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

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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.


▪ 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

Benjamin et al., Circulation. 2019 Mar 5;139(10):e56-e528.
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.

Arnett et al. ACC/AHA Primary Prevention Guidelines Circulation 2019
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

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.

Ahmed et al. Nutrition Obesity & Exercise Dec 2018
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

- Inflammation
- Glucose Metabolism and Insulin Resistance
- Body Mass Index
- Hypertension
- Traditional Lipids
- HDL Measures
- VLDL Measures
- Branched-Chain Amino Acids
- LDL Measures
- Apolipoproteins
- Small-Molecule Metabolites

Reduction, %
**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).

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.
Estruch 2018: Individuals following an energy-unrestricted Mediterranean diet PLUS extra-virgin olive oil OR nuts had lower rates of major CV events.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Mediterranean Diet</th>
<th>Control Diet</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted ITT analysis</td>
<td></td>
<td></td>
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<tr>
<td>Mediterranean diet with EVOO</td>
<td>96/2543</td>
<td>109/2450</td>
<td>0.70 (0.53–0.92)</td>
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<tr>
<td>Mediterranean diet with nuts</td>
<td>83/2454</td>
<td>109/2450</td>
<td>0.70 (0.53–0.94)</td>
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<tr>
<td>Adjusted ITT analysis</td>
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<tr>
<td>Mediterranean diet with EVOO</td>
<td>96/2543</td>
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<td>83/2454</td>
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<td>0.72 (0.54–0.95)</td>
</tr>
<tr>
<td>Excluding Site D and second household members (adjusted)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mediterranean diet with EVOO</td>
<td>77/2158</td>
<td>98/2138</td>
<td>0.66 (0.49–0.89)</td>
</tr>
<tr>
<td>Mediterranean diet with nuts</td>
<td>67/2109</td>
<td>98/2138</td>
<td>0.64 (0.47–0.88)</td>
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<tr>
<td>Excluding Sites D and B and second household members (adjusted)</td>
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<tr>
<td>Mediterranean diet with EVOO</td>
<td>73/1976</td>
<td>83/1906</td>
<td>0.71 (0.52–0.97)</td>
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<tr>
<td>Mediterranean diet with nuts</td>
<td>62/1977</td>
<td>83/1906</td>
<td>0.68 (0.49–0.95)</td>
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</tbody>
</table>
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?
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
Arnett et al. Circulation 2019
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

Medical Nutrition Therapy (MNT)

Cardio-metabolic factors

$\rightarrow$

34 primary studies (N=5704)
*including 10 randomized control trials (n=2526)

RESULTS

- Total Chol (mg/dL): -9.9
- LDL (mg/dL): -10.3
- Triglycerides (mg/dL): -15.9
- A1c (%): -0.38
- glucose (mg/dL): -0.53
- BMI (kg/m²): -0.39
- HDL (mg/dL): +1.6
- QALY (years): +0.75
- $ saved/patient year
- reduced meds: +$638 to +$1456.00 per yr.

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.

Ketogenic Diets

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

Authors
C Kirkpatrick, PhD, RDN, CLS
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G Sikand, MA, RDN, CLS
K Aspry, 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."

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.
Keto Meal Plan

Very Low CARB: 5-10% (20-50 g/day)

Moderate Protein: 25-30%

High Fat: 55-75%

THE KETOGENIC FOOD PYRAMID

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).

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 cheeses and creams.

Fat
Fats will make up a dominant portion of a Ketogenic Diet’s 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.
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
Prospective study (N=78) hx stroke, evaluated for MI, recurrent stroke & CV death
Does Lowering Inflammation Improve Cardiovascular Outcomes?
LDL Vs. Inflammation

LDL alone

LDL + 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
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.

Shah B et al. JAHA. 2018
EVADE 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:

<table>
<thead>
<tr>
<th></th>
<th>Vegan</th>
<th>AHA</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-point</td>
<td>96%</td>
<td>84%</td>
<td>0.09</td>
</tr>
<tr>
<td>Final</td>
<td>94%</td>
<td>74%</td>
<td>0.003</td>
</tr>
</tbody>
</table>

- 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.

Shah B et al. JAHA. 2018
# Secondary Endpoints: Lipid Profile

## AHA vs. Vegan diet

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

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%
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!