Just What the Doctor Ordered: Food as Therapy
Culinary Labs

Learning Objectives:

- Learn nutrition strategies and simple culinary skills to promote easy, quick, and affordable healthy cooking styles for self, future patients and the community;
- Identify healthy cooking approaches that are also culturally appropriate and budget friendly for cost conscious individuals & families;
- Identify the evidence based information to support identification of the healthiest overall dietary patterns, including but not limited to healthiest macronutrients (carbohydrates, fats, proteins);
- Understand how to plan menus, including portion size and life cycle concerns
- Understand the concept of dietary patterns and not individual nutrients in relation to risk for chronic disease and optimal health
- Clarify current nutrition controversies versus core, agreed upon concepts
- Recognize the importance of acting as a team leader or group member as necessary to facilitate optimal learning experiences

Format:

- Each culinary lab will begin with a brief introduction to identify the underlying nutrition concepts of the class
- Each culinary lab will identify core culinary skills incorporated into the lab’s lesson plans. Students will have the opportunity to watch very short pod-casts of the key culinary skills prior to starting the lab
- Labs’ intent is not to just provide ‘recipes’ but lifelong culinary skills and core nutrition concepts
- Students will participate in designated small groups and each group focuses on preparation of specific foods
- Time allowed to taste all food preparations and discuss the lab’s underlying nutrition concepts and practiced culinary skills
Lesson 1:

Culinary Skills/Techniques demonstrated today:
- cutting skills: slicing, chopping, mincing
- Roasting to enhance flavor: roasted vegetables
- Flavor enhancer: sweating vegetables
- How to cook beans (legumes), specifically lentils

Technique: How to slice, dice and mince vegetables


video link is also on the above page: (1 minute 54 sec)


How to ‘sweat’ vegetables:

https://www.youtube.com/watch?v=HukuAHtG5Mg

How to soak dry beans: (less than a minute)

http://www.marthastewart.com/967789/how-cook#973725

Excellent videos related to lentils:

http://www.lentils.ca/recipes-cooking/cooking-techniques/

How to roast vegetables:

Nutrition Concepts:

- Dietary patterns are an independent risk factor for many of today’s chronic diseases as demonstrated by RCT and epidemiologic studies
  - What is a Dietary Pattern?
  - Common Dietary Patterns include:
    - Western Diet – high processed foods, sugars, fats, fast foods, low dietary fiber
    - Prudent Diet- focus away from processed foods towards increased minimally processed foods in all food groups
    - Mediterranean Diet
      - Represents no one singular ‘diet’ or food plan but rather a style of eating. Generally higher intakes of total fat from unsaturated fats such as olive oil, fruits, vegetables, legumes, seeds, nuts/dairy such as yogurt, reduced amounts of animal based proteins, wine regularly
    - DASH (Dietary Approaches to Stop Hypertension)
      - Specified focus on whole grains, fruits, vegetables, low or fat free milk and dairy, nuts/seeds/legumes, 2-3 teaspoons of healthy fats daily, limited sweets and sugars
  - Nutrition Education messaging for Heart Health includes
    - Fat- quality & quantity; ↑soluble fiber; 2 g plant stanols & sterols ↓ plasma cholesterol; isoflavones-soy; sodium
Dietary Fiber- Basics and Metabolic Benefits

Beans (legumes) are an excellent source of total & SOLUBLE dietary fiber!

(Recommendation for 14g total fiber/1,000 kcal)

**Dietary Fiber definition:** non-digestible carbohydrate components of plants. These are not enzymatically digested to absorbable units; Includes non-digestible fibers and lignin, (*technically lignin is not a carbohydrate, but a complex polymer*)

- Examples: cellulose, pectin, lignin, gums, b-glucans, fructans, psyllium, resistant starches and resistant dextrins;

**Functional Fiber definition:** non-digestible carbohydrates which have been isolated, extracted or synthesized

**Classifications:** By solubility in water and ability to form viscous solutions

- **Insoluble:** lignin, cellulose, hemicellulose; high water absorption; MORE efficient at normalizing defecation (wheat/corn bran, avocado, banana, green beans, celery, potato skins, nuts, seeds, zucchini)
- **Soluble:** psyllium, b-glucans, pectins, fructans, hemicellulose, gums; they are FERMENTABLE in large intestine-forming short chain fatty acids (SCFA- acetate, propionate, butyrate) (legumes, oats, barley, prunes, berries, plums, broccoli, root vegetables, pears, eggplants)

**Metabolic benefits of soluble fiber (and hence beans of all types):**

- ↑ viscosity of a meal, thus delaying the gastric emptying time
- Delayed gastric emptying time, slows the rate of appearance into plasma
- Beneficial to glucose control and postprandial glucose levels (Anderson, 1979)
- Traps bile acids and dietary cholesterol for removal in feces, thus lowering plasma lipids
- Dietary fiber INDEPENDENTLY of dietary fat ↓ risk of CHD, Rimm, 1996
- Inverse relationship between dietary fiber (both types) and CHD
- 1998: FDA health claim: ‘viscous fibers are cholesterol lowering agents. Efficacy needs at least 3-7 grams of viscous fiber for benefit
- Production of SCFA- modulates intestinal microbiome (both types of fiber do this)
- Inverse relationship between fiber (all types) and inflammatory markers; Kuo, 2013
Sources of Dietary Fiber

**Soluble Fiber**
(e.g. pectins, gums)
- Oats, rye, barley
- Legumes
  - Beans, peas, soybeans
- Some fruits + fruit juices
  - Prune juice, plums, berries insides of apples + pears
- Some vegetables
  - Broccoli, carrots, artichoke
- Some root vegetables
  - Sweet potatoes, onions (skins are sources of insoluble fiber)

**Insoluble Fiber**
(e.g. cellulose, lignin)
- Wheat + corn bran
- Nuts and seeds
- Potato skins
- Some fruits
  - Avocado, bananas
- Some vegetables
  - Green beans, cauliflower, zucchini, celery

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**Table 2. Dietary fiber content of commonly consumed fruits, vegetables, grains, and other foods**

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving size</th>
<th>Total dietary fiber (g/serving)</th>
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<tbody>
<tr>
<td>Fruits</td>
<td></td>
<td></td>
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<tr>
<td>Prunes, dried</td>
<td>5 prunes</td>
<td>3.0</td>
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<tr>
<td>Orange</td>
<td>1 orange</td>
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<tr>
<td>Apple, large with skin</td>
<td>1 banana</td>
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<tr>
<td>Banana</td>
<td>1 banana</td>
<td>0.9</td>
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<tr>
<td>Radishes</td>
<td>1 miniature box (14 g)</td>
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<tr>
<td>Figs, dried</td>
<td>2 figs</td>
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<tr>
<td>Pear</td>
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<td>0.0</td>
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<tr>
<td>Peaches, canned</td>
<td>1/2 c</td>
<td>1.3</td>
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<tr>
<td>Strawberries, raw</td>
<td>1 c, sliced</td>
<td>3.9</td>
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<tr>
<td>Vegetables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beans, kidney, canned</td>
<td>1/2 c</td>
<td>4.9</td>
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<tr>
<td>Peas, split, cooked</td>
<td>1/2 c</td>
<td>8.1</td>
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<tr>
<td>Lentils, cooked</td>
<td>1/2 c</td>
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<td>Lettuce, iceberg</td>
<td>1 c, shredded</td>
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<td>Brussels sprouts</td>
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<td>Spinach, cooked</td>
<td>1/2 c</td>
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<td>Carrots, raw</td>
<td>1/2 c</td>
<td>1.8</td>
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<tr>
<td>Potatoes, boiled</td>
<td>1/2 c</td>
<td>1.6</td>
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<tr>
<td>Broccoli, raw</td>
<td>1/2 c</td>
<td>1.3</td>
</tr>
<tr>
<td>Celery, raw</td>
<td>1/2 c</td>
<td>1.0</td>
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<tr>
<td>Grains</td>
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<td></td>
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<tr>
<td>Wheat bran flakes</td>
<td>1/2 c</td>
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<tr>
<td>Raisin bran</td>
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<td>3.0</td>
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<td>Rye crispbread</td>
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<td>Other</td>
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<td></td>
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<td>Apple pie</td>
<td>1 piece</td>
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<td>Nuts, mixed, dry roast</td>
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<tr>
<td>Chocolate cake</td>
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<tr>
<td>Yellow cake</td>
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</table>
Group 1 - Black Eyed Beans (BEB)

Equipment:
√ Burner
√ Pot for beans
√ Strainer
√ Whisk
√ Small bowl for making vinaigrette, large bowl for salad
√ Cutting board
√ Knife for chopping vegetables

Pre-measured:
1/3 cup Balsamic Vinegar
1 tablespoon hot, sweet mustard
1 teaspoon creole seasoning
¼ cup extra virgin olive oil
Small bowl – 10 oz. frozen corn
¼ cup parsley fresh
1 bell pepper
1 red onion
3 stalks celery

