

IS THERE A BEST DIET (DIETARY PATTERN) FOR PREVENTION OF CARDIOVASCULAR DISEASE ?

**Geeta Sikand, MA, RDN, FAND, CDE, CLS,
FNLA**

**Associate Clinical Professor of Medicine
(Cardiology)**

Director of Nutrition

**University of California Irvine Preventive
Cardiology Program**

Disclosures

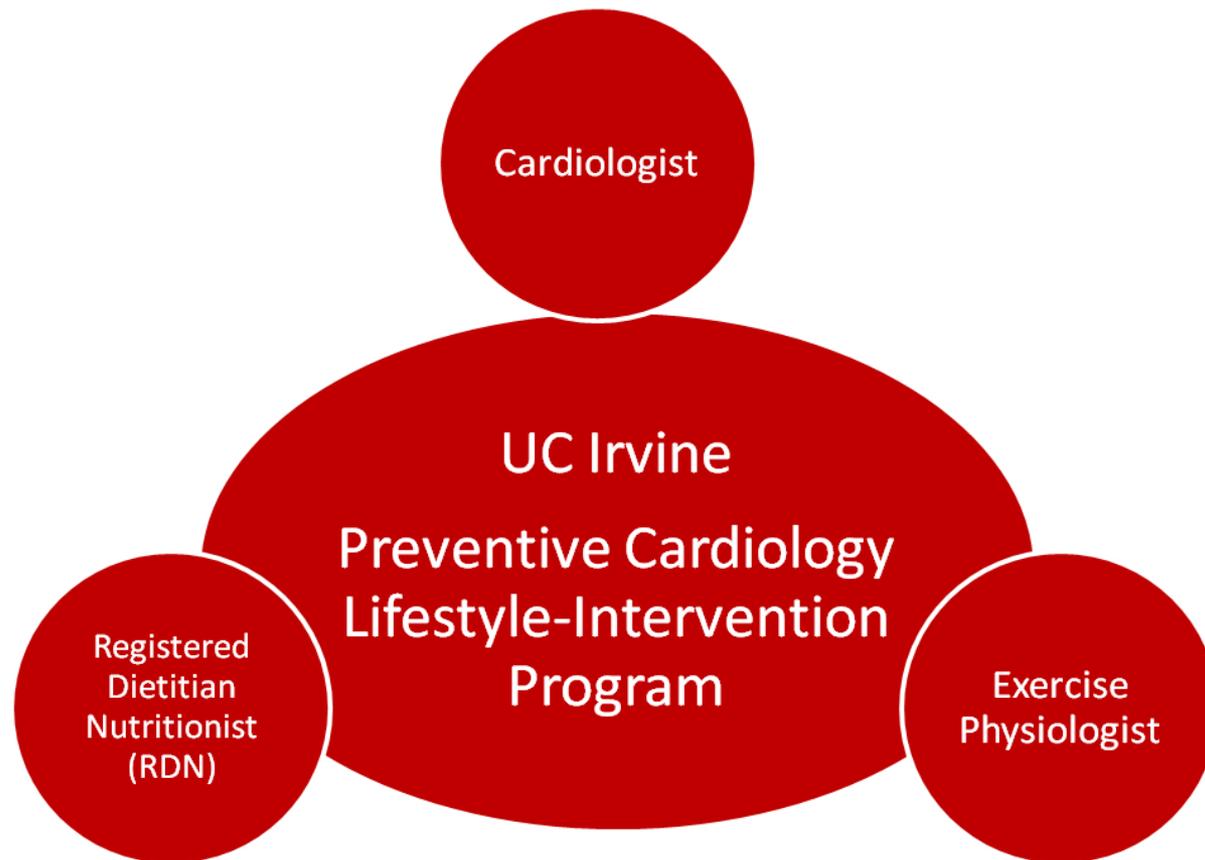
- No financial relationships to disclose



University of California Irvine

16-Week Preventive Cardiology Program

- 8 individualized visits with each discipline followed by monthly maintenance visits



