Discuss with your medical doctor before following this plan. This is not medical advice. Every patient has a different health history, takes different medicines, and has different genetics. There are drug interactions with certain foods and also disease state interactions with certain foods. Seek medical advice before starting an intensive nutritional change!

I have put together a prostate cancer diet after reading many, many different sources. I have listed the scientific resources that my opinions are pooled from. Doctors and healthcare authorities rely on research studies, and when you discuss changes to your cancer plan with them, it is a good idea to carry the study with you that you're basing your desire to change your cancer plan on. Most doctors will NOT encourage complementary diets and think they are a waste of patients' time and fretfulness. But there is research to support intensive dietary intervention, and if this research is put into doctors' hands, I believe they'll read it. If a patient brought me a research article (NOT a blog post or a newspaper article, but a REAL medical journal article), I always made time to read it when I was practicing.

Take a look at the diet I constructed and compare it to what's out there. Read. Read. And if what you eat is no big deal to you and you want to give nutritional intervention a try for prostate cancer, *with your doctor's approval*, go for it! If you can, try to eat organic; if you can't, try to eat organic at least on the foods you eat every day.

I read all comments (that don't go through to spam) and diligently consider them. If you have a story, refutation, helpful addition, or grammar correction, please comment. Lastly, medical research changes, and as this post "ages," there will be new diet information on prostate cancer. Do NOT use this post as medical advice!

Prostate Cancer Nutritional Intervention Plan (Reiteration: Discuss with your medical doctor before following this plan. This is not medical advice. Every patient has a different health history, takes different medicines, and has different genetics. There are drug interactions with certain foods and also disease state interactions with certain foods. Seek medical advice before starting an intensive nutritional change!)

1. Eat a total of 8 CUPS (or more) of a combination of vegetables and/or fruits DAILY. Measure the eight cups so you're not misjudging. Include as part of this the following foods.

- Eat ½ cup cooked or 1 cup raw organic BROCCOLI DAILY. (Substitute Brussels, cauliflower, cabbage, or kale if/when you get disgusted with broccoli.)
- Eat 1 serving size of CITRUS DAILY, such as grapefruits, lemons, limes, oranges.
- Eat ½-1 cup of CARROTS DAILY.
- Eat almost daily: Organic tomato products that have been simmered for a long time (spaghetti sauce, tomato soup, tomato juice) with a little fat (like olive oil). Do not use products in BPA-laden plastic containers or BPA-lined cans. I search for products in glass jars.
- Also add in some of the following fruits that you like each day: apples, apricots, plums, red raspberries, red grapes, pomegranates, and other colorful fruits.
- Also add in some of the following vegetables that you like each day: Mushrooms (shiitake, Maitake, Reishi), bell peppers, hot peppers, Brussels, cauliflower, cabbage, red cabbage, kale, spinach, arugula, collards, cabbage, onions, Romaine lettuce, radishes, beets, and other colorful and/or deeply green vegetables.
- Also rotate through starchier vegetables like carrots, pumpkin, sweet potato, winter squashes (acorn, butternut), and potatoes (simply prepared) for foods which will help fill you up.
- **2. Eat 1 ounce (roughly ¼ cup or 28 grams) of nuts and/or seeds every day.** Choose from sunflower seeds, pumpkin seeds, Brazil nuts, almonds, cashews, walnuts, pecans, pistachios, black walnuts, English walnuts, sesame seeds, and pine nuts.\* (The \* means see the postscript notes at the bottom of the post before my references.)
  Eat them as is, sprinkle them on salads, toss into stir fry, or grind them fresh into "nut butter."\*\* (See notes below.)

My personal favorites for health and cancer are sunflower seeds and pumpkin seeds, but each nut is special (and I'm not kidding...)—eat ones you enjoy. Also use hemp seeds (for GLA, omega-3, zinc), flax seed (it must be freshly ground PLEASE—I started using my coffee bean grinder for flax), and chia seeds (for omega-3).

