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Reality check: no such thing as a miracle food

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Cancer is a disease that invokes fear, so it is not surprising that the public is eager to identify ways to decrease their risk. Food is a familiar and universally shared experience, which makes it a popular cancer prevention topic for the media. Attention-grabbing headlines and sound bites draw readers/viewers in. Foods are often promoted as “anti-cancer foods” or “super foods”, which have the power to magically prevent or “cure” cancer. But, do such “miracle” foods really exist? Do we really have sufficient evidence to make these claims to an eager public?

As an example, a recent segment from the Dr. Oz show, entitled “Anti-Cancer Diet,” suggested that endive, red onion, and sea bass are anti-cancer foods that can decrease risk of ovarian cancer by up to 75% (1). The segment claimed that kaempferol, a flavonoid found in endive, induces apoptosis in ovarian cancer cells, and inhibits cancer progression by blocking angiogenesis. Several studies have demonstrated that kaempferol has apoptotic (2, 3) and anti-angiogenic activity *in vitro* (4-9), however, it is unclear whether these findings translate to free-living human populations consuming kaempferol in usual dietary quantities. An association between raw endive intake and ovarian cancer has been reported by only one prospective observational study, in which endive was one of 39 foods evaluated (10). Given the large number of statistical tests, it is likely that the reduction in risk of ovarian cancer related to higher endive intake might have been observed solely by chance (11). No association with ovarian cancer risk was observed for other vegetables that actually provide more kaempferol per serving than endive (**Table 1**) (12), such as kale (RR: 1.02, 95% CI: 0.31-3.35) and spinach (RR: 1.43, 95% CI: 0.86-2.37), and there was a lack of association with cooked endive (RR: 0.78, 95% CI: 0.48-1.26).

Flavonoids in red onions were also touted as being able to prevent ovarian cancer. A reduced risk of ovarian cancer related to higher onion intake, which was assessed after cancer diagnosis, was reported by one case-control study (13). Conversely, three large prospective studies (the European Prospective Investigation into Cancer Nutrition study, the Women's Health Study, and the Nurses’ Health Study), where data on usual dietary intake were collected prior to cancer diagnosis, reported no association between onion intake and ovarian cancer risk (14-16). The retrospective nature of case-control studies makes this study design subject to unique biases (especially recall bias), and it is essential to interpret findings from a single case-control study with caution (11). Additionally, red onions, rather than white or yellow onions, were specifically recommended, but whether red onions contain more flavonoids than white or yellow onions is questionable. A study comparing total flavonoid contents of the 10 onion varieties (1 red, 1 white and 8 yellow) showed that

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two varieties of yellow onions (Western Yellow and New York Bold) had the highest flavonoid contents (69.2 mg/100g and 55.2 mg/100 g, respectively), followed by red onions (Northern Red, 35.1 mg/100g) and other yellow onion varieties (17).

The other food identified in the episode of the Dr. Oz Show as having “anti-ovarian cancer” activity was sea bass because of the high content of omega-3 fatty acids which were also claimed to have anti-angiogenic activity. Yet, again, the evidence of an association between fish intake and ovarian cancer risk is not convincing. A meta-analysis of 2 cohort studies and 6 case-control studies concluded that high fish intake was associated with a marginally significant reduction in ovarian cancer risk; however, statistically significant inverse associations were observed only in case-control studies (18). Many different types of fatty, predatory fish are high in omega-3 fatty acids, several of which (including mackerel, salmon and herring) have much higher contents of omega-3 fatty acids compared to sea bass (**Table 2**) (19).

Media coverage of these so-called “miracle foods” is often just a marketing tool. Stories of “miracle foods” sell magazines and advertising space; food industries often sponsor research to show that their foods or products are superior, and supplement industries look to boost sales. In real life, however, we do not live on one single food item. We eat meals that consist of a considerable variety of foods, several times each day. When evaluating potential cancer prevention benefits from the foods we eat, we need to consider diet in its totality, as well as other lifestyle factors such as physical activity, and the potential influences of genetic and epigenetic factors.

Foods and food components consumed together may have synergistic or antagonistic effects on health outcomes. For example, apiaceous vegetables (carrots, celery, parsnips) appear to reduce the activity of cytochrome P450 1A2 (CYP1A2), while cruciferous vegetables (broccoli, kale, Brussel sprouts) induce CYP1A2 activity(20). A crossover feeding study compared the effects of diets containing cruciferous only, apiaceous only and a diet with both vegetable families and found that CYP1A2 activity observed on the high cruciferous diet was reduced by the addition of apiaceous vegetables to the diet (20).

In addition to interactions between different foods and food components, some dietary exposures may have both beneficial and detrimental health effects depending on the outcome in question. For example, moderate alcohol consumption has been shown to decrease risk for cardiovascular disease, but increase the risk for breast cancer (21, 22). Similarly, while sea bass may be a good dietary source of omega-3 fatty acids, it is also important to consider the mercury content of fatty fish (**Table 2**) (Note: a concern about sea bass as a potential source of mercury was mentioned in the written transcript of the episode posted on the Dr. Oz show website (23), but was not mentioned during the actual television segment).

Further complicating study interpretation is that intraindividual genetic differences may lead to differences in the health benefits of certain dietary interventions. For example, individuals with the methylenetetrahydrofolate reductase (*MTHFR*) *C677T TT* genotype have been found to be at higher risk of certain types of cancers in the setting of folate deficiency, and may receive greater benefits from higher dietary folate intake compared to individuals with the *CT* or *CC* genotypes (24).

