Nutrition in Clinical Care

Role of fruit juice in achieving the 5-a-day recommendation for fruit and vegetable intake

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Although there is strong evidence that consumption of fruit and vegetables is associated with a reduced rate of all-cause mortality, only a minority of the population consumes 5 servings a day, and campaigns to increase intake have had limited success. This review examines whether encouraging the consumption of fruit juice might offer a step toward the 5-a-day target. Reasons given for not consuming whole fruit involve practicalities, inconvenience, and the effort required. Psychologically, what is important is not only basic information about health, but how individuals interpret their ability to implement that information. It has been argued that fruit juice avoids the problems that commonly prevent fruit consumption and thus provides a practical means of increasing intake and benefitting health through an approach with which the population can readily engage. Those arguing against consuming fruit juice emphasize that it is a source of sugar lacking fiber, yet juice provides nutrients such as vitamin C, carotenoids, and polyphenols that offer health-related benefits. Actively encouraging the daily consumption of fruit juice in public health policy could help populations achieve the 5-a-day recommendation for fruit and vegetable intake.

INTRODUCTION

In many countries, although not all, half or 1 glass of unsweetened 100% fruit or vegetable juice counts toward 5 portions a day. Yet, some have claimed that fruit juice is little more than a source of sugar, predisposing consumers to weight gain and obesity,[1,2] and have proposed that fruit juice should not be included. The veracity of this argument has been examined, and given advantages in terms of the ease of consumption of juice, it was considered whether a recommendation to consume fruit juice might be a simple and effective means of moving toward the goal of 5 servings a day. It was concluded that 100% fruit juice should be distinguished from juice sweetened with sugar but that daily consumption would benefit large sections of the population.

In this area, the argument has tended to be based on a particular isolated nutrient, usually sugar, but to a lesser extent fiber. There is a need, however, to remember that 100% juice, the topic of this review, does not have added sugar and should be distinguished from sweetened juices and fruit cordials. Nevertheless, the World Health Organization[3] suggested limiting the levels of free sugars in the diet with the implicit assumption that, for public health purposes, all sources can be added together and treated as one. However, Public Health England,[4] when they considered the definition of free sugars, commented that current definitions reflected a "limited understanding of the extent to which the cellular structure of different types of processed foods containing naturally occurring sugars is broken down and the differences in the physiological

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response to sugar consumed in different forms." This includes the sugars found in fruit.

The first objective of this review was to establish the factors that make increasing fruit and vegetable consumption so difficult and to consider the extent to which juice can solve these problems. Then the alleged benefits and alleged negative consequences of drinking juice were examined. To date the debate has centered on sugar and fiber, although meta-analysis finds that additional portions of fruit and vegetables, but also fruit juice, decrease the risk of coronary heart disease and all-cause mortality.[5]

The wider context is that only a small minority of the population consumes the recommended amount of fruit and vegetables,[6,7] and campaigns to increase intake have had little success. If fruit juice offers the means of adding to efforts to consume 5 servings of fruits and vegetables per day in a more acceptable way than preparing and consuming intact items, should this become a recommended approach, albeit one that does not replace the existing intake of intact fruit and still favors the majority of intake being intact fruit?

FACTORS INFLUENCING WHETHER INDIVIDUALS ACHIEVE 5 SERVINGS A DAY

In one sense, 5-a-day campaigns have been extremely successful. It is widely known that the eating of fruit and vegetables is an essential aspect of a healthy diet. Supermarket shelves have many food items labeled with the banner "one of your five-a-day." There is no need to say this refers to 1 portion of the recommended fruit and vegetable servings or why it is beneficial: it can be assumed that people understand the implicit message.

However, because the majority of the population fails to consume the required amounts, it is apparent that it is insufficient to merely convey basic information to consumers. After identifying 50 trials with children, a Cochrane review concluded that "the evidence for how to increase fruit and vegetable consumption of children remains sparse."[8] To increase consumption there is a need to understand the basic motivations that prevent the choice of fruit and vegetables and to offer solutions that minimize their impact. In this context, it was argued that fruit juice successfully addresses many problems and therefore has the potential to help achieve the recommended intake.

The likelihood of consumption varies with a range of social and psychological parameters. A survey in New York found that 50% of the population ate <1 portions a day[6]: low levels of education and being male were associated with a lower intake. Other problems included no convenient access to fresh produce and the high cost of produce. In another US study, those trying or not trying to increase intake were compared.[7] Those not trying to change their diet were more likely to be male, younger, and have a higher body mass index (BMI). Barriers to consumption included the impression that fruits and vegetables took time to prepare; they do not stay fresh for long so are not readily available in the home; they were costly; and they do not satisfy hunger.[7]

Psychosocial factors

A review of psychological and social factors that influence consumption concluded that there was strong evidence that the eating of fruit and vegetables was influenced by self-efficacy, social support, and knowledge.[9] There was weaker evidence for the influence of attitudes/beliefs, perceived barriers to consumption, the intention to change, and autonomous motivation.

According to social cognitive theory,[10] self-efficacy is a major factor in determining the setting of goals and the resulting effort that is expended. There is a distinction between "outcome expectancy" (the estimation that a certain outcome will result following a given behavior) and "efficacy" (the belief you can successfully carry out that behavior). What is important is not only basic information, but how the individual interprets the relevance of that information to his or herself. That is, although it might be fully accepted that fruit and vegetable intake results in better health, an individual will have little motivation if there is also a perception that he or she is unable to perform the relevant behavior.

As an example, Kreausukon et al[11] compared interventions aimed at increasing intake, based on either giving basic information or, in addition, enhancing self-efficacy. The control group received information concerning general health and nutrition education, whereas a second group, in addition, received a program that focused on self-efficacy and planning. For example, they planned when, where, and how they intended to consume fruit and vegetables. Both the intention to consume and the amount consumed were greater in those who received self-efficacy training.