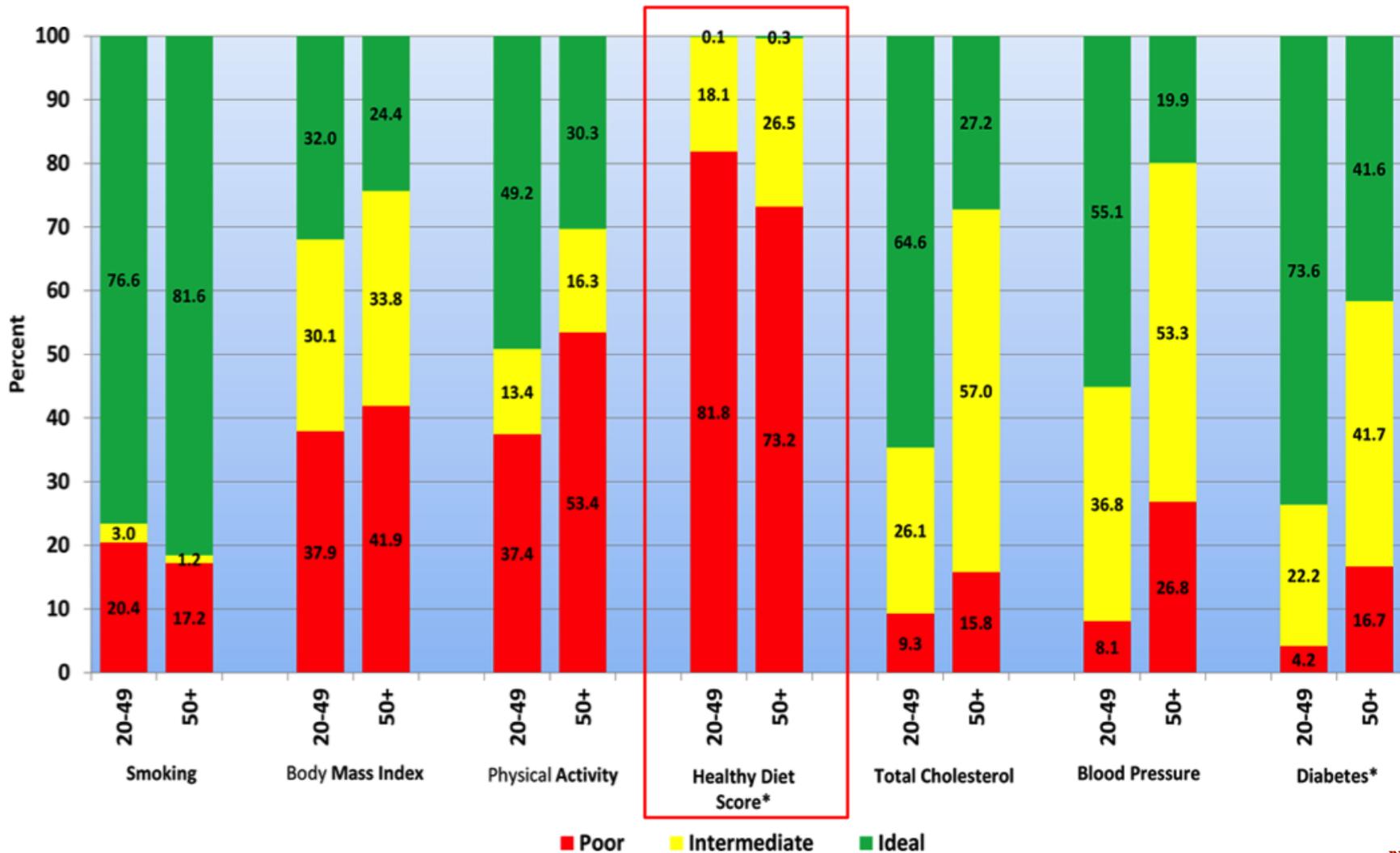
Objectives

- Describe evidence-based cardioprotective dietary patterns including Mediterranean (MED), Ketogenic (KETO) and Vegan.
- List recent 2019 AHA/ACC Nutrition Guidelines for atherosclerotic cardiovascular disease (ASCVD) prevention.
- Enumerate clinical and cost benefit of nutrition intervention by registered dietitians in the management of dyslipidemia and cardiometabolic risk factors.



AHA Heart & Stroke Statistics 2019

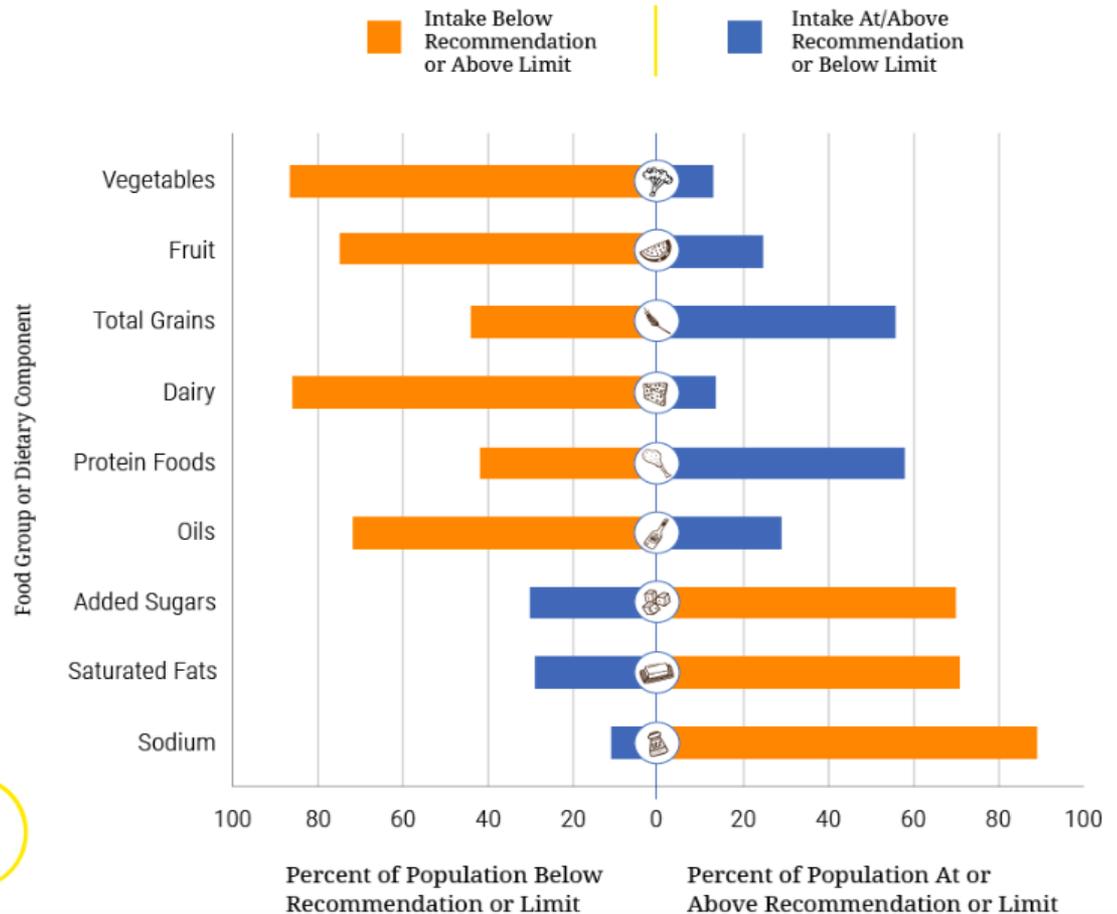
In the U.S. <1% of adults have an ideal Healthy Diet Score



DGAC 2015-2020: Typical American Diet

Intake is **below** recommendations in fruits and vegetables.

Intake is **above** recommendations for added sugars, saturated fats and sodium.



Rationale/Basis for Selecting a Cardioprotective Dietary Pattern

- RCTs: Each reduction of 1% in LDL-C or non-HDL-C is associated with 1% decrease in CHD event risk over 5 years.
- Weight loss of 5-8 kg if sustained, results in mean LDL-C reduction=5 mg/dL and an increase in HDL-C=2-3 mg/dL.
- A 3 kg weight loss reduces TG by 15 mg/dL.
- Diet and lifestyle patterns: also associated with non-traditional risk factors including markers of inflammation, insulin resistance, oxidative stress and thrombogenicity.



Which dietary pattern is best for Preventing CVD?

- DASH
- Mediterranean
- Vegetarian/Vegan
- Keto/Paleo/Atkins diet



AARP Study: Which Dietary Patterns are Effective for lowering CVD Risk & LDL-C?

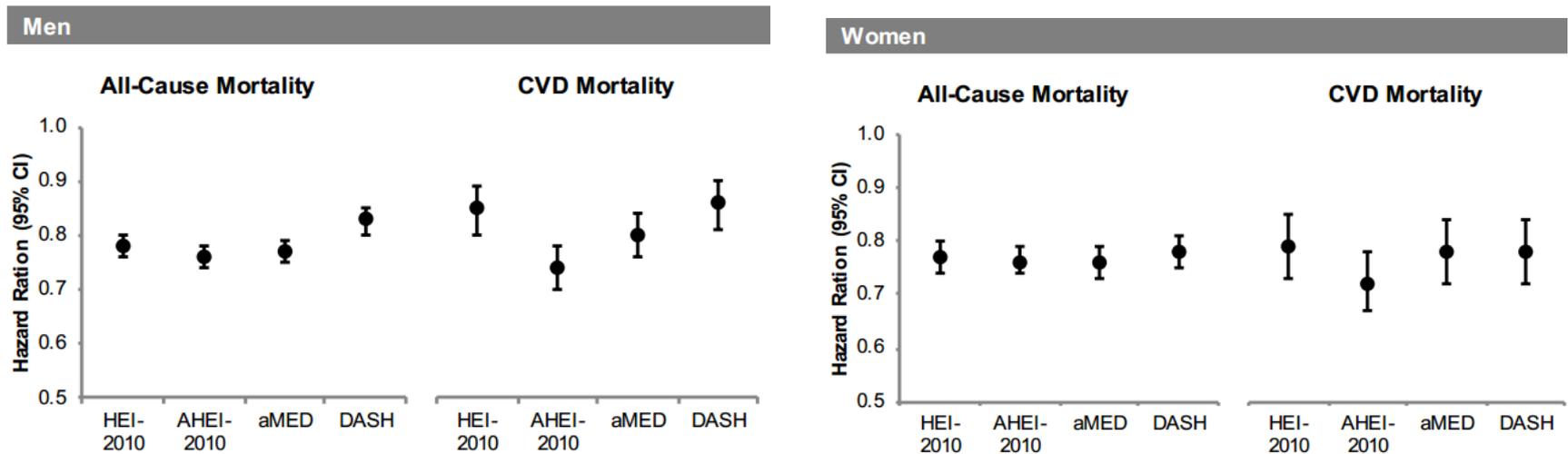
Examined >400,000 older men and women:

1. DASH (Dietary Approaches to Stop Hypertension)
2. Healthy Eating Index (HEI) (USDA diet)
3. Alternative Healthy Eating Index (AHEI) (AHA diet)
4. Mediterranean style dietary pattern

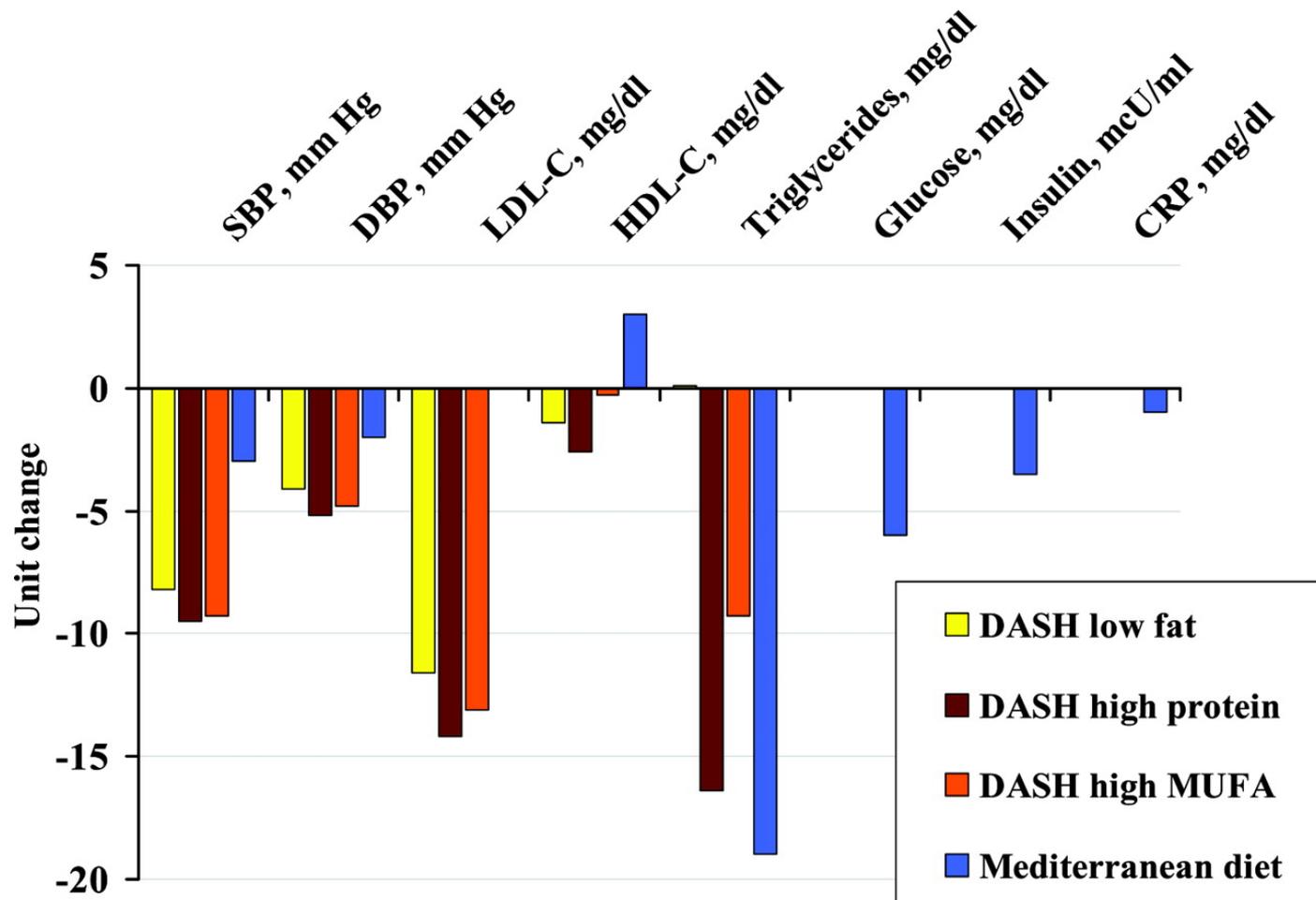
Conclusion: All whole foods dietary patterns are effective.



Evidence among men (n=242,321) and women (n=182,342)



Effects of Dietary Patterns on CVD risk factors in RCTs



Mozaffarian D et al. *Circulation*.
2011;123:2870-2891

Evidence-Based Cardioprotective Dietary Patterns

High intakes of

- Plants sources: fruits, vegetables, whole grain; legumes, nuts, and seeds
- Fish or seafood, lean meats, and non-fat or low-fat (1%) dairy products
- Plant-based oils in place of animal fats



Limit intake of

- High-fat red meat and high-fat dairy products
- Sweets, sugar-sweetened beverages



DASH and Mediterranean-style, HEI and AHEI dietary patterns



Womens' Health Study

Is a MED Diet associated with a lower risk of CVD events and if so, what are the underlying mechanisms?

- N=25,994 women
- Followed up to 12 years
- 40 Biomarkers evaluated
- –lipids, lipoproteins, apolipoproteins, inflammation markers, glucose metabolism, insulin resistance
- Data from Food Frequency Questionnaire categorized into three groups based on MED Diet adherence score: low, mid and highest.
- Primary Endpoints: MI, stroke, coronary artery revascularization, cardiovascular death.



