible steering columns, shatterproof glass, air bags.
  – Crash safety standards.
  – Safety inspections.

• Road:
  – Road engineering, guard rails, rumble strips.
  – Speed limits.
  – Stop signs, stop lights, caution signs.

• Culture:
  – Designated driver campaign.
  – Drunk-driving legislation.
  – Private advocacy, e.g. MADD.

Mozaffarian D, Circulation 2016
Among 115,602 US adults in 3 separate cohorts followed for 24 years. Multivariable-adjusted for age, sex, baseline BMI, sleep duration, smoking, physical activity, television watching, and other dietary habits.

Bertoia et al., Plos Med 2015
Long-term weight gain: Interaction between change in protein foods and change in glycemic load

Per one-serving/day increase in intake

4-year weight change (lb)

Redmeat, Processed Meats, Poultry, Seafood, Eggs, Legumes

Milk Fat Globule Membrane

Whipped Cream, Nuts, Yogurt, Cheese, Whole Milk, Low-fat Milk

FIGURE 1 Confocal laser scanning microscopy micrograph of milk fat globules from whipping cream (40% fat) stained with Alexa WGA 488 (invitrogen) and Nile red (Sigma-Aldrich) fluorescent dyes, fat appears red, and milk fat globule membrane appears green. Images were captured at magnification ×2,580 with an objective lens ×60. Scale bar = 10 μm.

FIGURE 2 Confocal laser scanning microscopy micrograph of milk fat globules in an emulsion made from butter oil, purified water, and sodium dodecyl sulfate (15% fat) stained with Nile red (Sigma-Aldrich) and Alexa WGA 488 (invitrogen) fluorescent dyes; fat appears as red, and milk fat globule membrane appears in green. Images were captured at magnification ×2,580 with an objective lens ×60. Scale bar = 10 μm.

Rosqvist et al., AJCN 2016
Milk Fat Globule Membrane

Change from baseline, mg/dL

-5 0 5 10 15

Total Chol. LDL-C HDL-C Triglycerides ApoB (g/L)

Whipped Cream
Butter

* P < 0.05

19 genes differentially expressed (P ≤ 0.001 each)

@DMozaffarian
Rosqvist et al., AJCN 2016

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Diet Quality – Not Counting Calories, Fats, or Carbs

BMI 28-40, nondiabetic, all advised for healthy diet quality: no calorie counting or weight loss goals

<table>
<thead>
<tr>
<th></th>
<th>12-mo Change Estimate (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Healthy Low-Fat Diet (n = 305)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>-5.29 (-5.93 to -4.65)</td>
</tr>
<tr>
<td>Body mass index*</td>
<td>-1.75 (-1.97 to -1.52)</td>
</tr>
<tr>
<td>Body fat %</td>
<td>-1.97 (-2.38 to -1.56)</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>-3.74 (-4.64 to -2.84)</td>
</tr>
<tr>
<td>Lipid level, mmol/L</td>
<td></td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol</td>
<td>0.40 (-0.37 to 1.38)</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol</td>
<td>-2.12 (-4.70 to 0.47)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-0.95 (-17.46 to -2.44)</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>-3.18 (-4.33 to -2.03)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-1.94 (-2.65 to -1.22)</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>-3.67 (-4.90 to -2.44)</td>
</tr>
<tr>
<td>Fasting insulin, µIU/mL</td>
<td>-2.64 (-3.79 to -1.49)</td>
</tr>
<tr>
<td>Insulin-30, µIU/mL*</td>
<td>-15.38 (-21.13 to -9.62)</td>
</tr>
</tbody>
</table>

@DMozaffarian
Gardner et al., JAMA 2018

Tufts University School of Nutrition Science and Policy

Gerald L. and Dorothy R. Friedman School of Nutrition Science and Policy
Short-Term Weight Loss (secondary prevention)