- 3. For meat, eat fish (3-6 ounces provides the vitamin D and omega-3 requirements—or close to it, depending on the fish): wild caught salmon, sardines, cod, herring, trout.\*\*
  - Eliminate or only rarely eat red meat and processed meats (bacon, ham, salami, hot dogs, beef jerky, and cold meat). Do not eat any charred meat.
  - Eliminate or only rarely eat poultry.
  - Eliminate or only rarely eat eggs.
- **4. Eat ½ cup or more of lentils and/or beans 5-7 days per week.** Navy beans and lentils are my personal health favorites but eat what you enjoy. Choose from black beans, kidney beans, pinto beans, etc.
- **5. Soy is unclear to me.** It seems okay (beneficial even) for prevention and for early, localized cancer. However, I would avoid soy for high grade prostate cancers until we have

further information. Choose minimally processed soy: soybean nuts, edamame, tofu, tempeh. Really research soy yourself and talk with your cancer team (doctors, nutritionists, etc.).

#### 6. Drinks to include and exclude

- A good quality, organic green tea, even consider matcha green tea daily if tolerated.
- Water with the juice and pulp of a fresh lemon squeezed into it daily or routinely.
- Pomegranate juice daily (100% juice, no added sugar), 8 ounces, IF you have MnSOD AA polymorphism\*\*\*
- Good quality water. Filtered tap water is usually fine.
- Coffee seems neutral or even beneficial.
- Almond milk or soy milk as needed to prepare appealing foods.
- Eliminate any animal milk products.
- Eliminate sodas, store-bought juices, and anything in plastic or BPA lined cans.

# 7. Force yourself to add herbs and spices (and fermented condiments), both fresh and dried, to your food. Any food you can add an herb or spice to, then find a way to do it.

- **Use turmeric daily** (best when heated in oil and served with black pepper, so consider using on your vegetables).
- Use ginger daily.
- **Use fresh garlic, one clove every day**, ideally that has been pressed, cut, or diced and allowed to sit for 10 minutes prior to cooking (for development of a beneficial compound called allicin).
- Hot peppers
- Cinnamon
- Parsley
- Cilantro
- Rosemary
- Oregano
- Fermented foods (kimchi, sauerkraut, pickles) that haven't been pasteurized
- Other spices as you explore: chives, cloves, cumin, etc. Don't miss a chance to add a herb or spice.

8. Use high quality oils for dressings, sauces, and cooking. Do not aim necessarily for a low-fat diet, but your diet should be/will be lower in fat than a standard diet by nature of eating more vegetables, fruits, legumes, whole grains, and fish.\*\*\* Good choices are: high quality, fresh, well-stored olive oil, avocado oil, coconut oil, red palm oil (for natural forms of vitamin E), rare use of grass-fed butter (for vitamin K2), and/or unrefined sesame oil (for something called GLA).

- **9. Eat only truly whole grains that you must prepare.**\*\*\*\* (Please understand that the kind you pour from a box and put almond milk on does not generally count towards the benefits of truly whole grains. You can't eat cereal from a box or bag and expect you're eating a cancer-fighter!) Use your prepared whole grains as an accent to your lentils/beans, vegetables, and fruits. Grains really do make foods fun, in my opinion. But DO NOT fall for processed whole grain products like crackers, most pre-made breads, bagels, cereals in a box/bag, etc. These are good whole grains to choose from:
  - Oatmeal (contain GLA, zinc, and prebiotics)
  - Flax (not really a grain but lots of grain-like benefits)
  - Buckwheat
  - Quinoa
  - Wild rice
  - Brown rice

# 10. Do NOT eat the following foods (but if you do, then by all means let the guilt go and renew your efforts as needed and as desired—this is your life):

- Sugar (Spare use of honey or maple syrup is thought to be fine and helps flavor salad dressings, vegetable curries, fruit desserts, etc.)
- Cereal (NO boxed cereals or granolas that contain sweeteners. 100% *completely whole* grain or grains/seeds that you grind are thought to be good, so make your own cereals.)
- Bread (unless you know it is 100% whole grain or unless it is helping you to eat
  densely nutritious foods---for example, if a toasted slice of bread helps you to eat
  sardines with avocado, onions, and cilantro, go for it)
- Meat, particularly red meat, is often correlated with increased cancer. Just avoid it.
  HOWEVER, if you have an intense craving for it that you can't overcome, then listen
  to your body and prepare a good quality red meat dish. (I've seen a cancer patient
  who was craving red meat because she had severe anemia which needed a blood
  transfusion. Her body told her what she needed. I was a little disappointed that she
  chose McDonald's hamburgers as her red meat source.)
- Dairy (If you can't leave out dairy, use grass-fed dairy and/or organic cheeses, ideally just as small accents to make your food taste better if you need to.)