Womens' Health Study

FINDINGS by MED Diet Adherence Score

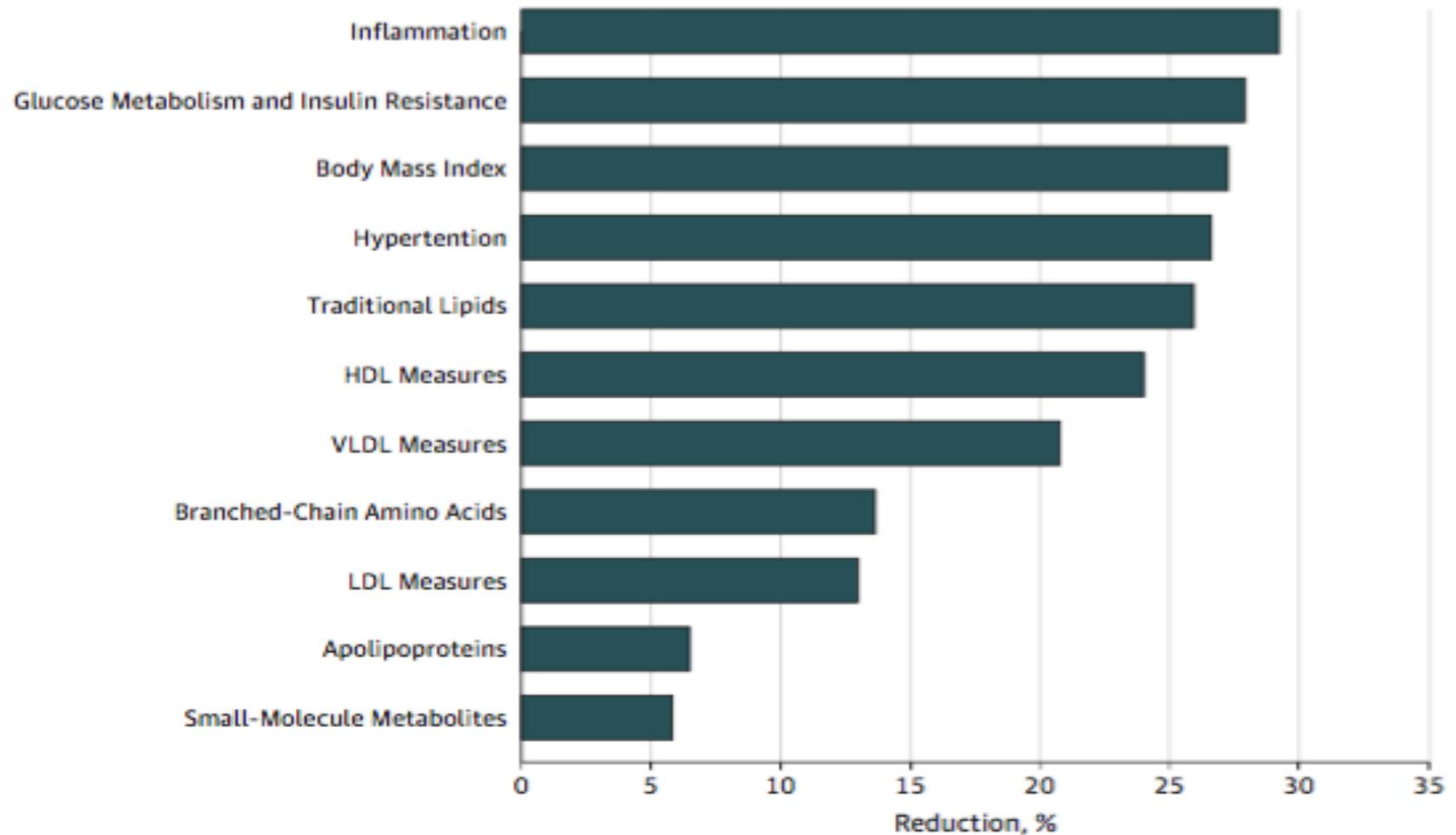
CVD risk reduction

- Middle diet adherence score 4-5: 0.77 (95% CI, 0.67-0.90) ***P* for trend < .001**
- Highest diet adherence score ≥ 6 : 0.72 (95% CI, 0.61-0.86) ***P* for trend < .001**
- Higher MED diet adherence was associated with **28% relative risk reduction in CVD events**
- Mechanisms: Improvement in Inflammation, glucose metabolism, insulin resistance and adiposity contributed most to these associations.



Womens' Health Study: % Reduction in CVD Events with MED Diet Explained by Potential Risk Mediators

Figure. Percentage Reduction in Cardiovascular Disease Events Associated With Mediterranean Diet Explained by Potential Risk Mediators



PREDIMED Study: Largest RCT to Assess the Effects of the MED Diet on CVD Prevention

- N=7447 Men/Women, ages 55-80 yrs. with T2DM or at least 3 major risk factors (no CVD).
- **Original study: Estruch, *New Engl J Med.* 2013.**
- **Retracted/Republished Estruch, *N Engl J Med.* 2018. (omitted 1588 participants)**

3 Groups (N=5859)

- 1. Mediterranean diet plus extra virgin olive oil.**
- 2. Mediterranean diet plus unsalted mixed nuts**
- 3. Control diet (reduced fat)**

- Median follow up ~4.8 years
- Adherence assessed by FFQ and biomarkers
- Both intervention groups also received more dietitian counseling.



Patient/Provider Scenario

Female, Age 50 yrs. BMI 36, T2D, high LDL-C,

My friend lost a bunch of weight on a very low carb diet like the keto diet. I would like to try the keto diet to lose weight.

What would you recommend?



2019 AHA/ACC Prevention Guidelines

Nutrition

- Encourage adults with **overweight or obesity** to seek comprehensive lifestyle counseling for achieving and maintaining weight loss including calorie restriction physically activity.
- Adults with **Type 2 diabetes**, and/or **high blood pressure**, should be counseled on lifestyle changes as a key part of their treatment plan.



Low Carb vs. High Carb diets

- Long term dietary patterns with low carb intake along with high animal derived fat/protein intake are associated with increased cardiac and non-cardiac mortality.
- High-carb diets (>70%) are also associated with a 23% increase in mortality rate.
- Optimal carb intake: 50% to 55% of energy intake.



2019 AHA/ACC Prevention Guidelines

Nutrition

Health care providers should **consider the “whole person.”**

- Share decision-making with patient—understand patients’ concerns so patient makes informed decisions.
- Use team-based care e.g. referring patients to specialists such as registered dietitians, psychologists and physical therapists.
- Understand psycho-social factors e.g. patients’ willingness/ability to change, health literacy, socioeconomic factors, culturally relevant lifestyle counseling and others.



Clinical and Cost Benefits of MNT by RDN for Management of Dyslipidemia

A systematic review and meta-analysis

J Clin Lipidol. 2018:12, 1113-1122

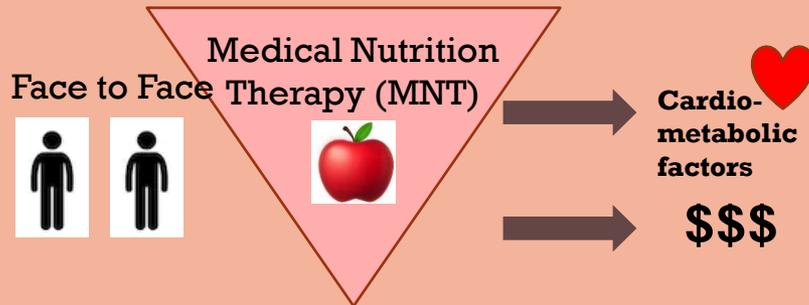
Authors

- **Geeta Sikand, MA, RDN, FAND, CDE, CLS, FNLA**
 - **Renee E. Cole, PhD, RDN**
 - **Deepa Handu, PhD, RDN**
- **Desiree deWaal, MS, RDN, FAND**
 - **Joanne Christaldi, PhD, RDN**
 - **Elvira Q. Johnson, MS, RDN**
- **Linda M. Arpino, MA, RDN, FAND**
 - **Shirley M. Ekvall, PhD, RDN**



Clinical and Cost Benefits of Medical Nutrition Therapy by Registered Dietitians for management of dyslipidemia: A systematic review and meta-analysis

METHODS



34 primary studies (N=5704)
*including 10 randomized control trials (n=25)

RESULTS

Total Chol (mg/dL):	-9.9	↑	HDL (mg/dL):	+1.6	
LDL (mg/dL):	-10.3		\$\$\$	QALY (years):	+0.75
Triglycerides (mg/dL)	-15.9		\$ saved/patient year	↓reduced meds:	+\$638
A1c (%):	-0.38		to +\$1456.00 per yr.		
glucose (mg/dL):	-0.53				
BMI (kg/m ²):	-0.39				

CONCLUSIONS: Evidence from this systematic review and meta-analysis demonstrates that multiple MNT sessions by an RDN are clinically effective and cost beneficial in patients with dyslipidemia and cardiometabolic risk factors.