Step 1:
Cooking of beans

√ Use 1 # bag of BEB
√ Put beans in a strainer
√ Rinse beans thoroughly in cold water
√ Check for tiny pebbles, remove
√ Add 4 cups cold water to pan, bring to a boil
√ Slowly (carefully) add 1 # beans
√ Phone timer for 23 minutes
√ At 23 minutes, take out 1 teaspoon of beans to test for doneness. Should be tender, not mushy.
√ Drain, rinse in cold water

Corn & Black Eyed Pea Salad
Source: Come on In!
Jr. League Jackson, Mississippi
Group 1

Step 2 & 3:

While beans are cooking, first read entire recipe! Then share these 2 tasks:

Task for student #1:

*Make vinaigrette:* Mix 1/3 cup Balsamic Vinegar
1 tablespoon hot, sweet mustard
1 teaspoon creole seasoning
1/4 cup extra virgin olive oil
1/4 cup chopped parsley
Whisk (briskly stir) together

Task for students #2 & 3:

*Chop*

1 green bell pepper – slice in half, remove seeds, slice in strips lengthwise.
  Slice cross wise into evenly chopped pieces.
1 medium red onion - watch podcast – chopping techniques
3 stalks of celery – slice thinly and evenly

When beans are cooked and drained give half of beans to Group 3.

**Final assembly**

✓ Place dressing in bottom of large bowl
✓ Use 1/2 of total reconstituted beans. (Give other half of cooked beans to group 3.)
✓ Add corn, 1/2 amount of beans, bell pepper, onion, celery to bowl
✓ Mix together
✓ Chill & enjoy!
Group 1 - Fresh Corn and Black Eyed (BEB Beans) Pea Salad

1/3 cup balsamic vinegar
1 tablespoon hot, sweet mustard
1/4 cup chopped, fresh parsley
1 teaspoon creole seasoning
1/4 cup extra virgin olive oil
1 - 10 oz. package frozen corn or 3 ears corn cooked
1/2 pound black eyed peas – (cooked beans)
1 medium green bell pepper, chopped
1 medium red onion, chopped
3 stalks celery, chopped

Source: Come on in!
Jr. League Jackson, Mississippi

Make the vinaigrette: mix vinegar, parsley, mustard, creole seasoning. Add oil. Stir.
Set aside in bottom of large bowl.

Combine corn, beans, bell pepper, onion, celery.

Add vegetables and beans to bowl

Toss dressing to vegetables and refrigerate until ready to serve.
Group 2 - Lentil Mason Jar Salad

Equipment:

√ Burner
√ Strainer
√ Whisk
√ Small bowl for making vinaigrette, large bowl for salad
√ Cutting board
√ Knife for chopping vegetables
√ Large liquid measuring cup

Premeasure:

1/3 cup rice wine vinegar  2 cups spinach
1 tablespoon honey          5 cups brown rice
1 teaspoon dijon mustard   Bowl for carrots
3 tablespoons olive oil    Bowl for cabbage
1/4 teaspoon salt & pepper Bowl for beans
10 teaspoons sesame seeds  Bowl for spinach

Step 1: Read entire recipe

Step 2:

√ Cook beans

√ Use _2 cup lentils
√ Put beans in a strainer
√ Rinse beans thoroughly in cold water
√ Check for tiny pebbles, remove
√ Add ___6_ cups cold water to pan, add lentils and bring to a boil
√ Set phone timer to ___15__ minutes (check at 12 minutes) Beans
√ When timer is ready, take out 1 teaspoon of beans to test for doneness, should be tender, not mushy.
√ Drain, rinse in cold water.
√ Cooked beans will be safely kept for 4 days in refrigerator.
Step 2 & 3:

While beans are cooking, first read entire recipe! Then share these 2 tasks:

Student #1 task:

*Make vinaigrette:* 2/3 cup rice wine vinaigrette
2 tablespoons honey
2 teaspoons dijon mustard
6 tablespoons extra virgin olive oil
Mix and place in a liquid measuring cup

*Salad:* ✓ Slice 2 cups raw spinach, place in bowl
 ✓ Using food processor, add 1 # carrots and pulse till carrots are shredded
 ✓ Remove from processor and measure 2 1/2 cups of carrots and place in small bowl
 ✓ Repeat above process with 1/2 of a small red cabbage
 ✓ Set up all bowls in a row to create Mason Jar Salads

- Set up the 8 Ball Jars
- Equally divide vinaigrette and add to the eight jars
- Set up bowls in any order: carrots, brown rice, red cabbage, lentils, spinach, seeds
- Distribute the ingredients evenly among the jars, in any order but seeds should be on top. You may choose how much of each ingredients to add, per your own preference. Do not shake or mix lentils jar salad until ready to serve to avoid getting soggy.
- Seal lid and eat within 4-5 days
- Refrigerate till ready to take home
Rainbow Lentil Mason Jar Salad – Group 2

Dressing:  

Source: Canadian Lentils

1/3 cup rice wine vinegar  
1 tablespoon honey  
1 teaspoon dijon or whole grain mustard  
3 tablespoons canola oil  
To taste, salt and ground black pepper

Salad:

1 ¼ cups thinly sliced carrots  
2 ½ cups cooked brown rice  
1 ¼ cups thinly sliced red cabbage  
2 ½ cups cooked green lentils or any type of cooked beans  
2 ½ cups thinly sliced kale, stem removed (use spinach)  
¾ cup toasted almonds (optional) (use sunflower seeds)

Line up five clean, 500 ml, wide mouth mason jars with fitted lids. For the dressing: whisk all dressing ingredients together and pour evenly into the mason jars.

For the salad: distribute the ingredients evenly amongst the five jars, starting with carrots and finishing with almonds, creating beautiful layers. Seal and refrigerate until you’re ready to eat within 4-5 days.

Keep dressing at the bottom, with denser salad vegetables to keep other items crisp and to avoid sogginess.
Group 3 - Black Eyed Bean Stew

Equipment:

✓ Burner
✓ Pot for stew
✓ Cutting board
✓ Knife
✓ Bowl for spinach, onion, carrots
✓ Garlic and garlic press

Pre Measured:

2 tablespoons olive oil
1/4 teaspoon salt
1/4 teaspoon pepper
1/4 teaspoon crushed red pepper
2 teaspoons fresh rosemary chopped

Step 1: Read the entire recipe before starting

Step 2:
✓ Slice 4 cups of spinach and put in bowl
✓ Peel, chop 1 small onion (see podcast)
✓ Slice carrots evenly in 1/2 inch pieces
✓ 3 ribs of celery - slice into 1/4 inch pieces
✓ 3 cups cooked beans from other group

Step 3:

Sweat the vegetables

✓ In large pan add all vegetables and 1/4 cup liquid. Cook over low to medium heat in a 10-12 inch saute pan. Do not cover pan and slowly cook.
✓ When vegetables start to soften 5-6 minutes, add crushed garlic. (Peel garlic, put in garlic press)
✓ Add 2 cups water, beans, rosemary, seasonings, bring to a boil but immediately reduce heat to low and simmer about 10-15 minutes till vegetables are tender. Add spinach, stir and serve.
White Bean (Use Black Eyed Peas) Stew  
with Rosemary and Spinach

Premeasured:

2 teaspoons extra virgin olive oil
1 yellow onion, peeled and chopped
2 cloves garlic, peeled and chopped
4 carrots, rinsed well, halved and sliced into ½ -inch slices
3 ribs of celery, rinsed well, halved and lengthwise and sliced into ¼-inch pieces
3 (15 oz) cans low-sodium cannellini beans, drained and rinsed  
   (or 3 cups cooked black eyed peas)
2 teaspoons chopped fresh rosemary
¼ teaspoon kosher salt
¼ teaspoon freshly ground black pepper
¼ teaspoon crushed red pepper flakes
4 cups fresh spinach leaves

In a large pot, heat the olive oil over medium-high heat. Add the onion and cook 5-6 minutes, stirring often, until beginning to soften. Add the garlic, carrots, and celery and continue to cook, 6 minutes more, stirring occasionally, until just a small amount of crispness remains. Do not overcook at this point.

Add 2 cups of water plus the beans, rosemary, salt, black pepper, and red pepper flakes. Heat to a boil. Reduce heat to medium and simmer, uncovered, for 12-15 minutes until the vegetables are tender.