Self-determination theory distinguishes autonomous from controlled motivation. When a person fully endorses a behavior and experienced choice, this is said to reflect "autonomous (intrinsic) motivation." When you feel coerced, experience pressure and obligation, this is said to reflect "controlled (extrinsic) motivation." McSpadden et al[12] reported that, whereas autonomous motivation was positively related to intake, there was a negative association with controlled or extrinsic motivation. An example of a question related to autonomous motivation is "I eat fruit and vegetables because I want to take responsibility for my own health" whereas a controlled motivation question was "... because I want others to approve of me." This type of finding is important because, when trying to change human behavior, some basic information is necessary, although this can be provided relatively easily; the difficult part is generating the motivation to act on that information.

The nature of motivation is particularly relevant when considering health-related behavior. Many such behaviors reflect extrinsic motivation: that is they are not carried out for current enjoyment but for some subsequent reward such as social approval. In contrast, intrinsic motivation results in freely chosen behavior that reflects core beliefs and values, and carrying it out generates spontaneous rewards and satisfaction.

It has been found that intrinsic motivation is more likely to result in better outcomes than extrinsic motivation.[13] There is a greater likelihood that you will continue to engage in a behavior when is intrinsically motivated,[14] when it is carried out for its own sake and thus there is engagement and effort. Deci and Ryan[15] identified 3 factors that lead to intrinsic motivation and hence the initiation of behavior: competence, one must have the ability to do the job; autonomy, one must be free to make one's own decision without any coercion; relatedness, one should feel cared for, supported, and connected to others.

Efficacy and social support[9] have parallels with the factors that benefit intrinsic motivation, competence and relatedness.[15] In addition, knowledge[9] and autonomy have been mentioned.[15] Below it is argued that fruit juice, rather than intact fruit, is more likely to generate feelings of self-efficacy and hence is more likely to be associated with long-term changes in diet.

Motivation to drink fruit juice

The major reasons for not consuming 5 servings of fruit and vegetables a day relate to practicalities, convenience, and the effort required. Fruit juice offers a solution to many of these problems, and hence has the potential to increase consumption. Juice is convenient, easily transportable and requires no preparation. It can be stored in bulk because it has a longer shelf life than fresh products. It does not need preparation, and because it can be stored at home, additional visits to the supermarket are unnecessary. It can be consumed on the move, and its taste makes it attractive to many. Juice is also a cheaper method of purchase: it can take about fifteen oranges to make a liter of juice, yet in a supermarket the juice costs about a quarter of the price of intact fruit.

From a psychological perspective the perceived problems related to fruit and vegetable consumption will reduce feelings of efficacy[10] and competence[15] and will reduce intrinsic motivation and hence the likelihood of regular consumption. Because consuming juice can overcome these problems, the likelihood of consumption is increased. "Efficacy" is central: there has to a belief that one can successfully carry out the necessary actions. The juiced rather than intact variety is associated with feelings of efficacy and competence, with the possibility that this will generate intrinsic motivation. Few people will feel unable to open a carton or bottle.

POSSIBLE NEGATIVE CONSEQUENCES OF CONSUMING JUICE

Even if one accepts the argument that it is easier to encourage the consumption of juice rather than intact items, any recommendation to consume juice requires evidence that a similar benefit results as with whole fruit. Those arguing that fruit juice should not have a role in the 5 servings a day, typically claim that the sugar in juice results in obesity and that the removal of fiber reduces its nutritional quality.

For brevity, a brief overview of the literature has relied on the quoting of systematic reviews and meta-analyses. Such balanced independent summaries prevent the cherry-picking of papers to support a preexisting point of view and, when considering public health, indicate the most common response.

Fruit juice, caloric intake, and obesity

When the French government reassessed their dietary guidelines in 2016, it was decided that fruit juices should be classified as a sugary drink rather than being placed in the fruit category. Although in France it is still possible to count juice as part of the 5 a day, there was clearly a concern about sugar and obesity. The medical campaigning group Action on Sugar[16] goes as far as recommending the removal of fruit juice from the diet to help reduce obesity. Such a view gained support from Jebb,[17] who, when she was the advisor on obesity to the United Kingdom government, suggested that orange juice should no longer be 1 of the 5 a day. She stated that orange juice contains as much sugar as fizzy drinks and is absorbed so quickly that by the time it gets to one's stomach one's body doesn't know whether it's Coca-Cola or orange juice. However, should sugar that is intrinsic to fruit be viewed in a similar manner to the sugar added to soda?

There is considerable evidence that the consumption of sugar-sweetened beverages (SSBs) is a risk factor for obesity, and because fruit juice contains intrinsic sugar, the 2 have often been lumped together. Sugar increases palatability and thus increases intake without there being sufficient calorie compensation at the next meal.[18] In addition, the reduced level of fiber in juice has been viewed as reducing satiety. However, an interesting approach was to give orange juice 3 times a day, either with or between meals[19]; when consumed with a meal, the juice resulted in lower fat mass and gamma-glutamyl transferase levels, a measure of liver functioning. In contrast, consumption between meals increased body fat and decreased insulin sensitivity. However, preload studies should be viewed only as hypothesis generating because energy compensation can take place over a longer period than these studies monitor.[20] The important question is whether, over time, drinking fruit juice increases body weight to the extent that there is an increased incidence of disease.

A meta-analysis illustrates a common problem.[21] When 20 cohort studies of children and 7 studies of adults were summarized, the consumption of SSBs was associated with weight gain over the course of a year. However, the definition of SSBs involved adding together soda, sweetened beverages, sports drinks, and generic fruit drinks. As such, nothing can be concluded about 100% fruit juice. There is a need to distinguish 3 types of drink; those sweetened with sugar that contain no fruit juice; drinks with less than 100% fruit juice that are sugar sweetened; and 100% fruit juice to which no extrinsic sugar has been added. Is 100% fruit juice only guilty by association, or does it predispose to obesity in its own right?