Journal of
Clinical
Lipidology

Sikand G et al. J Clin Lipidol. ...(October 2018) 12, 1113–1122



Ketogenic Diets

Masood W, Uppaluri KR. Ketogenic Diet. [Updated 2019)

<https://www.ncbi.nlm.nih.gov/books/NBK499830/>

- Trendy: 100 yrs. old
- Treatment of epilepsy
- Goal: achieve state of ketosis
- All you can eat meat?



A Scientific Statement from the National Lipid Association. Review of Current Evidence & Clinical Recommendations on the Effects of Low-Carbohydrate and Very-Low-Carbohydrate (including Ketogenic) Diets for the Management of Body Weight and other Cardiometabolic Risk Factors. J Clin Lipidol. October 2019. (published ahead of print) www.lipid.org

Authors

C Kirkpatrick, PhD, RDN, CLS

J Bolick, MS, RDN, CLS

PM Kris-Etherton, PhD, RDN , CLS

G Sikand, MA, RDN, CLS

K Aspary, MD

D Soffer, MD

KE Willard, MD

K C Maki, PhD, CLS



Who might benefit from a Very-low carb (including ketogenic) diet?

- "People with overweight/obesity who also have diabetes or elevated triglycerides might benefit from following a very low-carb diet for two to six months."

Kirkpatrick 2019, Lean 2019, Bueno 2013, Sikand 1988



Points to Consider for Patients on a Low- and Very Low-Carb Diet

- A clinician-patient discussion regarding risks and benefits of the diet and the need for medical oversight should occur before initiation.
- Personal preference should be considered when selecting a weight loss diet.
- Limit the use of a very-low-carb diet to 2-6 months to induce weight loss.
- Conduct baseline and follow-up lipid and lipoprotein assessments.
- Monitor glycemic control and adjust diabetes medication(s) as needed.
- Monitor vitamin K-dependent anticoagulation tx.



THE KETOGENIC FOOD PYRAMID

Keto Meal Plan
Very Low CARB:
5-10%
(20-50 g/day)
Moderate Protein:
25-30%
•**High Fat:**
55-75%

Carbohydrates

Keep carbohydrates to a maximum of 5% of your total daily calorie intake. Making up of mostly green cruciferous vegetables. **Avoid all sugars, starches, grains, bread, pasta, fruits** (except avocado).

5%

Protein

Protein is essential for muscle retention and muscle building but **too much protein can keep you out of Ketosis**. Limit your protein intake to 25% of your daily calorie intake. Excellent sources of protein are: Fatty cuts of meat, eggs, full fat cheeses. Avoid milk, fat reduced chesses and creams.

25%

Fat

Fats will make up a dominant portion of a Ketogenic Diets macronutrients. When fat intake is high and carbs are low the body will resort to using fat as fuel through **Ketosis** (put simply). When possible your fat intake should come from **Saturated Fats** (Butter, Coconut Oil etc) & **Monounsaturated Fats** (Avocado, Macadamia Nuts etc). Ensure you get ample Omega-3's in your diet as well.

70%



Keto diets: Popularity/Potential Benefits

- Rapid weight loss
- Improved lipid profile
- ↓TG, ↑HDL (↓/ ↑LDL?)
- No calorie or fat gm counting
- “Decadent” food choices
- Decreased hunger
- LBM spared; BMR maintained
- ↓HbA1C, ↓BP
- ↓use/dose of diabetes medications



Keto Diets: Potential Concerns

- Rigid/not nutritionally adequate.
- Not aligned with nutrition recommendations from various professional organizations.
- May restrict foods associated with cardioprotective benefits.
- Difficult compliance (>6 months) with long term benefits unproven.
- May increase LDL-C in some individuals.
- May encourage foods high in saturated fats and dietary cholesterol that increase ASCVD risk.



Keto Diet: Contraindications

- Patients using SGLT2 inhibitors (increase risk of ketoacidosis).
- Patients with a history of high TG due to an increased risk of acute pancreatitis.
- Severe hypertriglyceridemia or inherited severe hypercholesterolemia.
- Liver, pancreas or kidney conditions



Keto Diets: Follow up Outcomes

- Short term data, small interventions
- Results have shown to be limited in time.
- Review of 24 RCTs of ketogenic vs low-fat diets (N = 2,946)
- Keto Diet: -0.9 –2.2 kg more than low-fat diets at 6 to 24 months follow up.
- Past 30 years: major problem to be resolved with keto diets is the maintenance of the large weight loss.
- Ongoing challenge of weight maintenance remains the Achilles heel and needs further research.



Patient/Provider Scenario: Vegan diet

Patient asks

Since I have heart disease and inflammation (high hsCRP), I want to go on a Vegan diet?

What are your thoughts?