Many types of studies are needed to evaluate the impact of diet in cancer prevention, and no one study design is perfect. Drawing conclusions based on one study or a few studies of the same design, ignores the importance of limitations inherent in each study design. Large, observational studies are useful in hypothesis generating or testing whether findings from

laboratory research hold true in free-living human populations. However, the analyses from these studies are often cross-sectional, limiting the ability to interpret causality, and potential confounding by other environmental or lifestyle factors cannot be eliminated with certainty. In these large observational studies, dietary intake is usually assessed using a food frequency questionnaire (FFQ), which often asks individuals to report usual intake of food groups rather than individual food items. Intake of an individual food item is estimated by weighing each food item within the FFQ grouping using certain reference data such as age- or sex-specific consumption patterns (25). As a result, misclassification of individual food intake is unavoidable. In addition, data on food preparation methods and grouping of foods within meal events are rarely captured by FFQs, and thus cannot be included as potential effect modifiers. On the other hand, feeding studies and chemoprevention trials necessarily focus on single foods or nutrients, and thus do not represent real conditions in free-living human populations. Feeding studies are labor intensive and a considerable burden to participants, and as a result, are often not adequately powered to capture interactions between nutrients. Additionally, cancer is a relatively rare disease with a long onset, which limits the feasibility of using intervention trials with cancer incidence as an end point.

Nutritional scientists and epidemiologists should be cognizant of the public health messages that are taken away from their individual studies, and not sensationalize the findings or contribute to the media frenzy around a single study. Current systematic reviews and meta-analyses of the diet and cancer prevention literature conducted by World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) (26) and others are based on data from studies of single foods and nutrients simply because that is the type of data that is most commonly available. However, the actual WCRF/AICR dietary recommendations for cancer prevention are whole foods based (**Table 3**)(26). While perhaps not as “sexy” as Dr. Oz would like, the public needs more information about the effects of diet as a whole on cancer risk, as well as the importance of achieving and maintaining an ideal body weight, regular physical activity, and avoiding a sedentary lifestyle.

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Table 1

Major dietary sources of kaempferol

Food item	Kaempferol (mg[a])
Kale, raw	46.80
Mustard greens, raw	38.30
Welsh onions, raw	24.95
Watercress, raw	23.03
Chinese cabbage, raw	22.51
Cress, raw	13.00
Turnip greens, raw	11.87
Endive, raw	10.10
Chives, raw	10.00
Collards, raw	9.48
Radish leaves, raw	7.72
Fennel leaves, raw	6.50
Spinach, raw	6.38
Chinese cabbage (pak-choi), raw	4.35
Green onions, raw	3.60
Leeks	2.67
Chicory greens, raw	2.45
Kohlrabi, raw	2.43
Red lettuce, raw	2.24
Garlic chives, raw	2.12
Rocket, raw	1.78
Horseradish, whole	1.58
Parsley, raw	1.49
Tea (green or black), brewed	1.31

Data sources: U.S. Department of Agriculture. Agricultural Research Service. 2011.

USDA Database for the Flavonoid Content of Selected Foods, Release 3 (12).

[a]Per 100 gm edible portion.

Table 2

Omega-3 fatty acid (FA) and mercury contents in major dietary sources

Food item	Omega-3 FA (gm/100 gm)[a]	Mercury (ppm)[b]
Mackerel, Atlantic, raw	2.51	0.050
Salmon, Atlantic, farmed, raw	2.36	0.022
Anchovy, European, canned in oil, drained	2.10	0.017
Herring, Pacific, raw	1.83	N/A
Salmon, Atlantic, wild, raw	1.72	0.022
Herring, Atlantic, raw	1.63	N/A
Mackerel, Pacific, raw	1.56	0.088
Spanish mackerel, raw	1.44	0.454
Tuna, Bluefin, raw	1.30	0.368
Sardine, canned in oil, drained	0.98	0.013
Shark, raw	0.95	0.979
Trout, raw	0.91	0.071
Tuna, albacore, canned in water, drained	0.88	0.350
Swordfish, raw	0.79	0.995
Bass, freshwater, raw	0.75	0.354
Sea bass, raw	0.67	0.152
Sea trout, raw	0.48	0.235
Catfish, wild, raw	0.46	0.025
Mackerel, king, raw	0.42	0.730
Tuna, light, canned in water, drained	0.28	0.128
Tuna, yellowfin, raw	0.23	0.354
Cod, Pacific, raw	0.22	0.111
Cod, Atlantic, raw	0.19	0.111

[a] Per 100 gm edible portion. Including eicosapentaenoic acid (EPA, 20:5 n-3), docosapentaenoic acid (DPA, 22:5 n-3) and docosahexaenoic acid (DHA, 22:6 n-3). USDA National Nutrient Database for Standard Reference, Release 24 (19).

[b] U.S. Food and Drug Administration, Mercury Levels in Commercial Fish and Shellfish (1990-2010) (25).

Table 3

The 2007 WCRF/IACR recommendations for cancer prevention

	Recommendation
1.	Be as lean as possible within the normal range of body weight.
2.	Be physically active as part of everyday life, for at least 30 minutes every day.
3.	Limit consumption of energy-dense foods. Avoid sugary drinks.
4.	Eat mostly foods of plant origin, more of a variety of less-starchy vegetables, fruits, whole grains and legumes.
5.	Limit consumption of red meat (such as beef, pork and lamb) and avoid processed meat.
6.	If consumed at all, limit alcoholic drinks to 2 for men and 1 for women a day.
7.	Limit consumption of salt-preserved, salted, or salty foods and foods processed with salt.
8.	Aim to meet nutritional needs through diet alone. Don't use supplements to protect against cancer.
9.	Aim to breastfeed exclusively infants exclusively up to 6 months and continue with complimentary feeding thereafter.[a]
10.	Cancer survivors should follow the recommendations for cancer prevention after cancer treatments

Source: The WCRF/AICR Second Expert Report (24)

[a]Special population recommendations.