Children

Consumption by children has attracted particular attention. The American Academy of Pediatrics[22] acknowledges potential benefits but also the possibility of the detrimental consequences of drinking fruit juice. In those aged <6 years, there is the possibility of diarrhea, dental caries, and the development of an allergic reaction to orange. After this age, fewer issues arise, although the possibility of weight gain has been a concern for some. The consumption of whole fruit rather than a drink was encouraged, although it was unclear why these were viewed as alternatives: drinks quench thirst and prevent dehydration, whereas there are different motivations to eat whole fruit. A systematic review found that in those aged <12 years, SSBs were associated with total and central adiposity, whereas drinking 100% fruit juice was not.[23] However, in those aged <5 years, there was some evidence that juice was associated with greater body weight. A later review concluded, "Consumption of 100% fruit juice is associated with a small amount of weight gain in children ages 1 to 6 years that is not clinically significant, and is not associated with weight gain in children ages 7 to 18 years."[24] Again, it is essential to distinguish 100% fruit juice from sugar-sweetened products. The recommendation of the American Academy of Pediatrics is that no more than 4–6 fluid ounces, or 100–130 mL per day of juice, be consumed by young children.

Adults

The 2 Nurses Health Studies and the Health Professionals Follow Up cohort were integrated to produce a cohort of 120 877 participants,[25] and over 4 years changes in the intake of foods were related to changes in weight. An increased intake of french fries was associated with an annual increase in weight of 0.84 lbs (380 g); potato chips (crisps) with 0.42 lbs (192 g); SSBs with 0.25 lbs (113 g); and fruit juice with 0.08 lbs (35 g). In contrast, an increased fruit intake decreased weight by −0.12 lbs a year (55 g). It was suggested that the small effect of fruit juice on body weight reflected its consumption in small quantities and a tendency to have 1 rather than multiple servings. These findings assumed that the portion of fruit juice was 240 mL, and if instead the recommended portion of 150 mL had been consumed, the annual increase in weight would have been 0.05 lbs (22 g) a year. In fact, the findings cannot be taken at face value because the studies were not able to distinguish 100% fruit juice from sweetened beverages, and inevitably, in part at least, the results reflected added sugar.

In fact, many studies have found that the consumption of fruit juice was associated with lower body weight. Pereira and Fulgoni[26] used National Health and Nutrition Examination Survey data (NHANES) to examine the influence of 100% fruit juice. Although only 28% of participants consumed fruit juice, they were more insulin sensitive, had a lower risk of obesity, and were less likely to have metabolic syndrome. Similarly, a sample of 13 971 from the 2003–2006 NHANES survey found that those adults who consumed 100% orange juice had a lower BMI, waist circumference, and percentage body fat,[27] although these effects of orange juice were not found in children and adolescents. More recently, a Canadian study examined 26 340 individuals and found that fruit intake was inversely related to BMI, waist circumference, and the percentage of fat mass,[28] with a broadly similar pattern being associated with 100% fruit juice but not vegetables.

Celis-Morales et al[29] collected data in 7 European countries and identified factors that predicted adult obesity. A greater BMI was associated with a higher energy intake, eating red meat, and consuming SSBs. In contrast, a lower BMI was associated with a greater intake of whole grains, fruits and vegetables, and a Mediterranean diet, as well as consumption of fruit juice.

The picture is that at any point in time the consumption of fruit juice is associated with a lower BMI.[26–29] However, if you change your diet and consume additional calories, over time your body weight will rise[25]; this is true regardless of the source of additional calories. As such, fruit juice is no different than other food and is better than many because it produces a relatively small increase in weight. The Harvard studies[25] found that juice increased weight by only 0.05 lbs (22 g) a year, although there had been no correction for the increase in calorie intake that may well explain the finding. Similarly, when, over 3 years, weight was monitored in 49 106 postmenopausal women,[30] each additional daily serving of 100% fruit juice was associated with an annual gain of 0.13 lbs (59 g).

Hebden et al[31] reviewed studies that related fruit consumption to adiposity. Four of 6 cross-sectional studies found that fruit consumption was associated with a lower level of at least 1 measure of adiposity. However, none of 11 intervention trials found that increased consumption was influential in this respect, although the trials tended to be small and lasted 4–12 weeks.

Hebden et al,[31] also concluded that fruit juice increased weight over the long term—that is, allegedly fruit and fruit juice had opposite effects, This conclusion was based on 8 mostly large prospective cohorts, of which only 1, the smallest, had distinguished drinking fruit juice with or without added sugar. All other surveys used the Harvard Willett Food Frequency Questionnaire, which simply asks the frequency that fruit juices were consumed but does not distinguish juice to which sugar has and has not been added. When generically reporting the consumption of fruit juice, it is inevitable that 100% fruit juice and sugar-sweetened juice will be treated as one. As more extrinsically sweetened juice is consumed, it follows that nothing can be concluded about 100% fruit juice. Given that, when these types of juices are distinguished, the outcomes differs[23,26–29] this is a serious problem. The hypothesis that needs testing is that adding sugar to juices results in a heavier weight, whereas 100% fruit juice does not.

When Rampersaud and Valim[32] more specifically reviewed the relationship between orange and grapefruit consumption and anthropometric measures, they found a lower BMI in those who consumed juice, although intervention studies found no influence. They concluded that moderate consumption of citrus juices "do[es] not appear to negatively impact body weight, body composition, or other anthropometric measures in children and adults."[32]

The picture is that a dietary style commonly associated with a lower BMI includes both intact fruit and juice. However, in terms of increasing energy intake, since fruit juice is a minor problem compared with a range of more calorific foods,[25] it should be consumed in moderation to ensure that calorie intake does not markedly increase.

It is noteworthy that rather than playing a major role in calorie intake, fruit juice consumption decreases throughout life.[33,34] A systematic review found that Germans consumed the most fruit juice and Italians consumed the least, but in a range of countries, consumption decreased with age.[34] Thus, if a reduction of the consumption of fruit juice is recommended, it will affect a minority who drink juice, and this minority decreases consumption with age. In addition, for many years the juice industry has bemoaned the fact that overall consumption has continually declined. Between 2013 and 2016 consumption declined by 10% in Germany and Spain, 12% in the United Kingdom, and 15% in France.[35] Between 2008 and 2012, there were falls of 8% in Australia and 6% in New Zealand.[36] Between 1994 and 2016, consumption of orange juice in those under 20 years of age in the United States declined 10.5 pounds a year, and in adults there was a fall of 6.1 pounds.[37]

Fructose

One viewpoint has been to emphasize the influence of fructose, as in 2004 it was hypothesized that it was a primary cause of the obesity epidemic[38]: in the United States the increased consumption of high fructose corn syrup paralleled the rapid increase in the incidence of obesity.