Remove from heat, and stir in the spinach, which will wilt within seconds. Divide among bowls and serve.
Roasted Vegetables

1. Each red, yellow and orange bell pepper
2. Zucchini
3. Red onions

Prepare:
- ✔ Cube the onion(s)
- ✔ Slice zucchini evenly
- ✔ Cut bell pepper into strips

Mix:
- ¼ cup olive oil
- ½ cup Balsamic Vinegar
- 2 teaspoons herbs de province

Pour mixture over vegetables and toss to coat
Preheat oven to 400°
Place veggies on a cookie sheet with 1” sides or a roasting pan
Cook uncovered ~ 40 minutes until tender
Stir once at midway through cooking

Serves 7-8

May be stored for 5 days in refrigerator
- ~ 15% loss after cleaning (before cooking)
- @ 100 gram serving size, per 1 pound of vegetables is equal to ~ 4.8 servings
  Cost: varies per vegetable chosen but ~ 0.47¢/serving
- Use any vegetable – but cut evenly
How to Slice, Dice and Mince Onions: A Step-by-Step Guide

Mince the Onion
Mincing onions is basically chopping onions as finely as you can. Start with diced onions. Then, lay one hand flat across the tip of your knife and use a rocking motion to chop. Keep going until the onions reach an evenly sized fine dice.

Finished Minced Onions
Minced onions can add zip to burgers, meatloaf, salad dressings or dips. Rinsing minced onions with cold water makes them less potent.

Sliced, Diced and Minced Onions
Mastering this skill will make cooking easier and faster — no matter how you slice or dice it. Watch our how-to video (/videos/onion-hows-0154927.html) for more.

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USA most well-known legume varieties available.

Below you will find some of the most well-known legume varieties available.

Legumes are one of the most healthy and wise food choices today, both from the nutritional and culinary standpoint.
Legume Chef: USA most well-known legume varieties available.

- Lentil Crimson Decorticated
- Lentil Eston
- Lentil French Green
- Lentil Pardina
- Lentil Regular
- Lentil Red Chief Decorticated
- Lentil Richlea
- Lentil Large Green
- Pea Yellow Split
- Pea Austrian Winter
- Pea Whole Green
- Pea Green Split
- Pea Marrowfat
- Pea Whole Yellow
Beans for Powerful Nutrition!

Beans add nutrition and flavor to any meal. Follow the directions below for cooking and storing beans.

-1- Examine the beans and throw away any foreign particles or beans that are discolored or shriveled.

-2- Rinse the beans with water and then drain the water. Put the beans in a large pot and add fresh water to cover the beans.

-3- Heat the beans and water to boiling, then, turn the heat down to LOW and cover the pot. Since beans soak up water, you may need to add more water during cooking.

-4- Add seasonings to the beans while they cook. However, if you add salt, do so only after the beans are cooked, because salt toughens beans.

-5- When the cooked beans are soft, they are ready to eat.

### Suggested Cooking Times

<table>
<thead>
<tr>
<th>Bean Type (1 cup / 230 g)</th>
<th>Water for Cooking</th>
<th>Cooking Time</th>
</tr>
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<tbody>
<tr>
<td>Kidney</td>
<td>3 cups (710 mL)</td>
<td>2.0 hours</td>
</tr>
<tr>
<td>Black-eyed Peas / Cowpeas</td>
<td>2 1/2 cups (590 mL)</td>
<td>0.5 hours</td>
</tr>
<tr>
<td>Pinto</td>
<td>2 1/2 cups (590 mL)</td>
<td>0.5 hours</td>
</tr>
<tr>
<td>Navy</td>
<td>3 cups (710 mL)</td>
<td>2.0 hours</td>
</tr>
<tr>
<td>Black</td>
<td>2 1/2 cups (590 mL)</td>
<td>0.5 hours</td>
</tr>
<tr>
<td>Great Northern</td>
<td>3 cups (710 mL)</td>
<td>2.0 hours</td>
</tr>
<tr>
<td>Lima</td>
<td>3 cups (710 mL)</td>
<td>2.0 hours</td>
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</tbody>
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### Storage Directions

- Uncooked, dry beans should be stored in a tightly sealed container and kept in a dry area. Beans can be stored for up to one year for maximum flavor. While storage time does not affect nutrient value, beans may require longer cook times as they age.
- Cooked beans, if chilled, will keep for up to five days, in a covered container. Do not store beans in their original cooking pot! After cooking, place leftover beans in tightly covered containers, to allow for proper cooling and storage.

Eat More Beans for Health!

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US DRY BEAN Council
# Nutrient Profile

**Cooked Dry Beans: 1 Cup**

<table>
<thead>
<tr>
<th>Bean Type</th>
<th>Baby Lima</th>
<th>Black</th>
<th>Blackeye</th>
<th>Cranberry</th>
<th>Garbanzo</th>
<th>Gt. Northern</th>
<th>Large Lima</th>
<th>Navy</th>
<th>Pink</th>
<th>Pinto</th>
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<td>1g</td>
<td>1g</td>
<td>4g</td>
<td>1g</td>
<td>1g</td>
<td>1g</td>
<td>1g</td>
<td>1g</td>
<td>1g</td>
<td>1g</td>
</tr>
<tr>
<td>% Calories from Fat</td>
<td>6%</td>
<td>8%</td>
<td>10%</td>
<td>6%</td>
<td>26%</td>
<td>6%</td>
<td>8%</td>
<td>6%</td>
<td>6%</td>
<td>6%</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>Sodium</td>
<td>6mg</td>
<td>1mg</td>
<td>6mg</td>
<td>1mg</td>
<td>10mg</td>
<td>4mg</td>
<td>2mg</td>
<td>4mg</td>
<td>4mg</td>
<td>4mg</td>
<td>8mg</td>
<td>4mg</td>
</tr>
</tbody>
</table>
In a recommended 100-gram serving of lentils, there is:

- 18 grams of fibre or 72% of your daily recommended intake of fibre. That is more fibre than in a 100-gram serving of bran flakes!

- 25% of your daily recommended Potassium intake. Which is twice as much potassium as in a large banana!

- 50% of your daily recommended intake of Folate.

- 48% of your daily recommended intake of Iron.
Health & Nutrition

100 grams of Lentils

- 26 grams of protein.
- Only 1.5 grams of fat.

VS

108 grams of Steak

- 27 grams of protein.
- 18 grams of fat.
Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study

Marta Guasch-Ferré1,2, Frank B Hu3, Miguel A Martínez-González2,4, Montserrat Fito5, Mónica Bulló1,2, Ramon Estruch2,6, Emilio Ros2,7, Dolores Corella2,8, Javier Recondo2,9, Enrique Gómez-Gracia10, Miquel Fiol11, José Lapetra2,12, Lluís Serra-Majem13, Miguel A Muñoz14, Xavier Pinto2,15, Rosa M Lamuela-Raventós16, Josep Basora1,2, Pilar Buil-Cosiales2,4,17, José V Soriguer28, Valentina Ruiz-Gutierrez2,18, J Alfredo Martínez19 and Jordi Salas-Salvadó1,2*

Abstract

Background: It is unknown whether individuals at high cardiovascular risk sustain a benefit in cardiovascular disease from increased olive oil consumption. The aim was to assess the association between total olive oil intake, its varieties (extra virgin and common olive oil) and the risk of cardiovascular disease and mortality in a Mediterranean population at high cardiovascular risk.

Methods: We included 7,216 men and women at high cardiovascular risk, aged 55 to 80 years, from the PREvención con Dita MEDiterránea (PREDIMED) study, a multicenter, randomized, controlled, clinical trial. Participants were randomized to one of three interventions: Mediterranean Diets supplemented with nuts or extra-virgin olive oil, or a control low-fat diet. The present analysis was conducted as an observational prospective cohort study. The median follow-up was 4.8 years. Cardiovascular disease (stroke, myocardial infarction and cardiovascular death) and mortality were ascertained by medical records and National Death Index. Olive oil consumption was evaluated with validated food frequency questionnaires. Multivariate Cox proportional hazards and generalized estimating equations were used to assess the association between baseline and yearly repeated measurements of olive oil intake, cardiovascular disease and mortality.

Results: During follow-up, 277 cardiovascular events and 323 deaths occurred. Participants in the highest energy-adjusted tertile of baseline total olive oil and extra-virgin olive oil consumption had 35% (HR: 0.65; 95% CI: 0.47 to 0.89) and 39% (HR: 0.61; 95% CI: 0.44 to 0.85) cardiovascular disease risk reduction, respectively, compared to the reference. Higher baseline total olive oil consumption was associated with 48% (HR: 0.52; 95% CI: 0.29 to 0.93) reduced risk of cardiovascular mortality. For each 10 g/d increase in extra-virgin olive oil consumption, cardiovascular disease and mortality risk decreased by 10% and 7%, respectively. No significant associations were found for cancer and all-cause mortality. The associations between cardiovascular events and extra virgin olive oil intake were significant in the Mediterranean diet intervention groups and not in the control group.

Conclusions: Olive oil consumption, specifically the extra-virgin variety, is associated with reduced risks of cardiovascular disease and mortality in individuals at high cardiovascular risk.