<table>
<thead>
<tr>
<th>Weight loss goal</th>
<th>Weight of study (%)</th>
<th>WMD (95% CI), kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-fat vs low-carbohydrate intervention</td>
<td>2.26</td>
<td>-1.20 [-1.91 to 1.51]</td>
</tr>
<tr>
<td>Foster et al</td>
<td>2.38</td>
<td>-1.03 [-1.45 to 1.39]</td>
</tr>
<tr>
<td>Keogh et al</td>
<td>1.49</td>
<td>-0.90 [-1.65 to 0.38]</td>
</tr>
<tr>
<td>Goldbrand et al</td>
<td>2.34</td>
<td>-0.63 [-1.44 to 0.88]</td>
</tr>
<tr>
<td>Davis et al</td>
<td>2.53</td>
<td>-0.00 [-2.05 to 1.98]</td>
</tr>
<tr>
<td>Ellis et al</td>
<td>2.71</td>
<td>0.30 [-1.58 to 1.49]</td>
</tr>
<tr>
<td>Bham et al</td>
<td>2.20</td>
<td>0.75 [-0.25 to 1.63]</td>
</tr>
<tr>
<td>Lim et al</td>
<td>2.33</td>
<td>0.80 [-1.64 to 1.34]</td>
</tr>
<tr>
<td>Ghali et al</td>
<td>2.27</td>
<td>1.30 [-1.38 to 3.97]</td>
</tr>
<tr>
<td>McIsaac et al</td>
<td>0.85</td>
<td>1.40 [-1.65 to 3.95]</td>
</tr>
<tr>
<td>SMART Study</td>
<td>2.71</td>
<td>1.50 [-0.06 to 3.06]</td>
</tr>
<tr>
<td>Brinkworth/Tay et al</td>
<td>1.60</td>
<td>1.50 [-2.93 to 1.93]</td>
</tr>
<tr>
<td>DIRECT</td>
<td>2.74</td>
<td>1.80 [-0.34 to 3.79]</td>
</tr>
<tr>
<td>Foster et al</td>
<td>2.08</td>
<td>1.80 [-1.28 to 5.89]</td>
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<tr>
<td>Stone/Samuah et al</td>
<td>2.17</td>
<td>2.00 [-0.92 to 4.92]</td>
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<td>A to Z</td>
<td>2.55</td>
<td>2.10 [0.11 to 4.09]</td>
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<tr>
<td>Bazzano et al</td>
<td>2.52</td>
<td>3.50 [0.42 to 5.98]</td>
</tr>
<tr>
<td>Harvey-Berino</td>
<td>2.55</td>
<td>4.00 [-0.35 to 8.57]</td>
</tr>
</tbody>
</table>

Pooled WMD (heterogeneity F=0.41, p=0.33)

High-Fat Diets Superior to Low-Fat Diets

RCTs 1+ years in duration

@DMozaffarian

Tobias et al, Lancet Diab 2015

Probiotics and Glycemic Control: Randomized Trials

~1100 total subjects, duration 3-24 wks

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Participant</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IV, Random, 95% CI</td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>Asensi et al, 2013 (16)</td>
<td>54</td>
<td>7.9%</td>
<td>-1.51 [-1.73, -1.29]</td>
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<tr>
<td>Asensi et al, 2013 (28)</td>
<td>70</td>
<td>8.3%</td>
<td>-0.27 [-0.38, -0.16]</td>
</tr>
<tr>
<td>Bukowska et al, 1998 (17)</td>
<td>30</td>
<td>6.4%</td>
<td>-0.17 [-0.25, -0.09]</td>
</tr>
<tr>
<td>Eljahl et al, 2012 (12)</td>
<td>60</td>
<td>3.6%</td>
<td>-0.88 [-1.87, 0.11]</td>
</tr>
<tr>
<td>Ivey et al, 2014 (18)</td>
<td>77</td>
<td>8.1%</td>
<td>0.15 [-0.03, 0.33]</td>
</tr>
<tr>
<td>Ivey et al, 2014 (18)</td>
<td>79</td>
<td>8.0%</td>
<td>0.13 [-0.06, 0.32]</td>
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<tr>
<td>Jones et al, 2012 (18)</td>
<td>124</td>
<td>6.0%</td>
<td>0.50 [-0.04, 1.04]</td>
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<tr>
<td>Jung et al, 2013 (19)</td>
<td>50</td>
<td>6.8%</td>
<td>0.18 [-0.27, 0.63]</td>
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<tr>
<td>Laitinen et al, 2009 (20)</td>
<td>136</td>
<td>6.7%</td>
<td>-0.15 [-0.58, 0.28]</td>
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<tr>
<td>Lindsay et al, 2014 (21)</td>
<td>138</td>
<td>8.3%</td>
<td>-0.02 [-0.13, 0.09]</td>
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<tr>
<td>Mohamadshahi et al, 2014 (22)</td>
<td>40</td>
<td>1.6%</td>
<td>0.08 [-2.69, 0.93]</td>
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<tr>
<td>Naruszewicz et al, 2002 (15)</td>
<td>36</td>
<td>5.8%</td>
<td>-0.33 [-0.92, 0.26]</td>
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<tr>
<td>Rajkumar et al, 2014 (24)</td>
<td>30</td>
<td>8.1%</td>
<td>-0.63 [-0.97, -0.29]</td>
</tr>
<tr>
<td>Rajkumar et al, 2014 (24)</td>
<td>30</td>
<td>8.4%</td>
<td>-0.10 [-0.58, 0.38]</td>
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<tr>
<td>Shakeri et al, 2014 (25)</td>
<td>52</td>
<td>1.5%</td>
<td>-0.35 [-2.17, 1.48]</td>
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<tr>
<td>Sharafeddinov et al, 2013 (26)</td>
<td>36</td>
<td>2.4%</td>
<td>-0.09 [-1.48, 1.30]</td>
</tr>
<tr>
<td>Shivakoti et al, 2013 (27)</td>
<td>63</td>
<td>4.2%</td>
<td>-0.41 [-1.27, 0.45]</td>
</tr>
</tbody>
</table>

Total (95% CI): 0.00% [-0.31, -0.56]

Heterogeneity: $\tau^2 = 0.19$, $\chi^2 = 209.47$, df = 16 (P < 0.00001); $I^2 = 92%$ .

Test for overall effect: $Z = 2.41$ (P = 0.02).