One reason for being concerned about fructose consumption is that it has been proposed that the nature of its metabolism in the liver predisposes towards lipogenesis. However, a meta-analysis of 14 trials that considered the impact of exchanging fructose in the diet for other carbohydrates concluded that it did not increase postprandial triglycerides.[39] However, when fructose consumption resulted in excessive energy intake, the levels of postprandial triglycerides increased. That is, raising energy intake increases triglycerides, but the form of the sugar consumed is unimportant. Other meta-analyses of human data have come to similar conclusions, ie, "fructose does not cause biologically relevant changes in triglycerides or body weight."[40] In 11 studies carried out for up to 13 weeks, in only 1 did the levels of triglycerides increase, and in this case baseline values were unusually low, possibly resulting in regression to the mean. The triglyceride levels did not increase in women consuming up to 133 g/day and men consuming 136 g/day of fructose—that is, even intakes vastly in excess of normal levels of consumption were without effect.

In this context, the use of stable isotopes is particularly informative because it allows researchers to see, in the intact individual, where fructose ends up. The hypothesis is clear: if fructose is especially associated with fat deposition, then the isotope should end up in fat. A review of human isotopic tracer studies concluded that <1% of fructose was converted to plasma lipids.[41]

The World Health Organization[3] report on sugar intake commissioned a meta-analysis that considered 30 randomized controlled trials (RCTs) and 38 cohort studies.[42] It concluded that when sugars were exchanged for other carbohydrates, while maintaining a constant energy intake, body weight was not affected. In contrast, with ad libitum diets, a higher sugar intake was associated with increased weight. Thus, if food intake is modified, any change in body weight appears to reflect a change in total energy intake rather than the provision of fructose. Again, when 31 isocaloric and 10 hypercaloric trials were examined, in isocaloric trials fructose had no influence on body weight. However, when large amounts of fructose were added to the diet, body weight increased.[43] Because those who are overweight may differ metabolically—for example, in terms of insulin resistance or glucose tolerance—this group was considered separately. A similar conclusion resulted: "There is no evidence which shows that the consumption of fructose at normal levels of intake causes biologically relevant changes in triglycerides or body weight in overweight or obese individuals."[43]

A consistent picture has emerged. When fructose replaces other carbohydrates that provide a similar number of calories, there is no specific influence on body weight. Rather, weight gain reflects the general overconsumption of calories from any dietary source. As such, the fructose provided by fruit juice, other than the calories it provides, does not predispose to obesity. A major problem for those seeing sugar as the major cause of obesity is that the intake of added sugars has progressively decreased. In the United States between 1999–2000 and 2007–2008, the intake of added sugars was reduced from 100.1 gram/day to 76.7 gram/day,[44] yet the incidence of obesity continued to rise.

Fiber

Fiber plays an important role in a balanced diet because it helps to prevent heart disease, diabetes, and some cancers.[45] Thus, for some, a major problem associated with the consumption of juice is the removal of fiber. When juicing, the skin and pulp, both good sources of fiber, are often not included. However, when juice is made by pulping the whole fruit, fiber is provided.

In Europe, the recommended fiber intake is 25–32 g/day for women and 30–35 g/day for men.[45] Yet when data from 14 European countries were considered, the average intake was less than that recommended. In males aged 20–35 years, the highest average intake was 26 g/day in Germany, Norway, and the United Kingdom. The lowest average was 14 g/day in Belgium; whereas in France, Italy, and Austria it was 16 g/day.[46] In the United States the average intake was 16 g/day,[47] a value that compares with a recommendation of 38 g/day for men and 25 g/day for women.[48]

In this context, the drinking of juice has been viewed as reducing the intake of fiber. There appears, however, to be an implicit assumption that if an individual stops drinking juice they will start eating whole fruit. The basis for this unlikely expectation is unclear because the dietary roles played by fruit and a beverage are very different. Why should juice and intact fruit be viewed as alternatives? If an individual drinks juice at breakfast, its removal will result in consuming an alternative beverage. Throughout the day thirst will lead to having a drink, or individuals drink because it is appropriate in a social setting where fruit is not available or when consumption would be socially inappropriate.

There is also another implicit assumption—that fiber can be viewed in a homogeneous manner. However, there are many different types of fiber with different physiological consequences; for example, they impact differently on the gut microbiota.[49] Thus, too much emphasis should not be placed on increasing the intake of any 1 type of fiber, but rather it should be ensured that it is obtained from a range of fruit, vegetables, cereals, bran, nuts, and seeds. A more sophisticated recommendation is required than suggesting the removal of fruit juice from the diet. Although the findings need to be treated cautiously, a meta-analysis[50] found that cereal and, to a lesser extent, vegetable fiber were associated with lower total mortality, although fruit fiber was not.

Although the logic appears muddled, one argument for not consuming fruit juice is that it contains less fiber than intact fruit. Yet nobody would suggest stopping eating meat or fish because they contain no fiber: rather, the overall contribution made to the diet justifies their consumption. Similarly, any recommendation to consume fruit juice must be made in the context of the entire diet, such that the addition would have a positive impact.

In fact, there have been many reports that the consumption of juice is associated with a better quality diet, including a greater consumption of intact fruit and vegetables and hence more fiber. A roundtable of experts concluded that removing juice from the diet would reduce daily fruit consumption and increase the drinking of SSBs.[51] In the United Kingdom those drinking 100% fruit juice were 42% more likely to achieve 5 a day because there was also a greater intake of whole fruit and vegetables.[52] In a French representative sample, the consumption of juice was associated with a diet of higher quality with a higher intake of fruits and vegetables than with nonconsumers.[53] Importantly, fruit juice had a greater influence on the fruit and vegetable intake of those with lower socioeconomic status, such that the removal of juice from the diet of the financially less well-off would have a greater impact on the healthiness of their diet.