Trial registration: This study was registered at controlled-trials.com (http://www.controlled-trials.com/ISRCTN35739639). International Standard Randomized Controlled Trial Number (ISRCTN): 35739639. Registration date: 5 October 2005.

Keywords: Olive oil, Cardiovascular, Mortality, Mediterranean Diet, PREDIMED

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ABSTRACT

One of the best-studied diets for cardiovascular health is the Mediterranean diet. This consists of fish, monounsaturated fats from olive oil, fruits, vegetables, whole grains, legumes/nuts, and moderate alcohol consumption. The Mediterranean diet has been shown to reduce the burden, or even prevent the development, of cardiovascular disease, breast cancer, depression, colorectal cancer, diabetes, obesity, asthma, erectile dysfunction, and cognitive decline. This diet is also known to improve surrogates of cardiovascular disease, such as waist-to-hip ratio, lipids, and markers of inflammation, as well as primary cardiovascular disease outcomes such as death and events in both observational and randomized controlled trial data. These enhancements easily rival those seen with more established tools used to fight cardiovascular disease such as aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and exercise. However, it is unclear if the Mediterranean diet offers cardiovascular disease benefit from its individual constituents or in aggregate. Furthermore, the potential benefit of the Mediterranean diet or its components is not yet validated by concrete cardiovascular disease endpoints in randomized trials or observational studies. This review will focus on the effects of the whole and parts of the Mediterranean diet with regard to both population-based and experimental data highlighting cardiovascular disease morbidity or mortality and cardiovascular disease surrogates when hard outcomes are not available. Our synthesis will highlight the potential for the Mediterranean diet to act as a key player in cardiovascular disease prevention, and attempt to identify certain aspects of the diet that are particularly beneficial for cardioprotection.

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ABSTRACT

Background: The role of the Mediterranean diet among individuals with previous cardiovascular disease (CVD) is uncertain.

Objective: The aim of this study was to assess the association between the Alternate Mediterranean Diet (aMED) score and all-cause, cardiovascular, and cancer mortality in men and women with CVD from the Health Professionals Follow-Up Study and the Nurses’ Health Study.

Design: This study included 6137 men and 11,278 women with myocardial infarction, stroke, angina pectoris, coronary bypass, and coronary angioplasty. Diet was first assessed in 1986 for men and in 1980 for women with a food-frequency questionnaire (FFQ) and then repeatedly every 2–4 y. Cumulative consumption was calculated with all available FFQs from the diagnosis of CVD to the end of the follow-up in 2008.

Results: During a median follow-up of 7.7 y (IQR: 4.2–11.8) for men and 5.8 y (IQR: 3.8–8.0) for women, we documented 1982 deaths (1142 from CVD and 344 from cancer) among men and 1468 deaths (666 from CVD and 197 from cancer) among women. In multivariable Cox regression models, the pooled RR of all-cause mortality from a comparison of the top with the bottom quintiles of the aMED score was 0.81 (95% CI: 0.72, 0.91; P-trend < 0.001). The corresponding pooled RR for CVD mortality was 0.85 (95% CI: 0.67, 1.09; P-trend = 0.30), for cancer mortality was 0.85 (95% CI: 0.65, 1.11; P-trend = 0.10), and for other causes was 0.79 (95% CI: 0.65, 0.97; P-trend = 0.01). A 2-point increase in adherence to the aMED score was associated with a 7% (95% CI: 3%, 11%) reduction in the risk of total mortality.

Conclusion: Adherence to a Mediterranean-style dietary pattern was associated with lower all-cause mortality in individuals with CVD. Am J Clin Nutr 2014;99:172–80.
DASH DIET (dietary approaches to stop hypertension)

Research based

The DASH diet is based on the research studies: Dietary Approaches to Stop Hypertension, and has been proven to lower blood pressure, reduce cholesterol, and improve insulin sensitivity. Blood pressure control with the DASH diet involves more than just the traditional low salt or low sodium diet advice. It is based on an eating plan proven to lower blood pressure, a plan rich in fruits, vegetables, and low-fat or nonfat dairy. It emphasizes whole grains and contains less refined grains compared with a typical diet. It is rich in potassium, magnesium, calcium, and fiber. Your doctor may have recommended this eating plan; it is also recommended by:

- The National Heart, Lung, and Blood Institute (one of the National Institutes of Health, of the US Department of Health and Human Services)
- The American Heart Association
- The Dietary Guidelines for Americans
- US guidelines for treatment of high blood pressure

The DASH Diet Plan

The DASH diet eating plan is a diet rich in fruits, vegetables, low fat or nonfat dairy. It also includes mostly whole grains; lean meats, fish and poultry; nuts and beans. It is high fiber and low to moderate in fat. It is a plan that follows US guidelines for sodium content, along with vitamins and minerals. In addition to lowering blood pressure, the DASH eating plan lowers cholesterol and makes it easy to lose weight. It is a healthy way of eating, designed to be flexible enough to meet the lifestyle and food preferences of most people. It can be considered to be an Americanized version of the Mediterranean diet, and to be easier to follow, since it has more specific guidelines. The plan below is for the original DASH diet, which was designed to lower blood pressure, and was not specifically a weight loss plan. The pumped up versions for weight loss is lower in calories and discourages refined and processed foods, which are mostly empty calories. You can see sample menus for the original plan, the weight loss plan, and vegetarian plan.

Specifically the DASH diet plan includes:

<table>
<thead>
<tr>
<th>Type of food</th>
<th>Number of servings for 1600 - 3100 Calorie diets</th>
<th>Servings on a 2000 Calorie diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains and grain products (include at least 3 whole grain foods each day)</td>
<td>6 - 12</td>
<td>7 - 8</td>
</tr>
<tr>
<td>Fruits</td>
<td>4 - 6</td>
<td>4 - 5</td>
</tr>
<tr>
<td>Category</td>
<td>Amount</td>
<td>Amount</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Vegetables</td>
<td>4 - 6</td>
<td>4 - 5</td>
</tr>
<tr>
<td>Low fat or non fat dairy foods</td>
<td>2 - 4</td>
<td>2 - 3</td>
</tr>
<tr>
<td>Lean meats, fish, poultry</td>
<td>1.5 - 2.5</td>
<td>2 or less</td>
</tr>
<tr>
<td>Nuts, seeds, and legumes</td>
<td>3 - 6 per week</td>
<td>4 - 5 per week</td>
</tr>
<tr>
<td>Fats and sweets</td>
<td>2 - 4</td>
<td>Limited</td>
</tr>
</tbody>
</table>

**Who Should Follow the DASH Diet?**

The *Dietary Guidelines for Americans* recommend the DASH eating plan as a model for healthy eating for everyone! The whole family can enjoy the DASH diet. And of course, the DASH diet was developed to help people lower their blood pressure. It provides additional heart health benefits, lowering cholesterol and inflammation. New research shows that it is effective in lowering blood pressure in children as well as adults.
ABSTRACT

Background: Previous studies on diet and coronary heart disease (CHD) focused primarily on individual nutrients or foods.

Objective: We examined whether overall dietary patterns derived from a food-frequency questionnaire (FFQ) predict risk of CHD in men.

Design: This was a prospective cohort study of 44,875 men aged 40–75 y without diagnosed cardiovascular disease or cancer at baseline in 1986.

Results: During 8 y of follow-up, we documented 1089 cases of CHD (nonfatal myocardial infarction and fatal CHD). Using factor analysis, we identified 2 major dietary patterns using dietary data collected through a 131-item FFQ. The first factor, which we labeled the “prudent pattern,” was characterized by higher intake of vegetables, fruit, legumes, whole grains, fish, and poultry, whereas the second factor, the “Western pattern,” was characterized by higher intake of red meat, processed meat, refined grains, sweets and dessert, French fries, and high-fat

N= ~45,000

8 years
FFQ

2 dietary Patterns:

Prudent Pattern

Western pattern

AJCN, 2000
Benefits of the Mediterranean Diet: Insights From the PREDIMED Study

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\textsuperscript{d}Human Nutrition Department, Hospital Universitari Sant Joan, Institut d'Investigació Sanitària Pere Virgili, Universitat Rovira i Virgili, Reus, Spain
\textsuperscript{e}Institut d'Investigacions Biomèdiques August Pi i Sunyer, Hospital Clinic, University of Barcelona, Barcelona, Spain
\textsuperscript{f}Department of Preventive Medicine and Public Health, University of Valencia, Valencia, Spain
\textsuperscript{g}Cardiovascular and Nutrition Research Group, Institut de Recerca Hospital del Mar, Barcelona, Spain

\begin{table}[h]
\centering
\begin{tabular}{|l|}
\hline
\textbf{ARTICLE INFO} \\
\hline
\textbf{Keywords:} Mediterranean diet, Dietary intervention, Randomized trials, Primary prevention, Atrial fibrillation, Peripheral artery disease, Stroke, Type-2 diabetes \\
\hline
\textbf{ABSTRACT} \\
\hline
The PREDIMED (PREvención con Dieta MEDiterránea) multicenter, randomized, primary prevention trial assessed the long-term effects of the Mediterranean diet (MeDiet) on clinical events of cardiovascular disease (CVD). We randomized 7447 men and women at high CVD risk into three diets: MeDiet supplemented with extra-virgin olive oil (EVOO), MeDiet supplemented with nuts, and control diet (advice on a low-fat diet). No energy restriction and no special intervention on physical activity were applied. We observed 288 CVD events (a composite of myocardial infarction, stroke or CVD death) during a median time of 4.8 years; hazard ratios were 0.70 (95\% CI, 0.53–0.91) for the MeDiet + EVOO and 0.70 (CI, 0.53–0.94) for the MeDiet + nuts compared to the control group. Respective hazard ratios for incident diabetes (273 cases) among 3541 non-diabetic participants were 0.60 (0.43–0.85) and 0.82 (0.61–1.10) for MeDiet + EVOO and MeDiet + nuts, respectively versus control. Significant improvements in classical and emerging CVD risk factors also supported a favorable effect of both MeDiets on blood pressure, insulin sensitivity, lipid profiles, lipoprotein particles, inflammation, oxidative stress, and carotid atherosclerosis. In nutrigenomic studies beneficial effects of the intervention with MedDiets showed interactions with several genetic variants (TCF7L2, APOA2, MLXIP, LPL, FTO, MHC, COX-2, GCKR and SERPINE1) with respect to intermediate and final phenotypes. Thus, the PREDIMED trial provided strong evidence that a vegetable-based MeDiet rich in unsaturated fat and polyphenols can be a sustainable and ideal model for CVD prevention. \\
\hline
\end{tabular}
\end{table}

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Statement of Conflict of Interest: see page 56.
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E-mail address: mamartinez@unav.es (M.A. Martínez-González).
1 A complete list of PREDIMED INVESTIGATORS can be found at the end of this manuscript.

http://dx.doi.org/10.1016/j.pcad.2015.04.003
0033-0620/© 2015 Elsevier Inc. All rights reserved.
Cardiovascular (CV) disease (CVD) is the main cause of worldwide premature mortality. Coronary heart disease (CHD) and stroke ranked first and third, respectively, as the leading global causes of disability-adjusted years according to the global burden of disease estimates for 2010. Furthermore, the projections of mortality from CVD for 2030 are dismal and underline the need for preventive strategies as a public health priority. In this context, a high-quality diet and a healthy lifestyle at middle age are the most important factors for CVD prevention. Consequently, the diet-heart hypothesis has been a long-standing tenet in CVD prevention and nutritional epidemiology during the last 50 years. Recently, the relevance of overall high-quality food patterns, rather than the focus on single nutrients and foods, has emerged as a powerful paradigm to address the inherent complexity of dietary exposures and to assess their potential CVD preventive effects. Food patterns can be described as the amounts, proportions, combinations or varieties for the consumption of different foods and beverages and the frequency with which they are usually consumed. This approach allows the assessment of synergistic interactions and cumulative effects among different foods and nutrients, pre-empting confounding by alternative dietary exposures, avoids some problems of co-linearity between foods or nutrients and thus provides a strong methodological tool in nutritional epidemiology. Even though randomized dietary intervention trials are the hallmarks for acquiring knowledge on the effects of diet on CVD, most research in the field of dietary patterns is observational, with some potential for residual confounding and other possible sources of bias. These limitations have been the subject of ample but probably undue criticism.

A weakness of the diet-heart hypothesis is that most of the available experimental research in the field has not used hard clinical outcomes, but only intermediate risk biomarkers. The existence of multiple pathways leading from diet to CVD speaks against the simplistic approach of giving a high value to changes in any single biomarker. Moreover, the induction period can vary for the different pathways in which diverse biomarkers are involved, thus limiting the possibility of assessing multiple biomarker combinations at any time point. Furthermore, other lesser-known pathways could account for a substantial proportion of clinical CVD events. The most sensible approach, therefore, in order to investigate the diet-heart hypothesis is to use hard clinical CVD events as end-points of randomized controlled trials (RCTs). Most feeding trials, however, are usually short term and rarely include clinical end-points such as CVD events or death. The PREDIMED trial was designed to overcome both the problem of the single-nutrient approach and the limitations of assessing only intermediate risk markers. Indeed, the PREDIMED randomized trial used an overall food pattern as the intervention and assessed hard CVD events as end-points providing a high level of scientific evidence.

Scientific evidence of the cardio-metabolic benefits of the Mediterranean diet

The abundant and consistent observational evidence that was available to support the benefits of the Mediterranean diet (MeDiet) and, specifically, of tree nuts and olive oil, on CV health prompted us to choose this traditional dietary model enriched with olive oil or nuts as the intervention. Table 1 summarizes the results of meta-analyses and systematic reviews assessing the effects of MeDiet on different cardiometabolic outcomes.

The MeDiet is defined as the traditional dietary pattern found in the early 1960s in Greece, Southern Italy, Spain and other olive-growing countries of the Mediterranean basin. It is a frugal diet that uses generous amounts of olive oil as main culinary fat and has a high consumption of plant-derived foods (fruit, vegetables, legumes, nuts and seeds, and whole grain cereals); frequent but moderate intake of wine (especially red wine), usually with meals; moderate consumption of seafood and dairy products (especially yogurt and cheese, but not whole milk, butter or cream), poultry and eggs; and low consumption of sweet desserts, red and processed meats. In comparison with other healthy patterns, such as the DASH diet, the healthy US dietary pattern or the Alternative Healthy Eating Index, the consumption of fruit and fish is usually higher in the MeDiet, while the consumption of dairy products tends to be lower. In healthy vegetarian food patterns, meat and seafood are not consumed, but eggs and dairy are most frequently included. Legumes, nuts/seeds, and processed soy are all higher in a healthy vegetarian food pattern than in the healthy U.S.-style or Mediterranean-style patterns.

A considerable scientific advantage of the MeDiet over other healthy dietary patterns was the availability of a previous randomized trial, the Lyon Diet Heart study, conducted in myocardial infarction survivors (i.e., it was a secondary prevention trial). It showed that a MeDiet enriched with alpha-linolenic acid, but not olive oil, provided a strong protection against recurrent CHD.

Our hypothesis when designing the PREDIMED trial was that the MeDiet would be superior to a low-fat diet for primary CVD prevention. This hypothesis had never been tested previously using a RCT design.

Design and methods of the PREDIMED study

The PREDIMED study was a primary prevention trial which tested the long-term effects of the MeDiet on incident CVD in men and women at high CVD risk aged 55–75 years (men) or...
Table 1 – Scientific evidence on the Mediterranean diet.
Systematic reviews assessing the association between adherence to the Mediterranean diet and cardio-metabolic outcomes.