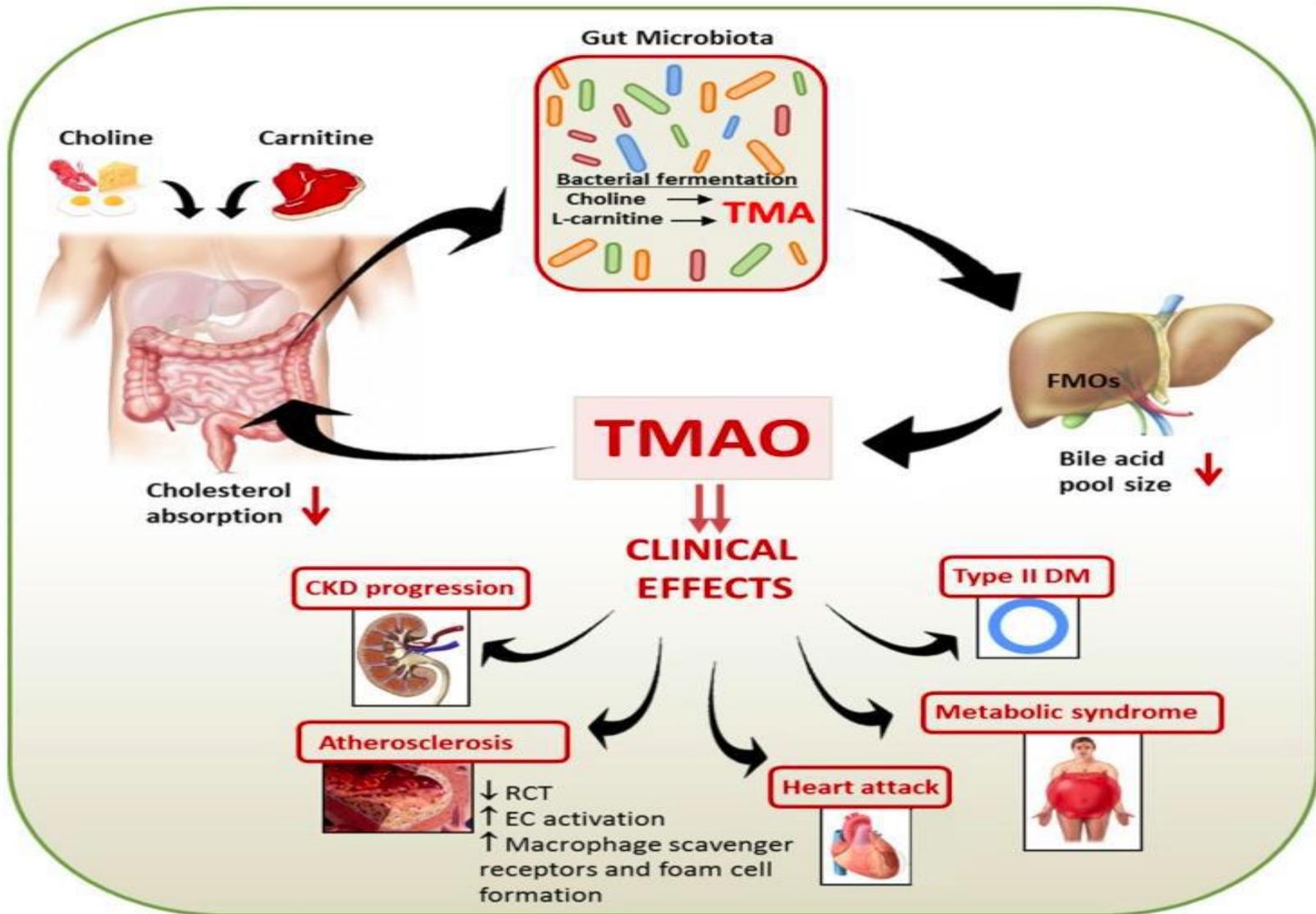


Role of Animal Products in Inflammation and Atherosclerosis



Trimethylamin N-Oxide (TMAO)

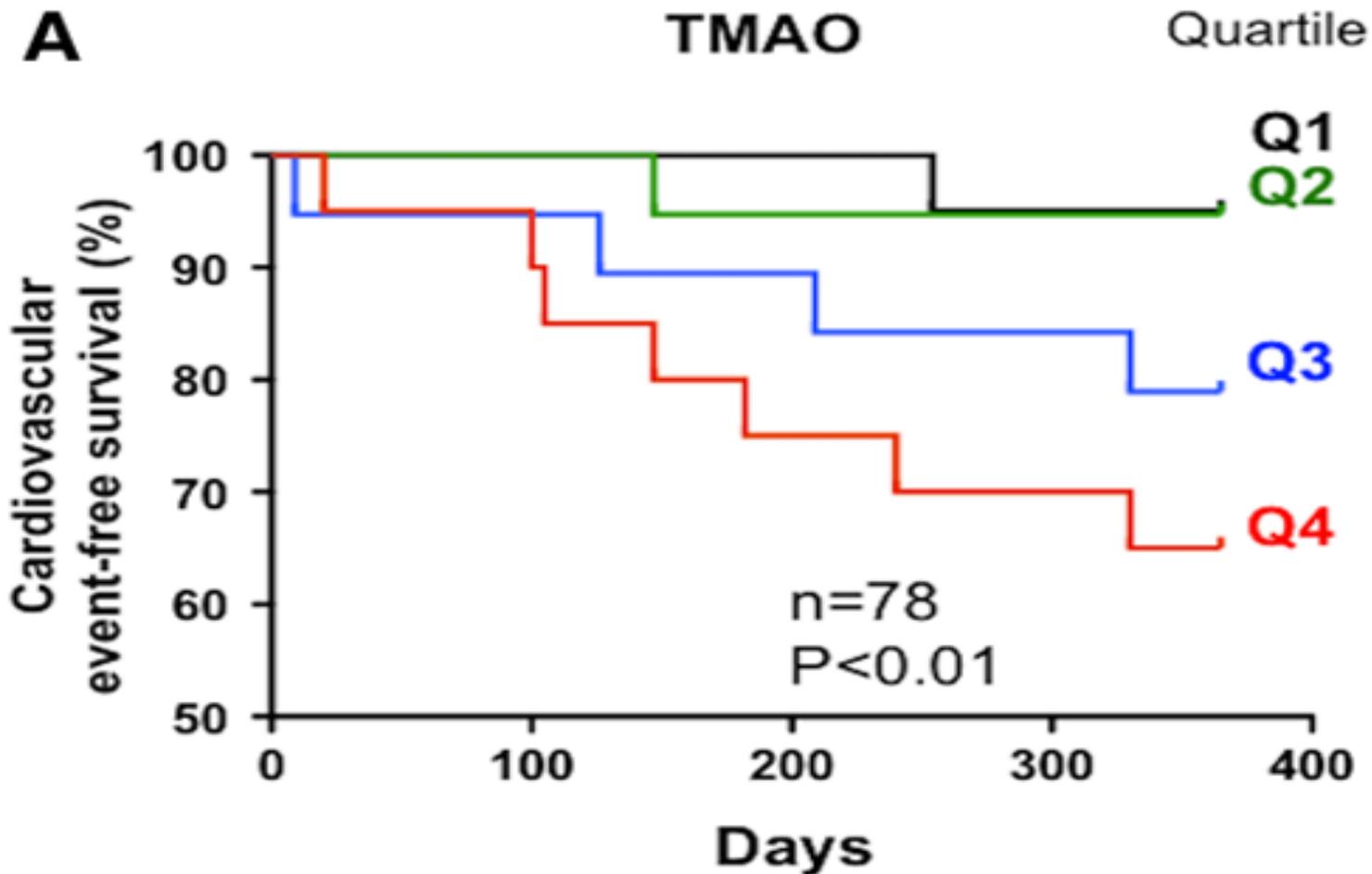
Velasquez MT et al. Toxins. 2016



Trimethylamin N-Oxide

(Haghikia A et al. *Arterioscler Thromb Biol.* 2018)

Prospective study (N=78) hx stroke, evaluated for MI, recurrent stroke & CV death