Possible negative influences of fruit juice

In summary, the fructose associated with fruit sugar is no more likely to be stored as body fat than other sugars. Although when juiced, less fiber is consumed than with intact fruit, there is no reason to believe that intact and juiced fruit should be viewed as alternatives; they are consumed in different circumstances. In fact, those consuming juice tend to consume more intact fruit and vegetables with an associated greater intake of fiber.

BIOACTIVE MOLECULES

When considering the role of fruit juices, a major factor is that they are a rich source of vitamin C, carotenoids, and polyphenols. However, to demonstrate a parallel between juice and intact fruit, there is a need to show that they act in a similar manner.

A first question is does processing influence the properties of juice? Commercial rather than domestic squeezing has been reported to extract 25% more vitamin C, and pasteurization slightly increased the levels extracted from solids. Pasteurization, concentration, and freezing did not affect the total antioxidant capacity due to vitamin C.[54] Similarly, when 7 juices were compared, fresh and commercially processed juices (no extrinsic sugar) were similar in terms of total phenolic content and antioxidant activity. However, the levels were lower when fruit drinks were sweetened with sugar and contained a smaller proportion of fruit juice.[55] The importance of polyphenols in juices is indicated by their high correlation with total antioxidant activity: it is associated with the total phenolic rather than vitamin C content,[56] although levels will differ with the method of preparation and may decline depending on nature of storage.

A second question is whether juice consumption impacts human physiology? Because fruit juice delivers compounds that improve antioxidant status, Crowe-White et al[57] subjected the topic to systematic review. The summated evidence from 10 trials suggested that 100% fruit juice improved a range of antioxidant biomarkers and the levels of other nutrients. For example, adding orange juice to the normal diet 3 times a day for 3 weeks increased the blood levels of vitamin C (59%), folate (46%), carotenoid (22%), and flavanone (8 fold).[58] Silveira et al[59] asked normal-weight individuals to consume red orange juice each day for 8 weeks. Low-density lipoprotein (LDL) cholesterol and C-reactive protein levels decreased, whereas antioxidant activity in serum increased and insulin resistance and systolic blood pressure declined.

Vitamin C

Water-soluble vitamin C fulfills a wide range of functions. Having antioxidant properties, it protects against the damage caused by free radicals that have a role in aging and the development of cancer, heart disease, and arthritis. It is also involved in healing wounds and maintaining connective tissues and the structure of blood vessels, skin, and bone. Various fruit juices are good sources of vitamin C, including guavas, kiwi, black currents, strawberries, oranges, and papayas.

Sixty-two percent of British children aged 4–10 years consumed fruit juice, something true of only 37% of those aged >65 years. In children, beverages provided 32%–39% of their vitamin C: 14%–19% came from fruit juice and 8%–20% came from soft drinks. Although fruit provided 22% of the vitamin C of those aged 4–10 years, the percentage fell to only 12% in those aged 11–18 years. However, the contribution of fruit juice increased in adults to 19%–24%.[60] Thus, fruit juices make a substantial contribution to the total intake of vitamin C, although there are subgroups who are at risk of deficiency. When 15 769 individuals aged 12–74 years in the United States were studied, although the average intake and blood levels of vitamin C were above the suggested levels, 14% of males and 10% of females were deficient, with smokers being particularly at risk.[61]

Another meta-analysis considered 29 trials and concluded that supplementation with vitamin C reduced blood pressure.[62] When nurses were followed for 16 years and the development of coronary heart disease was monitored,[63] a higher intake of vitamin C was associated with a lower risk. When serum ascorbate concentrations were assessed during the second NHANES survey, mortality 12–16 years later was greater in men, but not women, in those with a low intake of vitamin C.[64] Ashor et al[65] pooled the data from 44 clinical trials where orange juice had been added to the diet. They found improvements in endothelial functioning in those with atherosclerosis, diabetes, or heart failure. The effects were stronger in those with a higher risk of cardiovascular disease.

A meta-analysis[66] considered the influence of vitamin C on the glycemic response. Vitamin C reduced the levels of blood glucose in those with type 2 diabetes mellitus (T2DM) if the intervention was >30 days. The effect on fasting insulin levels was greater after a meal and in those who were older.

A British study that considered those with a low income found that 25% of men and 16% of women had blood levels of vitamin C indicative of deficiency, with a further 20% having levels in the depleted range.[67] Although a poor diet is the most usual cause of poor vitamin C status, smoking, pregnancy, a low income, and strenuous exercise may play a part. When those of normal weight were compared with those who were obese, the latter had a lower intake of vitamin C and were more likely to be deficient.[68]

In summary, a good vitamin C status is associated with a range of health benefits. Because juices make a substantial contribution to the level of vitamin C intake, their removal from the diet may reduce vitamin C status with the risk of an adverse influence on health.

Carotenoids

More than a thousand carotenoids fall into 2 classes, xanthophylls and carotenes, that are found in fruit and vegetables that are colored orange, red, or yellow. Humans do not synthesize carotenoids, so to benefit they must be part of the diet. Carotenoids act as antioxidants, and beta-carotene can be converted into vitamin A. Vegetables, such as carrots and spinach, are a good source of carotenoids, but carotenoids are also found in plums, apricots, mangoes, colored melons, peaches, nectarines, sour cherries, and some citrus fruits such as red grapefruits, tangerines, and oranges. Particular attention has been directed to lycopene, a bright red carotenoid found in tomatoes, guavas, watermelon, papaya, and pink and red grapefruit.

The levels of carotenoids in the human skin are an indicator of the antioxidant status of the body. Although there are richer sources of carotenoids, adding orange juice to the diet increases the bodily levels. Drinking orange juice for 25 days increased carotenoid status by 10%–15%, depending on starting values.[69] Values, however, returned to baseline levels within 3 days of stopping drinking the juice.