<table>
<thead>
<tr>
<th>Systematic Review</th>
<th>N (Studies)</th>
<th>Exposure</th>
<th>Outcome</th>
<th>Effects of Increased Adherence to MeDiet&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esposito 2013&lt;sup&gt;31&lt;/sup&gt;</td>
<td>16</td>
<td>MeDiet (randomized trials)</td>
<td>Weight loss</td>
<td>−1.75 kg (−2.38; −0.64)</td>
<td>Greater weight loss with energy restriction and longer follow-up</td>
</tr>
<tr>
<td>Buckland 2008&lt;sup&gt;38&lt;/sup&gt;</td>
<td>21</td>
<td>MeDiet (randomized trials)</td>
<td>Weight loss</td>
<td>Beneficial (13 studies); no evidence (8 studies)</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>Nordmann 2011&lt;sup&gt;28&lt;/sup&gt;</td>
<td>6</td>
<td>MeDiet (randomized trials)</td>
<td>Risk factors</td>
<td>Beneficial</td>
<td></td>
</tr>
<tr>
<td>Grosso 2014&lt;sup&gt;24&lt;/sup&gt;</td>
<td>58</td>
<td>MeDiet (randomized trials)</td>
<td>Risk factors</td>
<td>Beneficial</td>
<td></td>
</tr>
<tr>
<td>Schwingshackl 2014&lt;sup&gt;18&lt;/sup&gt;</td>
<td>17</td>
<td>MeDiet</td>
<td>Flow-mediated dilatation</td>
<td>WMD = −1 mg/l (−1.5; −0.5)</td>
<td>Qualitative systematic review for adiponectin levels also increased</td>
</tr>
<tr>
<td>Schwingshackl 2014&lt;sup&gt;14&lt;/sup&gt;</td>
<td>17</td>
<td>MeDiet</td>
<td>High-sensitivity CRP</td>
<td>WMD = −1.86% (0.23−3.48)</td>
<td></td>
</tr>
<tr>
<td>Kastorini 2011&lt;sup&gt;30&lt;/sup&gt;</td>
<td>50</td>
<td>MeDiet (randomized trials)</td>
<td>Metabolic syndrome</td>
<td>RR = 0.50 (0.29−0.85)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Significant beneficial effects were found for each of the metabolic syndrome criteria</td>
</tr>
<tr>
<td>Esposito 2013&lt;sup&gt;35&lt;/sup&gt;</td>
<td>14</td>
<td>MeDiet</td>
<td>Metabolic syndrome</td>
<td>Beneficial</td>
<td>Qualitative systematic review for long-term studies were fairly homogenous (I² = 0%) and showed a stronger risk reduction RR = 0.75 (0.68−0.83)</td>
</tr>
<tr>
<td>Schwingshackl 2014&lt;sup&gt;15&lt;/sup&gt;</td>
<td>9</td>
<td>MeDiet</td>
<td>Type-2 diabetes</td>
<td>RR = 0.81 (0.73−0.90)</td>
<td>Quantitative meta-analysis: subgroups by region, health status, and degree of confounding control rendered similar results.</td>
</tr>
<tr>
<td>Koloverou 2014&lt;sup&gt;16&lt;/sup&gt;</td>
<td>17</td>
<td>MeDiet</td>
<td>Type-2 diabetes</td>
<td>RR = 0.77 (0.66−0.89)</td>
<td></td>
</tr>
<tr>
<td>Esposito 2010&lt;sup&gt;33&lt;/sup&gt;</td>
<td>9</td>
<td>MeDiet</td>
<td>Type 2 diabetes and glycemic control</td>
<td>Beneficial</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>Esposito 2014&lt;sup&gt;33&lt;/sup&gt;</td>
<td>5</td>
<td>MeDiet (observational)</td>
<td>Type-2 diabetes</td>
<td>Beneficial</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>Esposito 2014&lt;sup&gt;33&lt;/sup&gt;</td>
<td>5</td>
<td>MeDiet (randomized trials)</td>
<td>Glycemic control</td>
<td>Beneficial</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>Georgoulis 2014&lt;sup&gt;20&lt;/sup&gt;</td>
<td>17</td>
<td>MeDiet</td>
<td>Type-2 diabetes and other outcomes</td>
<td>Beneficial</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>Roman 2009&lt;sup&gt;39&lt;/sup&gt;</td>
<td>20</td>
<td>MeDiet</td>
<td>CVD and risk factors</td>
<td>CVD</td>
<td>Beneficial</td>
</tr>
<tr>
<td>Widmer 2014&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Not stated</td>
<td>MeDiet and its components</td>
<td>CVD and risk factors</td>
<td>CVD</td>
<td>Beneficial</td>
</tr>
<tr>
<td>Ros 2014&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Not stated</td>
<td>MeDiet</td>
<td>CVD</td>
<td>Beneficial</td>
<td></td>
</tr>
<tr>
<td>Whayne 2014&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Not stated</td>
<td>MeDiet</td>
<td>CVD</td>
<td>Beneficial</td>
<td>Qualitative systematic review: this meta-analysis was subsequently updated</td>
</tr>
<tr>
<td>Sofi 2008&lt;sup&gt;23&lt;/sup&gt;</td>
<td>4</td>
<td>MeDiet (+2/9 points)</td>
<td>CVD</td>
<td>Beneficial</td>
<td></td>
</tr>
<tr>
<td>Sofi 2010&lt;sup&gt;21&lt;/sup&gt;</td>
<td>8</td>
<td>MeDiet (+2/9 points)</td>
<td>CVD</td>
<td>RR = 0.91 (0.87−0.95)</td>
<td></td>
</tr>
<tr>
<td>Sofi 2014&lt;sup&gt;21&lt;/sup&gt;</td>
<td>20</td>
<td>MeDiet (+2/9 points)</td>
<td>CVD</td>
<td>RR = 0.90 (0.87−0.92)</td>
<td></td>
</tr>
<tr>
<td>Martínez-González 2014&lt;sup&gt;22&lt;/sup&gt;</td>
<td>2</td>
<td>MeDiet (randomized trials)</td>
<td>CVD</td>
<td>RR = 0.62 (0.45−0.85)</td>
<td>The heterogeneity disappeared after removing 3 studies assessing only fatal cases</td>
</tr>
<tr>
<td>Martínez-González 2014&lt;sup&gt;22&lt;/sup&gt;</td>
<td>16</td>
<td>MeDiet (observational, +2/9 points)</td>
<td>CVD</td>
<td>RR = 0.90 (0.86−0.94)</td>
<td></td>
</tr>
<tr>
<td>Martínez-González 2009&lt;sup&gt;25&lt;/sup&gt;</td>
<td>5</td>
<td>MeDiet</td>
<td>CVD</td>
<td>Beneficial</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>de Lorgeril 2008&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Not stated</td>
<td>MeDiet</td>
<td>CVD</td>
<td>Beneficial</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>Rees 2013&lt;sup&gt;36&lt;/sup&gt;</td>
<td>11</td>
<td>MeDiet</td>
<td>CVD</td>
<td>No evidence</td>
<td>Qualitative systematic review</td>
</tr>
<tr>
<td>Systematic Review</td>
<td>N (Studies)</td>
<td>Exposure</td>
<td>Outcome</td>
<td>Effects of Increased Adherence to MeDiet&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Comment</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------</td>
<td>----------</td>
<td>---------</td>
<td>---------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Panagiotakos 2004&lt;sup&gt;42&lt;/sup&gt;</td>
<td>6</td>
<td>MeDiet</td>
<td>CHD</td>
<td>8%–45% relative risk reduction RR = 0.71 (0.5–0.89)</td>
<td>The selection of trials apparently had little connection with the concept of MeDiet. Qualitative systematic review</td>
</tr>
<tr>
<td>Psaltoupoulou 2015&lt;sup&gt;27&lt;/sup&gt;</td>
<td>22</td>
<td>MeDiet</td>
<td>Stroke</td>
<td>RR = 0.71 (0.5–0.89)</td>
<td>Quantitative meta-analysis: meta-regression suggested stronger protection among males.</td>
</tr>
<tr>
<td>Tyrovolas 2010&lt;sup&gt;34&lt;/sup&gt;</td>
<td>9</td>
<td>MeDiet</td>
<td>CVD and cancer</td>
<td>Beneficial</td>
<td>Qualitative systematic review: The authors support the case for the urgent need of a trial such as PREDIMED.</td>
</tr>
<tr>
<td>Martinez-Gonzalez 2004&lt;sup&gt;46&lt;/sup&gt;</td>
<td>14</td>
<td>Feeding randomized trials</td>
<td>CVD and cancer</td>
<td>Unknown</td>
<td>Qualitative systematic review: This meta-analysis was subsequently updated.</td>
</tr>
<tr>
<td>Sofi 2009&lt;sup&gt;37&lt;/sup&gt;</td>
<td>8</td>
<td>MeDiet (+2/9 points)</td>
<td>All-cause mortality</td>
<td>RR = 0.91 (0.89–0.94)</td>
<td>Quantitative meta-analysis: I² = 33%</td>
</tr>
<tr>
<td>Sofi 2010&lt;sup&gt;32&lt;/sup&gt;</td>
<td>9</td>
<td>MeDiet (+2/9 points)</td>
<td>All-cause mortality</td>
<td>RR = 0.92 (0.90–0.94)</td>
<td>Quantitative meta-analysis: I² = 47%</td>
</tr>
<tr>
<td>Sofi 2014&lt;sup&gt;41&lt;/sup&gt;</td>
<td>18</td>
<td>MeDiet (+2/9 points)</td>
<td>All-cause mortality</td>
<td>RR = 0.92 (0.91–0.93)</td>
<td>Qualitative systematic review: Opinion of experts around the world</td>
</tr>
<tr>
<td>Trichopoulou 2000&lt;sup&gt;43&lt;/sup&gt;</td>
<td>3</td>
<td>MeDiet</td>
<td>All-cause mortality</td>
<td>Longer survival</td>
<td>Qualitative systematic review:</td>
</tr>
<tr>
<td>Serra-Majem 2006&lt;sup&gt;60&lt;/sup&gt;</td>
<td>35</td>
<td>MeDiet</td>
<td>A variety of outcomes</td>
<td>Beneficial</td>
<td></td>
</tr>
<tr>
<td>Trichopoulou 2014&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Not stated</td>
<td>MeDiet</td>
<td>A variety of effects</td>
<td>Beneficial</td>
<td></td>
</tr>
<tr>
<td>Madenelo-Fernández 2014&lt;sup&gt;45&lt;/sup&gt;</td>
<td>14</td>
<td>Interventions to promote MeDiet</td>
<td>Adherence to MeDiet</td>
<td>Beneficial</td>
<td>Qualitative systematic review: hard end-points were not assessed</td>
</tr>
</tbody>
</table>

<sup>a</sup> Risk ratios in meta-analyses of epidemiologic studies, usually adjusted for multiple confounders, compared the highest versus the lowest category of adherence to the MeDiet. Outcome changes describe the mean changes for the MeDiet versus comparator diets in meta-analyses of RCTs; only statistically significant changes are shown. Values between brackets are 95% confidence intervals.