**11. Supplements:** I believe in minimal supplementation and that food should be the source of our supplementation. I like to try to eat so I'm getting vitamin D, vitamin E, selenium, zinc, omega-3, magnesium, etc., through my diet. But, there are certain nutrients that I think are hard to get that could benefit prostate cancer, and those are iodine and vitamin K2. Iodine can come from seafood and seaweed, if a person wants to research those. Vitamin K2 could come from natto (which contains soy and is hard to find in the USA) or from high quality, high fat dairy (which I don't really think agrees greatly with prostate cancer). These might be two supplements worth discussing with your doctor about supplementation (but PLEASE read and research so you have medical studies IN HAND on these---doctors nearly universally believe we get enough iodine and most have never heard of vitamin K2 yet).

That's it for now. Best wishes to you, your family, and your life. Remember, I didn't write this plan for you. It hasn't been tested or tried and could worsen cancer! So if you want to use any or all of it, you need to talk with your doctor. Please take good care of yourself.

Terri F

#### Notes:

\*I encourage you to grind your own "nut butters" rather than buying them pre-ground. Some stores have places you can grind your own. Nuts and seeds are rich in oils that can be oxidized and damaged by air and light. The fresher the "nut butter," the better for the body. I would not use peanut products routinely because of the molds they can grow before processing.

\*\* There is a good physician who believes no nuts or seeds should be used in cancer because they have fat. His name is Dean Ornish, MD. He is very well-known and believes in very low fat intake. However, with all the benefits I found for nuts and seeds, with ALL the cancer-fighting components they have, and with the many studies that show that those who eat more nuts have better outcomes, I just can't exclude them from a cancer diet. BUT, I do think that perhaps the problem with nuts and seeds is the fact that their oils and fats are so easily damaged. Fats and oils work in the cell membrane, and if they're dysfunctional, our cell membranes won't work optimally. So I think QUALITY should be stressed for nuts and seeds and their oils. Although I, a humble, independent researcher, disagree with Dr. Ornish, a power-house of knowledge and research, I want you to definitely know and read up on his work. He has a prostate cancer study with successful outcomes on his diet. That would obviously be a better researched and accepted diet than I have printed above!

Besides nuts, Dr. Ornish also eliminates all meat (including fish) and then he supplements omega-3, selenium, vitamin E, and vitamin D. This doesn't make sense to me. Repeatedly in nutritional medicine, certain supplements are thought to be helpful and end up being detrimental, whereas the foods that contain them don't seem problematic! I believe that very often (not always), isolated supplementation can pose more harm than benefits. I think it's better to allow fish and nuts than it is to eliminate them and then supplement back a tiny fraction of what they provide.

\*\*\*Drinking pomegranate only seems to help if a person has the MnSOD AA polymorphism:

- Prostate Cancer, Nutrition, and Dietary Supplements (PDQ). Health Professional Version. PDQ Integrative, Alternative, and Complementary Therapies Editorial Board. Published online: August 16, 2018. https://www.ncbi.nlm.nih.gov/books/NBK83261/#CDR0000719335\_162
- Note: I was able to figure out my MnSOD status (SOD2; rs4880) by using my 23 and Me raw data input into Promethease.

\*\*\*\*Grains are like nuts in that they have precious, easily damaged oils. Once they're ground, their oils will be oxidized and damaged. I suggest eating them whole (like cooked quinoa or brown rice) OR grinding them fresh yourself. I use a coffee grinder and then use the freshly ground grain or seed (flax, buckwheat, quinoa, brown rice, etc) to make my own bread or sprinkle on foods.

#### **References:**

Note: References have been roughly categorized. However, many references overlap and could appear in other sections as well. Please ask if you have any questions about the references. If you know of another reference that you've read that supports or refutes any of this information, great! Please comment on it so I can consider it and add notes or addendums to my diet.