As needed, beta-carotene is converted into vitamin A, which has important roles in the functioning of the immune system, mucus membranes, vision, and the skin. Given the clear evidence that the consumption of fruit and vegetables reduces the incidence of various diseases,[5] their powerful antioxidant properties makes it likely that carotenoids are part of the underlying mechanism.

Due to the antioxidant properties of carotenoids, their consumption is being related to the incidence of head and neck cancer. A meta-analysis of epidemiological studies found that when compared with the lowest level of intake, higher levels of beta-carotene were associated with a relative risk of 46% of developing oral cancer and 57% of developing laryngeal cancer. In addition, lycopene, alpha-carotene, and beta-cryptoxanthin were all associated with a reduction in the rate of oral and pharyngeal cancer of at least 26%.[70] Similarly, a meta-analysis[71] considered prospective studies that had related blood concentrations of carotenoids to the development of breast cancer. An inverse association was found between the total level of carotenoids and the subsequent development of cancer; more specifically, there was a negative association with beta-carotene. Intakes of beta-carotene and alpha-carotene have also been associated with the incidence of gastric cancer.[72] In addition, those consuming higher rather than lower levels of alpha-carotene, beta-carotene, and lutein/zeaxanthin had a reduced risk of developing non-Hodgkin's lymphoma.[73]

However, the evidence is not all positive; no association was found in meta-analyses between carotenoids and the risk of colorectal cancer.[74] Similarly, a review[75] found no association between carotenoids or vitamin A and the development of Parkinson's disease.

Particular attention has been paid to lycopene, the most powerful antioxidant found in food. A review of a total of 692 012 individuals found relationships between lycopene consumption and the risk of prostate cancer. The risk decreased by 1% for every additional 2 mg of lycopene consumed and reduced by 3.5% for each additional 10 mg/dL of circulating lycopene.[76] Similarly, a meta-analysis found that a greater exposure to lycopene was inversely associated with a lower risk of cardiovascular disease.[77]

The above series of meta-analyses provides evidence of a beneficial association between both the intake and blood levels of carotenoids and various disease states. There have been, however, relatively few intervention studies. Forty elderly men with benign prostrate hyperplasia received either 15 mg/day lycopene or a placebo for 6 months. The level of serum prostate-specific antigen was reduced in those taking lycopene, but not the placebo, and prostate enlargement continued in the placebo group but not the lycopene group.[78] However, in a similar trial, men with high-grade prostatic intraepithelial neoplasia consumed either lycopene or a placebo for 6 months. No differences in prostrate-specific antigen resulted, and the prevalence of cancer, atrophy, and inflammation were similar.[79] In African Americans who had been recommended for a prostrate biopsy, lycopene supplementation for 3 weeks did not change the DNA oxidation product 8-oxo-deoxyguanosine or the lipid peroxidation product malondialdehyde in prostrate tissue.[80]

While accepting that RCTs offer the strongest evidence, there are good reasons not to place too great a reliance on the present intervention data. There are relatively few studies of short durations, when disorders such as cancer may develop over many years, even decades. To date, the intervention studies are best seen as pilot studies because they have used small sample sizes and therefore had little chance of picking up any but dramatic improvements, when any effect is more likely to be subtle. Future intervention studies that look for changes in the risk of developing the disease will need to be on a large scale and over an extended period.

Because epidemiology tracks the development of disease over many years, it is appropriate to use the criteria of Bradford-Hill[81] that allow a causal relationship to be presumed. In the same way that such an approach was necessary to relate cigarette smoking and lung cancer, the influence of carotenoids may well be insidious, impacting only slowly over time. Bradford-Hill[81] suggested that the larger the association, the more likely it was to be causal: several of the above meta-analyses reported large effect sizes. That the conclusion is supported by a series of meta-analyses satisfies the second criterion; there must be consistency with similar findings being reported by different researchers using different samples. The cause must occur before the effect: in this instance either dietary intake or blood levels were related to the subsequent development of disease. A biological gradient is also supportive, and some of the above meta-analyses related a range of intakes of carotenoids or blood levels to a lower incidence of disease.[76] A consistency of epidemiological and laboratory findings was also supportive, and in this instance, lycopene has, in vitro, been reported to reduce the growth of cancerous cells.[82] Finally, plausibility—are there mechanisms that would be expected to relate cause to effect? In the present instance, the antioxidant effect of carotenoids provides a plausible mechanism. In summary, the existing evidence looks promising, although in an ideal world, clinical trials would confirm the beneficial influence of carotenoids. However, if the influence of these phytochemicals is long term, their effects will be difficult to demonstrate using this approach.

Polyphenols

Fruit high in polyphenols includes blueberries, cherries, cranberries, pomegranates, apples, apricots, grapefruits, oranges, red grapes, raspberries, strawberries, blackberries, gooseberries, plums, and kiwis. One group of flavonoids, the anthocyanins, which give plants their red, purple, and blue color, are attracting increasing interest for their antioxidant, anti-inflammatory, and antiviral properties. They are found particularly in purple grapes, cherries, raspberies, blueberries, and plums.

Silveira et al[83] examined the pharmacokinetics of the main flavanone glycosides found in oranges, hesperidin, and narirutin: they found no differences in the dynamics of freshly squeezed and processed juice. After a single drink, levels peaked 2 hours after consumption and approached 0 after 12 hours, with none being measurable after 24 hours. Manach et al[84] calculated the time scale following consumption of the levels of plasma polyphenols. Gallic acid and isoflavones were the most readily absorbed, followed by catechins, flavanones, and quercetin glucosides, although the kinetics differed. When part of the diet, the half-life of anthocyanins have been found to vary 1–4 hours; flavonols, 1–13 hours; flavanones, 1–3 hours; flavanols, 1–3 hours; and isoflavones, 4–8 hours.[84]

Generalizations are difficult given the thousands of phenolic compounds that exist; there is, however, an impression that to maintain a high plasma concentration of polyphenols they need to be consumed regularly. For example, the flavones in orange juice, hesperidin, and naringin, have a half-life of about 2 hours in the blood. There remains a need for a greater understanding of the relationship between metabolic outcomes and consuming 100% fruit juice.[57]