<sup>b</sup> An apparent erratum was corrected. The authors presented the log of hazard ratio (95% CI) as −0.69 (−2.16 to −1.16), but this is impossible, the correct upper limit should probably be −0.16 (as we have assumed).

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60–80 years (women). PREDIMED was a multicenter, nutritional intervention RCT carried out in Spain from 2003 to 2011. The study was funded by the official Spanish agency for scientific research, Instituto de Salud Carlos III. A Web site (www.predimed.es) and the supplemental material published together with the final results provide full details of the study protocol. We selected participants from >200 primary care facilities affiliated with 11 recruiting sites. All participants were at high risk for CVD, but had no history of previous CVD episodes at enrollment. Criteria for recruitment were the presence of either type 2 diabetes mellitus (T2DM) or ≥3 risk factors (smoking, overweight or obesity, hypertension/HTN, dyslipidemia/DLP, and family history of early-onset CVD). Participants were randomized into one of three diets: 1) MeDiet supplemented with extra-virgin olive oil (EVOO); 2) MeDiet supplemented with nuts; and 3) control diet (advice on a low-fat diet).

Full-time registered dietitians delivered the intervention. Throughout the study, participants attended quarterly individual visits and group sessions in which they were instructed to follow the allocated diets. Participants also attended quarterly group sessions where they received written material with information on key Mediterranean foods and seasonal shopping lists, menus and specific recipes for a typical week. This material was discussed in detail with the dietitians. Allotments of EVOO (1 L per week, including a minimum of 50 mL/day for participants and the rest for family meals) or mixed nuts (30 g/day: 15 g walnuts, 7.5 g almonds and 7.5 g hazelnuts plus extra allocations for the family) were supplied at no cost to each participant randomly assigned to the MeDiet groups on a quarterly basis during the group sessions with dietitians. Participants in the control diet group attended similar quarterly sessions with explanations and written material on the low-fat diet and they received non-food gifts in these sessions. The three diets were energy-unrestricted and no intervention on physical activity was conducted.

A validated 14-point MeDiet screener was used by dietitians as a tool to both assess actual adherence to the MeDiet and enhance future adherence. These 14 items were:

1. Use of olive oil as the main culinary fat
2. Consumption of ≥4 tablespoons/day of olive oil (including oil used for frying, salads, out-of-house meals, etc.)
3. Consumption of ≥2 servings/d of vegetables
4. Consumption of ≥3 servings/d of fruits
5. Consumption of <1 serving/d of red meat, hamburger or meat products (ham, sausage, etc.)
6. Consumption of <1 serving/d of butter, margarine, or cream
7. Consumption of <1 serving/d of sweetened and/or carbonated beverages
8. Consumption of ≥1 serving/d of wine
9. Consumption of ≥3 servings/week of legumes
10. Consumption of ≥3 servings/week of fish or shellfish
11. Consumption of <3 servings/week of commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits or custard
12. Consumption of ≥3 servings/week of nuts (including peanuts)
13. Preferential consumption of chicken, turkey or rabbit meat instead of veal, pork, hamburger or sausage
14. Consumption of ≥2 servings/week of sofrito, a sauce made with tomato and onion, leek or garlic and simmered with olive oil.

Validated food frequency questionnaires covering 137 foods were collected yearly by the dietitians. This repeated collection of dietary data allowed us to use the PREMIDEM trial as a unique setting for subsequent cohort studies analyzed as a prospective observational follow-up study with repeated measurements of diet, thus improving the quality of our dietary assessment.10

Fasting blood and spot urine were obtained and serum, plasma and DNA samples were saved. Objective biomarkers of adherence to the supplemental foods (urinary hydroxytyrosol as marker of EVOO consumption and plasma α-linolenic acid as marker of walnut consumption) were determined in random sub-samples.

The pre-specified primary end-point of the trial was incident CVD (a composite of non-fatal myocardial infarction/MI, non-fatal stroke or CVD death). This composite event occurred in 288 participants during a median follow-up of 4.8 years. The trial was neither powered nor designed to independently assess each of the three components of the combined end-point. Secondary outcomes included total mortality, T2DM, metabolic syndrome (MetS), peripheral arterial disease (PAD), atrial fibrillation (AF), neurodegenerative diseases and major cancers. An event adjudication committee, whose members were blinded to group allocation, was responsible for event ascertainment. All participants provided written informed consent and the protocol was approved by the institutional review boards of all participating centers.

Main results of the PREMIDEM trial

We randomized 7447 participants into the three PREMIDEM intervention groups. The groups were well-balanced with respect to their baseline characteristics and pharmacologic treatments. Though small, between-group differences in some baseline characteristics were observed, but they were not clinically meaningful. Furthermore, we adjusted all risk estimates for these variables. The mean age of participants was 67 years, 57% were women and the mean body mass index was 30 kg/m². The baseline prevalence of diabetes was nearly 50% and the prevalence of DLP and HTN was higher than 70% and 80%, respectively.

Compliance with the intervention in the two MeDiet groups was adequate.48 Our tracking of objective biomarkers in random participant subsamples also indicated compliance with the intended dietary intervention. However, the achieved absolute difference in adherence to the MeDiet (according to the 14-item screener) between the intervention group and the control group was modest, amounting to a maintained difference of 2 points out of 14. There were no between-group differences in physical activity during the study. No diet-related adverse effects occurred.

We assessed the effect of baseline adherence to the 14-point score with respect to the subsequent incidence of the primary CVD end-point during follow-up.49 As shown in Fig 1, the effect was remarkable. The multivariable-adjusted hazard ratio for participants with a baseline 14-item screener in the 2nd-3rd quintile who scored between 8 and 9 points was 0.72 (95% confidence interval [CI]: 0.55–0.94), and for those with the highest adherence (two upper quintiles, scoring 10–14 points) it was 0.47 (CI: 0.35–0.65).

The observed rates per 1000 person-years for the primary end point were 8.1, 8.0, and 11.2 in the MeDiet + EVOO, MeDiet + nuts, and control groups, respectively. The unadjusted hazard ratios were 0.70 (CI, 0.53–0.91) for the MeD + EVOO and 0.70 (CI, 0.53–0.94) for the MeDiet + nuts. The relative risk reductions, absolute risk reductions and number needed to treat are shown in Table 2 after multivariable adjustment for sex, age, adiposity variables, and baseline CVD risk factors. No effect on all-cause mortality was apparent. Significant disease risk reductions were also observed for incident T2DM (in the subset of participants initially free of T2DM)50,51 and for other CVD outcomes, such as PAD52 and AF.53 Hence, the PREMIDEM study showed with an RCT design for the first time that a diet supplemented with either EVOO or nuts is useful in the primary prevention of CVD, PAD, AF, and T2DM in individuals at high risk.

A beneficial effect of the intervention on MetS status was also observed in the PREMIDEM trial.54,55 In comparison with the control group, participants randomized to either MeDiet were more likely to show reversion of MetS, with HR 1.35 (CI 1.15–1.58) for the MeDiet + EVOO, and HR 1.28 (CI 1.08–1.51) for the MeDiet + nuts. Similarly, the PREMIDEM MeDiet interventions were shown to reduce blood pressure and the risk of HTN56,57 and to slow the progression of subclinical atherosclerosis, as determined by changes in ultrasound-assessed carotid intima-media thickness and plaque.58,59

Number of events hypothetically prevented with the Mediterranean diet

Table 3 shows the number of hard clinical CVD events that could be prevented in a hypothetical cohort of 1000 persons undergoing the nutritional intervention with the MeDiet used in the PREMIDEM trial. These results suggest that even a modest intervention with the MeDiet has the potential to
account for a sizable reduction in the number of clinical events in a relatively short period of time.

**Observational studies and trials in the context of the PREDIMED trial**

Although some authors have suggested that RCTs with hard clinical events as end-points are the only solution to circumventing the problems of measurement error inherent to observational designs in nutritional epidemiology, trials are far from perfect, and also present considerable limitations. These problems include the frequent suboptimal compliance, losses to follow-up, and the ethical need to prematurely halt the trial when there is sufficient evidence of benefit, even when the number of observed events is lower than anticipated. In addition, some degree of contamination of the control group with aspects of the intervention intended only to the active intervention arms of the trial is unavoidable. Moreover some exposures or outcomes cannot be assessed with RCTs.