Painting to begin post: Severin Roesen, Wikimedia Commons, https://commons.wikimedia.org/wiki/File:Severin\_Roesen\_-\_Two-Tiered\_Still\_Life\_with\_Fruit\_and\_Sunset\_Landscape\_-\_Google\_Art\_Project.jpg On eating tons of vegetables and fruits:

- Nguyen JY, Major JM, et al. Adoption of a Plant-Based Diet by Patients with Recurrent Prostate Cancer. Integrative Cancer Therapies. 2006. 5(3): 214-223.
- Richman EL, Carroll PR, Chan JM. Vegetable and fruit intake after diagnosis and risk of prostate cancer progression. International Journal of Cancer Journal International du Cancer. 2012; 131(1): 201-210.

#### On eating tomato products:

- Chan J et al. Diet after diagnosis and the risk of prostate cancer progression, recurrence, and death. Cancer Causes and Control. 2006; 17:199-208
- Haseen F et al. Is there a benefit from lycopene supplementation in men with prostate cancer? A systematic review. Prostate Cancer & Prostatic Diseases. 2009; 12:325-33
- Mroz L. Dietary Advice for Prostate Cancer Patients. Research Gate. 2016. 10.13140/RG.2.1.1539.1125. (https://www.researchgate.net/publication/301542461\_Dietary\_Advice\_for\_Prostate\_Cancer\_Patients)

#### On eating broccoli:

• Canene-Adams K, Lindshield BL, Wang S, et al. Combinations of Tomato and Broccoli Enhance Antitumor Activity in Dunning R3327-H Prostate Adenocarcinomas. Cancer Res. 2007; 67(2): 836-843.

- Richman EL, Carroll PR, Chan JM. Vegetable and fruit intake after diagnosis and risk of prostate cancer progression. International Journal of Cancer Journal International du Cancer. 2012; 131(1): 201-210.
- Kirsh V A, Peters U, et al. Prospective Study of Fruit and Vegetable Intake and Risk of Prostate Cancer. J Natl Cancer Inst 2007;99: 1200-1209.
- Lassed S,Deus CM,Lourenço N, et al. Diet, Lifestyles, Family History, and Prostate Cancer Incidence in an East Algerian Patient Group. BioMed Research International Volume. 2016. Article ID 5730569.

## On eating citrus and the named fruits:

- Keizman D, Frenkel MA, et al. Effect of PectaSol-C modified citrus pectin (P-MCP) treatment on PSA dynamics in patients with nonmetastatic, biochemically relapsed prostate cancer: Results of the interim analysis of a prospective phase II study. Journal of Clinical Oncology 2017 35:15\_suppl, e16588-e16588. (MY NOTE: Modified citrus pectin is not the same as plain old pectin.)
- Paller CJ, Pantuck A, Carducci MA. A Review of Pomegranate in Prostate Cancer. Prostate cancer and prostatic diseases. 2017;20(3):265-270.
- Perez-Cornago A, Travis RC, Appleby PN, et al. Fruit and vegetable intake and prostate cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). International Journal of Cancer. 2017;141(2):287-297. doi:10.1002/ijc.30741.
- Lodi A, Saha A, et al. Combinatorial treatment with natural compounds in prostate cancer inhibits prostate tumor growth and leads to key modulations of cancer cell metabolism. Precision Oncology. 2017; 1 (1) DOI: 10.1038/s41698-017-0024-z

## On adding in the specified vegetables, especially carrots:

- See above references under "eating large amounts of vegetables and fruits."
- Patel S, Goyal A. Recent developments in mushrooms as anti-cancer therapeutics: a review. 3 Biotech. 2012;2(1):1-15.
- Xu X, Cheng Y, Li S. et al. Dietary Carrot Consumption and the Risk of Cancer. Eur J Nutr. 2014. 53: 1615.

# On eating nuts:

- Want W, Yang M, Kenfield SA, et al. Nut consumption and prostate cancer risk and mortality. British Journal of Cancer. 2016. 115: 371–374.
- Sparccarotella KJ, Kris-Etherton PM, et al. The effect of walnut intake on factors related to prostate and vascular health in older men. Nutrition Journal. 2008. 7:13.
- [My note: Dietary zinc beneficial but supplement not.] Epstein MM, Kasperzyk JL, Andrén O, Giovannucci EL, Wolk A, Håkansson N, Andersson SO, et al. Dietary zinc and prostate cancer survival in a Swedish cohort. Am J Clin Nutr. 2011 Mar;93(3):586-93.