A particular interest is the role played by polyphenols in preventing cancer, heart disease, osteoporosis, and neurodegenerative disorders. A meta-analysis of 22 prospective studies related flavonoid consumption to all-cause mortality[85]: a high intake reduced the risk of all-cause mortality (relative risk, 0.74). More specifically when 143 studies that considered cancer were integrated, in prospective studies the consumption of isoflavones was associated with a decreased risk of lung and stomach cancers, and an effect on breast and colorectal cancers just missed statistical significance.[86] Some types of cancer appear to be more susceptible because no influence was found with either esophageal or colorectal cancer.[87]

A large prospective cohort of health professionals[88] reported that the intake of anthocyanidins, but not other flavonoids, was associated with a reduced risk of T2DM. Similarly in Finland, consuming blueberries, a rich source of anthocyanidins, was related to a lower risk of T2DM.[89] A meta-analysis considered the association between the intake of flavonoids and risk of T2DM in 312 015 individuals followed up for up to 28 years. A higher intake of flavonoids reduced the risk of the disorder (relative risk, 0.89), which declined by 5% for each additional 300 mg that was consumed each day.[90]

Because there are suggestions that flavonoids may influence the immune system, a systematic review related consumption to the incidence of upper respiratory tract infections and indices of immune functioning.[91] Flavonoid supplementation decreased the incidence of respiratory infection by 33%, although measures of immune functioning were unaffected. Polyphenols did not, however, delay the onset of cognitive decline in older adults.[92]

Summarizing the influence of the bioactive molecules supplied by fruit and fruit juice, meta-analyses of prospective cohort studies (but not RCTs) have found the consumption of carotenoids to be associated with a decreased incidence of a range of cancers. In particular, lycopene consumption has been found, in a dose-response manner, to be associated with a reduced rate of prostrate cancer. Similarly, a higher flavonoid intake results in lower all-cause mortality, and the intake of isoflavones reduces the incidence of lung and stomach cancer. The intake of flavonoids, in a dose-dependent manner, reduces the incidence of T2DM. An increased intake of vitamin C is associated with lower blood pressure and better control of blood glucose in T2DM.

FRUIT JUICE AND DISEASE

A series of prospective cohort studies and RCTs have considered the impact of consuming fruit juice (as opposed to particular bioactive molecules) on the risk of disease.

Cardiovascular disease

Aune et al[5] considered 22 studies where the consumption of fruit had been related to aspects of cardiovascular disease. Benefits were found with up to 10 portions a day, when the relative risk was 27% lower than when no fruit was consumed. In particular, there was evidence that a high rather than low intake of either apples/pears or citrus fruits was protective.

However, when considering juice, interventions lasted >4 weeks in only a minority of studies. A cohort study[93] related the intake of fruit juice over a 20-year period to the risk of cardiovascular disease. A higher consumption of juice was associated with a lower incidence of hypertension, although the levels of LDL, high-density lipoprotein (HDL), and triglycerides were not influenced. Consuming 330 mL of pomegranate juice each day for 4 weeks reduced both systolic and diastolic blood pressure.[94] Similarly, after drinking 500 mL of orange juice each day for a month, the diastolic blood pressure of overweight men was reduced.[95] Again, when men with mild hypertension consumed Concord grape juice, both diastolic and systolic blood pressure were reduced.[96] However, other studies did not find that juice affected blood pressure.[97–100]

Vascular functioning has also been considered. In a cross-over trial, those at an increased cardiovascular risk received 500 mL of red orange juice or a placebo for 7 days.[101] Flow-mediated dilatation, a measure of the risk of cardiovascular disease, improved after consuming orange juice. However, there are other reports that fruit juice did not influence vascular functioning.[94,99,100]

Similarly, blood lipids have been examined. Overweight women who engaged in aerobic training for 12 weeks either did or did not drink 500 mL of orange juice each day. The consumption of juice resulted in lower total cholesterol and LDL, higher concentrations of HDL, and a better LDL/HDL ratio.[102] In another RCT, those with metabolic syndrome consumed 300 mL a day of a mixture of citrus-based juices for 6 months.[103] Again, the levels of total cholesterol, LDL, and HDL declined. However, in other trials, fruit juice did not affect blood lipids.[95,98,99]

In summary, a series of reports found that fruit juice reduced the risk of disease, although the findings are inconsistent and the amount of juice consumed tended to be in excess of the currently recommended level. In addition, most trials have been for a short period and have involved a small number of participants. Positive findings have, however, been reported often enough to suggest there should be further study of risk of cardiovascular disease.

Diabetes

Systematic reviews have consistently reported that consumption of SSBs is associated with a greater risk of T2DM.[104,105] The evidence concerning fruit juice is less clear, although there are reports that, although SSBs increased the risk of T2DM, 100% fruit juice did not.[106–108]

Imamura et al[105] considered 17 cohorts and found an association between SSBs and diabetes. Similarly, drinking artificially sweetened beverages and fruit juice was also associated with a greater incidence of diabetes. The authors, however, commented that the findings were likely to involve bias, including the misclassification by participants of sugar sweetened fruit-based drinks as 100% fruit juice. Importantly there was a difference depending on whether the incidence of diabetes depended on self-report rather than medical records or biochemical assay. In the former instance, fruit juice was associated with the incidence of diabetes, although the relationship disappeared when more reliable medical or biochemical information was the basis for diagnosis.

Xi et al[104] carried out a larger review. They considered 7 prospective studies that allowed the comparison of sugar-sweetened fruit juice and 100% fruit juice. Four studies provided 191 686 participants and 12 375 cases of T2DM in those who consumed sweetened fruit juice. They were contrasted with 137 663 participants who drank 100% fruit juice, who provided 4906 instances of T2DM: meta-analysis found that consuming sugar-sweetened fruit juice increased the risk of T2DM, whereas drinking 100% fruit juice did not.