**Does Lowering
Inflammation Improve
Cardiovascular
Outcomes?**

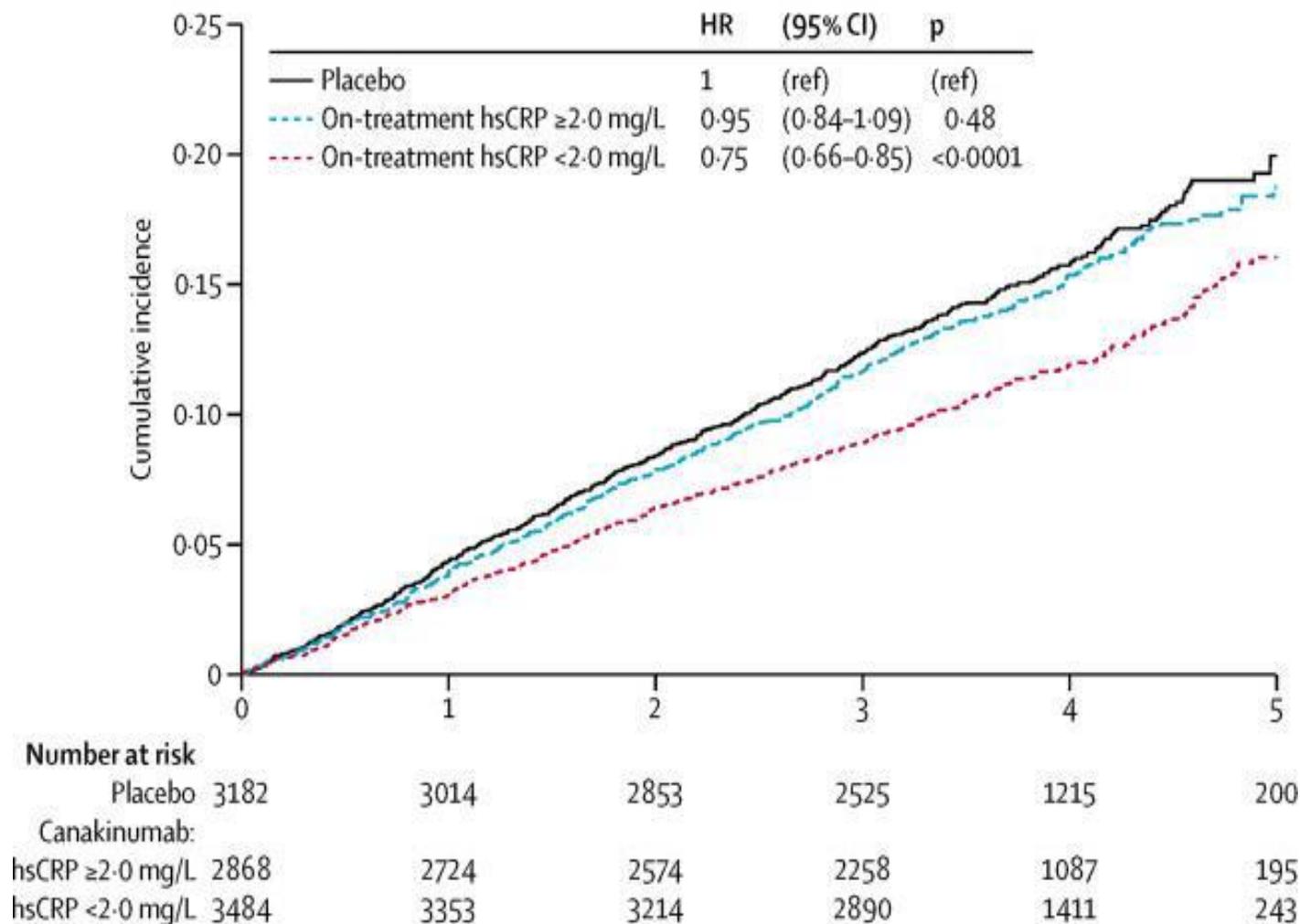


LDL Vs. Inflammation



Secondary Analysis from CANTOS

Magnitude of hsCRP reduction is associated with benefit



Nonfatal MI, nonfatal stroke, or cardiovascular death

Ridker PM, et al. *Lancet*. 2018



Limitations of Canakinumab

- Increased risk of fatal infections and leukopenia
- Subcutaneous injection every 3 months
- Annual cost is ~\$64 K per patient if used every 3 months



Prior Vegan Trials

Ornish D et al. JAMA. 1983

Ornish D et al. Lancet. 1990

Dod HS et al. AmJ Cardiol. 2010

Change in inflammatory biomarkers (n=23):

- CRP (mg/ml) Pre: 2.07 vs. Post: 1.6 (p=0.03)
- IL-6 (pg/ml) Pre: 2.53 vs. Post 1.24 (p=0.02)

Change in % diameter stenosis after-before intervention varied by diet adherence:

- Most adherence 1.25-1.61 (most benefit)
- Medium adherence 1.11 to 1.24
- Least adherence 0.7 to 1.07

Limitations:

- Vegan arm included multiple interventions provision of food, encouragement of exercise, stress management, yoga, meditation vs no intervention in control group.
- No lipid-lowering meds. during study period.



Effect of a Vegan versus AHA DiEt in Coronary Artery Disease (EVADE CAD Study)

- First rigorous RCT in US to evaluate the effects of a vegan diet vs. AHA recommended diet.
- Examined multiple parameters of inflammation, gluco-metabolic, and lipid profiles in patients with established CAD on guideline-directed medical therapy.

Shah B et al. JAHA. 2018



EVADe CAD Study

- Prospective blinded-endpoint study
- Patients (n=100) with angiography-defined CAD.
- Randomized to a Vegan diet vs. American Heart Association (AHA)-recommended diet.
- Both groups counseled to include nuts and unsaturated oils (olive oil used for all recipes).
- Both groups: same exposure to dietician, support, tools, groceries, etc. except substitution of animal-based protein for plant-based protein.



EVAADE CAD Study: Vegan Diet Arm

- Fresh plant foods (**Whole-Foods Plant-Based diet**)
- No processed foods
- No animal product of any kind, including meat, fish, eggs, cheese, and other dairy products



EVADE CAD Study: AHA-Recommended Diet Arm

- 7 servings of whole grain foods (5-10 g/day of soluble fiber)
- 5 servings of vegetables or nuts
- 4 servings of fruits
- 2 to 3 servings of fat-free or low-fat milk or milk products
- <5 ounces per day of lean meats or poultry or fish
- consumption of fish (esp oily fish) at least 2 x a week
- <7% intake of saturated fat, <1% intake of *trans* fat
- <200 mg of cholesterol
- <2300 mg of sodium
- Minimize intake of partially hydrogenated fats.



EVADe CAD Study Timeline

Participants who passed the screening were asked to:

- Return 7 to 10 days after PCI for **BASELINE** visit.
- Follow the diet they are randomized to for 8 weeks.
- Return at 4 weeks for an **INTERIM** visit.
- Return at 8 weeks for a **FINAL** visit.
- Twice weekly phone calls with dietitian to recall all food eaten in the past 24 hours, answer any questions regarding diet, and provide counseling where needed.



EVADE CAD study

Adherence to Diet

- **Withdrawals:**

2 subjects from the Vegan group withdrew from the study prior to the 4-week interim visit.