- Richman EL, Kenfield SA, Chavarro JE, et al. Fat Intake After Diagnosis and Risk of Lethal Prostate Cancer and All-Cause Mortality. JAMA Intern Med. 2013;173(14):1318–1326. doi:10.1001/jamainternmed.2013.6536
- Azrad M et al. Flaxseed-derived enterolactone is inversely associated with tumor cell proliferation in men with localized prostate cancer. <u>I Med Food</u> 2013 Apr; 16(4): 357–60.
- "Flaxseed Supplementation (Not Dietary Fat Restriction) Reduces Prostate Cancer Proliferation Rates in Men Presurgery." Cancer, Epidemiology, Biomarkers & Prevention. December 2008 17; 3577.

# On eating fish:

- Chavarro JE, et al. A 22-y prospective study of Fish intake in relation to prostate cancer incidence and mortality. American Journal of Clinical Nutrition. 2008; 88(5):1297-303.
- Castelló A, Boldo E, et al. Mediterranean Dietary Pattern is Associated with Low Risk of Aggressive Prostate Cancer: MCC-Spain Study. The Journal of Urology, 2018; 199 (2): 430 DOI: 10.1016/j.juro.2017.08.087

# On eliminating processed meats and charred meats, eggs, poultry:

- Zheng W, Lee S-A. Well-done Meat Intake, Heterocyclic Amine Exposure, and Cancer Risk. Nutrition and cancer. 2009;61(4):437-446. doi:10.1080/01635580802710741.
- Alexander DD, et al. A review and meta-analysis of prospective studies of red and processed meat intake and prostate cancer. Nutrition Journal. 2010; 9:50.2.
- John EM, et al. Meat consumption, cooking practices, meat mutagens, and risk of prostate cancer. Nutrition and Cancer. 2011; 63(4):525-37.3.
- Richman EL et al. Egg, red meat, and poultry intake and risk of lethal prostate cancer in the prostate-specific antigen-era: Incidence and survival. Cancer Prevention Research. 2011; 4(12):2110-21.4.
- Punnen S, et al. Impact of meat consumption, preparation, and mutagens on aggressive prostate cancer. PLoS One. 2011; 6(11):e27711.5.
- Frattaroli J, et al. (Dean Ornish) Clinical events in prostate cancer lifestyle trial: Results from two years of follow-up. Urology. 2008; 72(6):1319-23.
- (PDF) Dietary Advice for Prostate Cancer Patients. Available from: https://www.researchgate.net/publication/301542461\_Dietary\_Advice\_for\_Prostat e\_Cancer\_Patients [accessed Jul 25 2018].

# On eating lentils:

 (PDF) Dietary Advice for Prostate Cancer Patients. Available from: <a href="https://www.researchgate.net/publication/301542461">https://www.researchgate.net/publication/301542461</a> Dietary Advice for Prostate e Cancer Patients [accessed Jul 28 2018] • Li J, Mao Q-Q. Legume intake and risk of prostate cancer: a meta-analysis of prospective cohort studies. Oncotarget. 2017;8(27):44776-44784. doi:10.18632/oncotarget.16794.

## On eating soy:

- Yan L, & Spitznagel EL. Soy consumption and prostate cancer risk in men: a revisit of a meta-analysis. American Journal of Clinical Nutrition. 2009; 89(4):1155-11632.
- Goetzl MA, et al. Effects of soy phytoestrogens on the prostate. Prostate Cancer & Prostatic Diseases. 2007; 10(3):216-2233.
- Kwan W, et al. A phase II trial of a soy beverage for subjects without clinical disease with rising prostate-specifc antigen after radical radiation for prostate cancer. Nutrition & Cancer. 2010; 62(2):198-207
- Applegate CC, Rowles JL, Ranard KM, Jeon S, Erdman JW. Soy Consumption and the Risk of Prostate Cancer: An Updated Systematic Review and Meta-Analysis. *Nutrients*. 2018;10(1):40. doi:10.3390/nu10010040.