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Ruan et al, Plos One 2015

Fasting Glucose: -0.31 mmol/L [-0.56, -0.06]

Fasting Insulin: -1.29 uU/ml [-2.17, -0.41]

HOMA-IR: -0.48 [-0.83, -0.43]
Global Pandemic of Obesity

2,009 population-based studies in 112 million adults, with measured BMI from 1985 to 2017

Globally, obesity explained by rural rise (60%), urbanization (12%), urban rise (28%)

Ezzati et al., Nature 2019

Produce Prescriptions - “Fresh Food Farmacy”

Diabetics: HbA1c ≥ 8.0, self-reported food insecurity

Intervention:
- 15-20 hours of group classes with a health coach
- Home kit: measuring cups, recipes, nutritional info
- Weekly fresh F&V, whole grains, and lean proteins to prepare healthy, nutritious meals for the whole family: 2 meals/day for 5 days/week

Support:
- Weekly diabetes self-management support group
- Access to online wellness module on nutrition
- Access to free, interactive cooking and nutrition classes by dietitians and health coaches

458 patients screened, 128 eligible (28%), and 95 enrolled

https://www.geisinger.org/freshfoodfarmacy
https://catalyst.nejm.org/prescribing-fresh-food-farmacy/
Low-Carb Diets for Type 2 Diabetes

Intention-to-treat (Missing Values Imputed)

Open label, nonrandomized, 1 year intervention among 262 patients with type 2 diabetes (vs. 87 patients with usual care), 83% completion

Advice to consume <30 g/d carbohydrate (<6%E), 20% protein, incorporate dietary fats to satiety

Dairy Fat Biomarkers and Risk of Diabetes

63,682 participants with 15,180 incident diabetes cases from 16 prospective cohort studies across 12 countries

Imamura et al., Plos Med 2018
## Nuts & Weight Change: Randomized Trials

<table>
<thead>
<tr>
<th></th>
<th>Body weight</th>
<th>Nuts reduce body weight</th>
<th>Nuts increase body weight</th>
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<tr>
<td><strong>Body weight</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>WMD (95% CI)</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Time of follow-up</td>
<td></td>
<td></td>
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<tr>
<td>&lt;24 wk</td>
<td>20</td>
<td>-0.39 (-1.29, 0.51)</td>
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<tr>
<td>≥24 wk</td>
<td>8</td>
<td>-1.24 (-3.85, 1.36)</td>
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<tr>
<td>Study focus</td>
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<tr>
<td>Energy restriction</td>
<td>2</td>
<td>-2.61 (-12.1, 6.84)</td>
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<tr>
<td>No energy restriction</td>
<td>26</td>
<td>-0.18 (-0.76, 0.37)</td>
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<tr>
<td>Study design</td>
<td></td>
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<tr>
<td>Randomized parallel</td>
<td>11</td>
<td>-1.65 (-4.13, 0.83)</td>
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<tr>
<td>Randomized crossover</td>
<td>17</td>
<td>-0.03 (-0.62, 0.56)</td>
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<tr>
<td>Quality</td>
<td></td>
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<tr>
<td>&lt;14 points</td>
<td>15</td>
<td>-0.17 (-1.70, 1.36)</td>
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<tr>
<td>≥14 points</td>
<td>13</td>
<td>-0.76 (-2.21, 0.69)</td>
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<tr>
<td>Intervention diet</td>
<td></td>
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<tr>
<td>Supplementation with nuts</td>
<td>17</td>
<td>-0.08 (-0.65, 0.48)</td>
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<tr>
<td>Replacement with nuts</td>
<td>11</td>
<td>-1.68 (-4.01, 0.65)</td>
<td></td>
</tr>
</tbody>
</table>

Flores Mateo et al, AJCN 2013

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## Carbohydrate Quality: How To Define Simply?

- Whole grain content
- Fiber content
- Glycemic response
- Food structure

The Whole Grain Kernel

- Endosperm (source of complex carbohydrates, starchy endosperm with protein)
- Bran (fiber, B vitamins, minerals, and phytochemicals)
- Germ (potential fats, amino acids, essential fatty acids, and trace minerals)

![Whole Grain Kernel](image)

![Glucose Levels](image)

Mozaffarian D. Curr Athero Reports 2005
Choosing Carbs: Best Rule of Thumb?

- Best way to choose healthy whole grains?
  - Industry-sponsored “whole grain stamp”
  - Three USDA definitions, each using the ingredients list
  - Carb to fiber ratio (AHA)

|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

- Best: Ratio of total carb to fiber
  - > 10:1 = Avoid
  - < 10:1 = A good choice (many options)
  - < 5:1 = A great choice (fewer options)

Mozaffarian RS et al, Public Health Nutr 2013

Ultraprocessed vs. Minimally Processed

Hall et al. Cell Metab 2019

Tufts Gerald I. and Dorothy R. Friedman School of Nutrition Science and Policy
Grains and Sugars: What's The Healthy Choice?

Diet quality alters energy expenditure

Calorie-controlled feeding study.
No changes in weight.
No changes in physical activity.

Ebbeling et al. JAMA 2012