In this context, the symbiosis between properly designed RCTs and large cohort studies with appropriate and careful control of potentially confounding variables, and due precautions to improve dietary measurements, are currently the best possible option to ascertain the health effects of dietary exposures. Adequately designed and tested food frequency questionnaires (FFQs) have been shown to have acceptable validity when compared to reference measures. In addition, adjustment for total energy intake, usually applying the residual method along with the use of repeated FFQs in long-term prospective cohort studies, further improves their validity estimates.

The availability of validated FFQs of each participant with yearly repeated measurements is a unique strength of the PREDIMED trial. Furthermore, biomarker analyses have corroborated the validity of our dietary assessment tools. Most follow-up studies have collected measurements of dietary intake only at baseline and this is a limitation in nutritional epidemiology because diet may change during follow-up. The PREDIMED study has provided a large body of evidence on the associations between diet and diverse health outcomes taking advantage of the validated FFQs.

**Mechanisms of protection by the Mediterranean diet**

CVD protection by the MedDiet can be explained by a beneficial effect on classical and emergent CV risk factors. Although the underlying mechanisms of protection against CVD by the MedDiet are not fully understood, the richness of this dietary pattern in antioxidant and anti-inflammatory molecules is likely to be relevant. On one hand, this can be due to their anti-oxidant capacity, such as cell redox state modulating enzyme systems. On the other hand, nutrients have the capacity of modulating gene and protein expression and, subsequently, metabolite production. Previous nutrigenomic studies have revealed that the MedDiet has a protective effect on the expression of several proatherogenic genes involved in vascular inflammation, foam cell formation, and thrombosis.

**Genomics and the Mediterranean diet**

We investigated whether the effects of the MedDiet or its components might differ depending on genetic variants. We found several gene–diet interactions in determining both intermediate and CVD phenotypes. Suffice it to say that we observed that the association of the MCAR rs17782313 or the FTO rs9593609 polymorphisms with T2DM was modulated by the MedDiet. When adherence to the MedDiet was low (≤9 out of 14 points), carriers of the variant alleles had higher T2DM risk than wild-type subjects. However, when adherence to the MedDiet was high (≥9 points), these associations disappeared. These gene–diet interactions remained after adjustment for BMI. Adherence to the MedDiet was found to interact with the TCF7L2-rs7903146 (C>T) polymorphism in relation to fasting glucose, total cholesterol, low-density lipoprotein cholesterol and triglycerides. When adherence to the MedDiet was low, participants with the TT genotype had higher fasting glucose concentrations and lipids than CC + CT individuals but when adherence was high, these differences were not apparent. Moreover, TT subjects had a higher stroke incidence in the control group compared with CC, whereas the dietary intervention with MedDiet was associated with reduced stroke incidence in TT homozygotes but not CC homozygotes. Both genetic and epigenetic effects on microRNA target site polymorphisms were also analyzed. A gain-of-function microRNA-410 target site polymorphism (rs137027C) in the lipoprotein lipase gene, interacted with the MedDiet intervention in the association with triglyceride levels and stroke incidence. The interplay between genetic and epigenetic factors may contribute to better understand some biological mechanisms underlying CVD progression. Overall these results highlight the relevance of the multi-level omics approaches to a more comprehensive investigation of the mechanisms accounting for the MedDiet protective effects.
Table 2 - Relative risk reduction, absolute risk reduction and number needed to treat associated with the PREDIMED primary prevention intervention for several hard clinical events (assuming median follow-up = 4.8 years).

<table>
<thead>
<tr>
<th>Clinical Event</th>
<th>Mediterranean Diet Supplemented With Extra-Virgin Olive Oil</th>
<th>Mediterranean Diet Supplemented With Mixed Nuts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative risk reduction</td>
<td>Absolute risk reduction</td>
</tr>
<tr>
<td>Primary CVD end-point</td>
<td>30% (8.0%; 46%)</td>
<td>1.34% (0.36%; 2.05%)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>40% (15%; 57%)</td>
<td>3.52% (1.23%; 5.02%)</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>64% (35%; 79%)</td>
<td>1.18% (0.64% 1.45%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>38% (12%; 55%)</td>
<td>1.54% (0.48%; 2.22%)</td>
</tr>
</tbody>
</table>

Fully adjusted estimates for the hazard ratios from Cox regression models were used to compute the relative risks (RR). The relative risk reduction (RRR) was computed as RRR = (1 - RR). The absolute risk reduction (ARR) was computed taking into account the baseline incidence of events in the control group (I0) after a median follow-up of 4.8 years and applying the estimates for the relative risks, i.e. ARR = I0 (1 - RR).

Conclusions

The findings from the PREDIMED trial, the Lyon Diet-Heart trial, and many large prospective cohorts are fully consistent. These large observational and experimental studies are also supported by mechanistic investigations aimed at assessing classical and emergent CVD risk factors and pathophysiological pathways. Anti-inflammatory effects and reduced oxidative stress are very likely explanations for the protection observed in the PREDIMED trial. Taken together, these research findings converge, demonstrating that the traditional Mediterranean diet offers an affordable, attractive, and easily achievable protection against CVD.

Importantly, these findings suggest that an overall dietary pattern that is rich in high-unsaturated fat from natural vegetable sources is preferable for CV health than a low-fat diet. In addition, the Mediterranean diet has been shown to effectively control the residual risk observed after standard pharmacologic treatment of DLP anomalies and HTN in high-risk individuals. Taking into account the advanced age of many participants in the PREDIMED trial and in some of the available cohorts, it can be concluded that it is not too late to improve the food pattern to improve CV health.

Table 3 - Number of expected prevented cases with the PREDIMED primary prevention intervention for several hard clinical events (median follow-up: 4.8 years) in a hypothetical cohort of 1000 subjects. Both Mediterranean diet groups were merged together.

<table>
<thead>
<tr>
<th>Clinical Event</th>
<th>Number of Prevented Cases (95% CI) per 1000 Hypothetical Participants Receiving the PREDIMED MeDiet-Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary CVD end-point</td>
<td>13 (4-20)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>26 (7-41)</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>10 (6-13)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>11 (2-18)</td>
</tr>
</tbody>
</table>

Statement of conflict of interest

MA Martínez-González received grants for research from the International Nut Council, Reus, Spain; J. Salas-Salvado has received grants for research from the International Nut Council, Reus, Spain and is a non paid member of its Scientific Advisory Committee; Ramon Estruch no conflicts of interest; D. Corella no conflicts of interest; M. Fito no conflicts of interest and E. Ros has received grants for research from the California Walnut Commission, Sacramento, CA, U.S. and is a non paid member of its Scientific Advisory Committee;

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Role of the funders: Funding sources had no role in the design and conduct of the study, collection, management,
Appendix A. Complete list of PREDIMED Investigators

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Hospital Universitario de Bellvitge, Hospital de Llobregat, Barcelona, Spain: X. Pinto, E. de la Cruz, A. Galera, Y. Soler, F. Trías, I. Sarasa, E. Padres, and E. Corbella.


Other investigators of the PREDIMED network: J.A. Tur (University of Balearen Islands), V. Ruiz-Gutierrez (Instituto de la Grasa, Sevilla), M.P. Portillo (University of Basque Country) and G. Saez (University of Valencia); all in Spain.

REFERENCES


59


White Bean Stew with Rosemary and Spinach

You will not believe how much nutrition is loaded into this hearty vegetarian stew. There’s fiber, iron, potassium, vitamins A, C and K, the list goes on! The best part is that there is equally high amount of flavor. Plus, you can cook it up in just 30 minutes.

Developed by Sara Quessenberry for Cleveland Clinic Wellness

Yield: 4 Servings

Ingredients:

2 tablespoons extra virgin olive oil
1 yellow onion, peeled and chopped
2 cloves garlic, peeled and chopped
4 carrots, rinsed well, halved and sliced into ½-inch pieces
3 ribs celery, rinsed well, halved lengthwise and sliced into ¼-inch pieces
3 (15-ounce) cans low-sodium cannellini beans, drained and rinsed
2 teaspoons chopped fresh rosemary
¼ teaspoon kosher salt
¼ teaspoon freshly ground black pepper
¼ teaspoon crushed red pepper flakes
4 cups fresh spinach leaves

Instructions:
In a large pot, heat the oil over medium-high heat. Add the onion and cook 5-6 minutes, stirring often, until beginning to soften. Add the garlic, carrots, and celery and continue to cook, 6 minutes more, stirring occasionally, until just a small amount of crispness remains. Do not overcook at this point.

Add 3 cups of water plus the beans, rosemary, salt, black pepper, and red pepper flakes. Heat to a boil. Reduce heat to medium and simmer, uncovered, for 12-15 minutes until the vegetables are tender.

Remove from heat, and stir in the spinach, which will wilt within seconds. Divide among bowls and serve.

Nutrition Info Per Serving: (4 servings) 479 calories, 8 g total fat, 1 g saturated fat, 25 g protein, 80 g carbohydrate, 18 g dietary fiber, 5 g sugar, 0 mg cholesterol, 210 mg sodium