#### On drink choices:

- Guo Y, Zhi F, Chen P, et al. Green tea and the risk of prostate cancer: A systematic review and meta-analysis. Arora. S, ed. Medicine. 2017;96(13):e6426. doi:10.1097/MD.000000000006426.
- Perez-Cornago A, Travis RC, Appleby PN, et al. Fruit and vegetable intake and prostate cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). International Journal of Cancer. 2017;141(2):287-297. doi:10.1002/ijc.30741.
- Paller CJ, Pantuck A, Carducci MA. A Review of Pomegranate in Prostate Cancer. Prostate cancer and prostatic diseases. 2017;20(3):265-270. doi:10.1038/pcan.2017.19.
- Sen A et al. Coffee and tea consumption and risk of prostate cancer in the European Prospective Investigation into Cancer and Nutrition. Int J Cancer. 2018 Jun 26. doi: 10.1002/ijc.31634. [Epub ahead of print]
- Jiadong Xia, Jie Chen et al. An Up-to-date Meta-analysis of Coffee Consumption and Risk of Prostate Cancer. Urology Journal. 2017; 14(5).

#### On using herbs and spices:

- Zheng J, Zhou Y, Li Y, Xu D-P, Li S, Li H-B. Spices for Prevention and Treatment of Cancers. Nutrients. 2016;8(8):495. doi:10.3390/nu8080495.
- Arunkumar, A., Vijayababu, M.R., Srinivasan, N. et al. Mol Cell Biochem (2006) 288: 107. <a href="https://doi.org/10.1007/s11010-006-9126-6">https://doi.org/10.1007/s11010-006-9126-6</a>
- Yoon J, Yae, Kim, et al. 2'-Hydroxycinnamaldehyde inhibits cancer cell proliferation and tumor growth by targeting the pyruvate kinase M2. Cancer letters. 2018. 434. 10.1016/j.canlet.2018.07.015.

• Lodi A, Saha A, et al. Combinatorial treatment with natural compounds in prostate cancer inhibits prostate tumor growth and leads to key modulations of cancer cell metabolism. Precision Oncology. 2017; 1 (1) DOI: 10.1038/s41698-017-0024-z

## On use of added oils and not necessarily aiming for low fat numbers:

 Richman EL, Kenfield SA, Chavarro JE, et al. Fat Intake After Diagnosis and Risk of Lethal Prostate Cancer and All-Cause Mortality. *JAMA Intern Med*. 2013;173(14):1318–1326. doi:10.1001/jamainternmed.2013.6536

#### On eating whole grains:

- [Flax] Simon JA, et al. The relation of alpha-linolenic acid to the risk of prostate cancer: A systematic review and meta-analysis. American Journal of Clinical Nutrition. 2009; 89(5):1558S-1564S.
- (PDF) Dietary Advice for Prostate Cancer Patients. Available from: https://www.researchgate.net/publication/301542461 Dietary Advice for Prostate Cancer Patients [accessed Jul 25 2018].
- Azrad M et al. Flaxseed-derived enterolactone is inversely associated with tumor cell proliferation in men with localized prostate cancer. <u>J Med Food</u> 2013 Apr; 16(4): 357–60.

#### On foods to eliminate:

- Zheng W, Lee S-A. Well-done Meat Intake, Heterocyclic Amine Exposure, and Cancer Risk. Nutrition and cancer. 2009;61(4):437-446. doi:10.1080/01635580802710741.
- Park S-W, Kim J-Y, Kim Y-S, Lee SJ, Lee SD, Chung MK. A Milk Protein, Casein, as a Proliferation Promoting Factor in Prostate Cancer Cells. The World Journal of Men's Health. 2014;32(2):76-82. doi:10.5534/wjmh.2014.32.2.76.
- Chan JM, Stampfer MJ, et al. Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study. Am J Clin Nutr. 2001 Oct;74(4):549-54.
- Rohrmann S, Platz EA, Kavanaugh CJ, et al. Meat and dairy consumption and subsequent risk of prostate cancer in a US cohort study. Cancer Causes Control. 2007 Feb;18(1):41-50.
- Raimondi S, Mabrouk JB, et al. Diet and prostate cancer risk with specific focus on dairy products and dietary calcium: a case-control study. Prostate. 2010 Jul 1;70(10):1054-65. doi: 10.1002/pros.21139.

#### On fat intake:

 Richman EL, Kenfield SA, Chavarro JE, et al. Fat Intake After Diagnosis and Risk of Lethal Prostate Cancer and All-Cause Mortality. JAMA Intern Med. 2013;173(14):1318–1326. doi:10.1001/jamainternmed.2013.6536