- **Adherence:**

	Vegan	AHA	P Value
Mid-point	96%	84%	0.09
Final	94%	74%	0.003

- **Low in AHA group due to portion control of animal protein.**



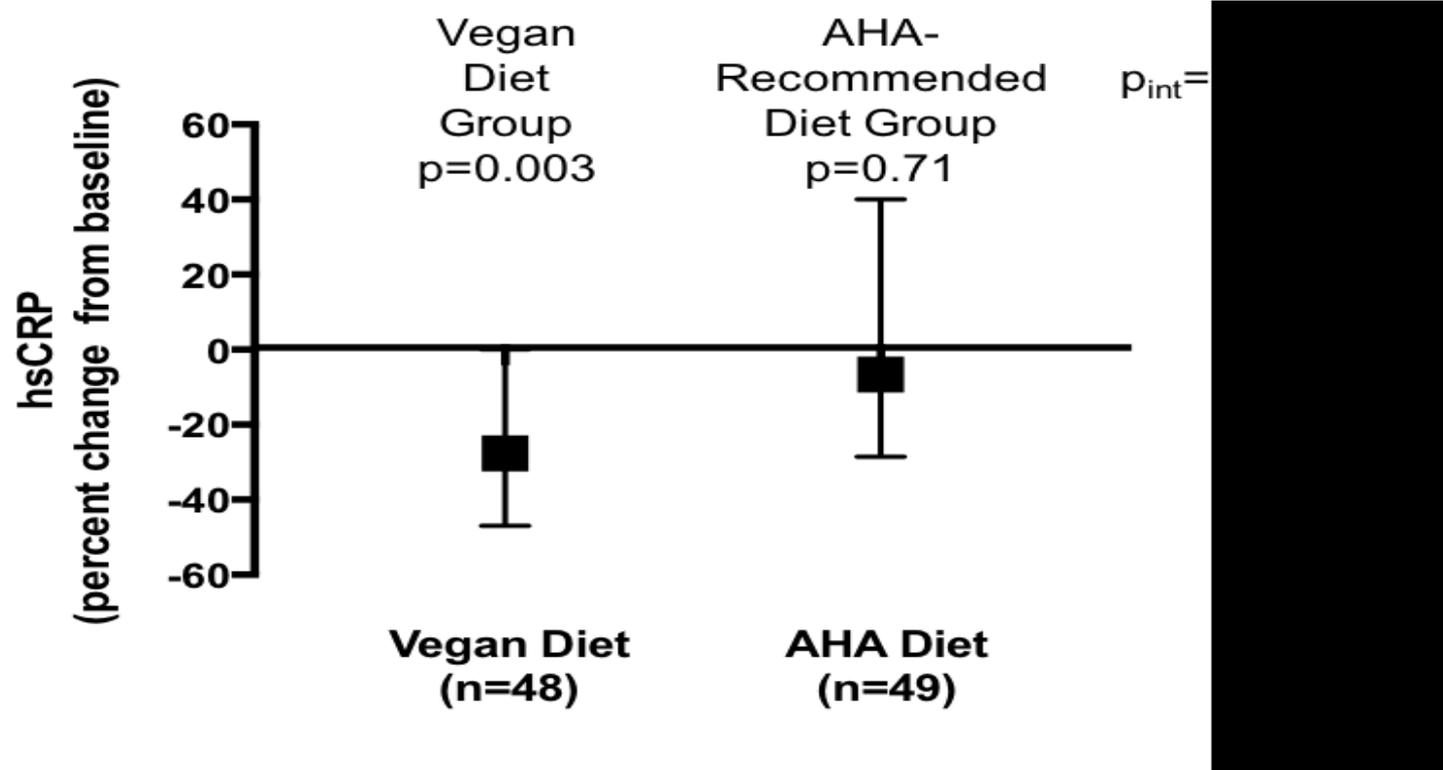
EVADe CAD study

Results: Primary Endpoint: hsCRP

Vegan diet group (n=48): -28% [-47,0]

AHA diet group (n=49): -7% [-29,+40]

Between groups P= 0.026



EVADE CAD Study Results

Secondary Endpoints

Anthropometrics, Glycemic status and Quality of Life

Both groups had significant weight loss (BMI and waist circumference), glycemic control and quality of life. No difference between diet groups.



Secondary Endpoints: Lipid Profile

AHA vs. Vegan diet

	Beta Estimate	95% CI	p-value
AHA-recommended diet	Reference diet	---	---
Vegan diet			
▪ Non-HDL cholesterol, mg/dL	0.92	0.84-1.00	0.05
▪ LDL-cholesterol, mg/dL	0.88	0.80-0.96	0.008
▪ LDL size, nm	1.00	0.99-1.00	0.40
▪ LDL-particle number, nmol/L	0.91	0.82-1.02	0.10
▪ Small LDL-particle number	1.17	0.96-1.42	0.12
▪ Oxidized LDL, U/L	0.92	0.82-1.03	0.13
▪ Triglycerides, mg/dL	1.06	0.94-1.21	0.35
▪ HDL-cholesterol, mg/dL	1.02	0.97-1.08	0.42
▪ HDL size, nm	0.99	0.96-1.01	0.23
▪ HDL-particle number, umol/L	1.07	1.02-1.13	0.01

Significance set at <0.0015

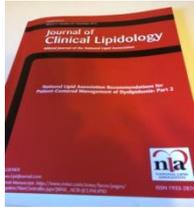


EVADE CAD Study: Conclusions/Limitations

- In patients with CAD and elevated hsCRP despite guideline-directed medical therapy, a vegan diet may be considered to further lower hsCRP.
- Both diet groups had significant weight loss, glycemic control and QOL. The Vegan diet does not appear to provide significant added benefit vs. the AHA- recommended diet in terms of weight loss, glycemic control, or lipid profile improvement (marginal LDL improvement).
- Results not generalizable: Only 14% of screened participants joined the study.



Predicting Reductions in LDL-C and Non-HDL-C



Diet low in saturated and trans fat and
dietary cholesterol: -5 to -10%

Loss of 5% of body weight: -3 to 5%

2 g /day plant sterols/stanols

or

7.5 g/day viscous fiber: -4 to -10%

Total reduction: -12 to -25%



2019 AHA/ACC Prevention Guidelines Nutrition Summary

Adults should eat a heart-healthy **dietary pattern**:

- Emphasize **plant-based foods** such as vegetables, fruits, legumes, nuts, whole grains, lean protein and fish.
- Limit foods high in **saturated fats and dietary cholesterol** (e.g. meat, organ meats, full-fat dairy products, eggs and tropical oils (coconut and palm oil)).
- Minimize trans fat, sodium (salt), processed meats, refined carbohydrates and sweetened beverages.
- If overweight, reduce 5-10% of body weight.
- Partner with a Registered Dietitian to personalize dietary patterns to patients' nutrition goals and to provide support and accountability.
- Include dietary adjuncts viscous fiber, plant sterols/stanols, soy, long chain omega-3 fatty acids.



Take Aways: Educate patients on how to separate fact from fiction

- –Do I have to become a vegan to lower my cholesterol?
- –Do I need to go on a keto diet to lose weight?

Most Importantly...

- Meet your patients where they are.....
- Be specific!
- Provide alternatives.
- Set short-term and long-term goals.
- Encourage working with a Registered Dietitian for accountability and support.



Thank You!