Given the unavoidable difficulties that arise when interpreting this type of epidemiological study, it is important to consider RCTs. An obvious hypothesis is that the sugar in fruit juice has consequences for glycemic control that, over time, predisposes to diabetes. A meta-analysis of 18 RCTs[109] summarized the effect of juice on insulin and the control of blood glucose. After consumption for at least 2 weeks, 100% fruit juice was found to have no effect on fasting blood glucose, fasting insulin, the Homeostatic Model Assessment for Insulin Resistance, or glycated hemoglobin—that is, fruit juice had no effect on glycemic control. This finding is similar to those randomized intervention trials that found little or no impact of increasing fruit and vegetable intake on biomarkers associated with metabolic diseases.[110]

Cancer

Eating 5 servings a day of fruits and vegetables is part of the dietary recommendations of the World Cancer Research Fund/American Institute for Cancer Research. A protective effect is said to be "probable" for mouth, pharynx and larynx, esophagus, stomach, and lung cancer, whereas it is "limited suggestive" for nasopharynx, lung, ovary, endometrium, pancreas, and liver cancer.[111] The role of dietary fiber in colorectal cancer was rated as "convincing."

Because fruits and vegetables are associated with only a few types of cancer, their potential may be limited in this area. However, dietary flavonoids, of which citrus fruits and their juices are a rich supply, interfere with "carcinogen activation, stimulate carcinogen detoxification, scavenge free radical species, control cell cycle progression, induce apoptosis, inhibit cell proliferation, oncogene activity, angiogenesis and metastasis as well as inhibit hormones or growth-factor activity."[112]

Cirmi et al[113] produced a systematic review that considered the potential of citrus juices to act as anticancer agents, looking at animal, in vitro, and human observational studies. It was concluded that citrus juices were a "potential resource against cancer." They, however, found only 2 human studies, and no conclusion was warranted until a range of longitudinal studies become available. The review of Aguilera et al[114] found that, although some studies found that juice had a positive influence, others did not, and there was a need for studies that examined possible confounding variables such as an interaction with other dietary bioactive substances. In addition, emphasis should not be solely placed on diet as a list of other risk factors needs to be considered. At present, the role of fruit juice is unclear.

Gout and nonalcoholic fatty liver disease

A meta-analysis considered 2 studies that included 125 299 participants and 1533 cases of gout concluded that fructose consumption was a risk factor. For example, Choi and Curhan[115] studied 46 393 men for >12 years and related the intake of soft drinks to the development of gout. The consumption of SSBs, but not diet soft drinks, increased the risk. It was suggested that fructose intake was involved because both fructose-rich fruits and fruit juices were risk factors.

It has also been proposed that fructose is a risk factor for nonalcoholic fatty liver disease. However, because it is known that obesity, insulin resistance, and T2DM are risk factors, any specific effect of fructose should be distinguished from any associated calories and change in body weight. Chiu et al[116] integrated the findings from 7 isocaloric trials where fructose intake was compared with similar amounts of other carbohydrates. The effect of fructose was similar to other forms of carbohydrate; fructose as such did not predispose to the disorder. In contrast, when additional energy was added to a diet (21%–35% increase), changes in both intra-hepatocellular lipids and alanine aminotransferase suggested liver damage. Thus, only when fructose is consumed at levels greatly in excess of the typical level of intake was there a problem, an effect that may well reflect consuming excess energy rather than specifically the consumption of fructose.

DISCUSSION

There are varying views concerning the impact on health of consuming 100% fruit juice. At one extreme it is viewed as a source of sugar that leads to obesity, and at the other it is seen as providing a range of bioactive molecules that benefit health. Yet, if one looks at the views of the national bodies setting food policy, after considering the full range of evidence, the majority give the same advice: fruit juice may contribute to the 5-day recommendation for fruit and vegetable consumption. For example, the US Dietary Guidelines state that 100% fruit juice may be consumed but in moderation.[117] The potential benefits are considerable because there is overwhelming evidence that the consumption of fruits and vegetables benefits health.[5,118,119] Because juice contains the same molecules as intact fruit, it is likely to have a contribution to make, although the emphasis needs to be on 100% fruit juice, rather than juices that are sugar sweetened. Unfortunately, to date, most of the literature has not distinguished 100% fruit juice, and therefore conclusions and recommendations confuse it with sugar-sweetened juice. However, both with weight gain in children[23] and diabetes in adults,[104] meta-analyses have found that sugar-sweetened juices are similar to other SSBs, although both differ from 100% juice. The negative consequences of SSBs were not found in those consuming 100% juice.

Yet, it is a minority of the population who achieve the recommended intake of fruits and vegetables,[5,6,46,120] and for practical reasons and convenience, there is resistance to making dietary changes.[6,7] However, if it is acceptable to count juice as 1 of the 5 servings a day, given the low level of fruit and vegetable intake, the recommendation that it be consumed on a daily basis is a small step to take. In the absence of alternatives, encouraging the daily drinking of fruit juice offers a simple and convenient way to increase the intake of fruit.

Those who advocate reducing the drinking of juice tend to worry that it leads to obesity; as in a similar manner to all food items, excessive consumption has the potential to result in weight gain. However, the majority of the population do not drink any fruit juice,[26,60,61] and the total amount consumed by the population has been declining for many years.[35–37] The frequency of consumption declines with age,[33,34] and when consumed, the average intake is small. Particularly in poorer sections of the population, juice may be the main source of fruit, and individuals would suffer if it was removed from the diet; it is this group that would be predicted to benefit most from adding juice to the diet.[52]

However, any decision to encourage consumption would need to be accompanied by appropriate health education. Infants should not have a bottle that they can suck at will; there should be appropriate dental hygiene; consumption is better with a meal; there should be only moderate consumption; juice should not replace existing fruit and vegetables in the diet.

Although public health policy naturally considers the entire diet, there has been a tendency at a particular time to pay disproportionate attention to a specific nutrient. In the late 1970s the reduction of fat intake became a major objective. Salt reduction has been emphasized more recently. Currently the reduction of sugar is a major priority: for example, many of those wishing to reduce fruit juice in the diet emphasize the sugar content. Yet food items should be eaten in moderation as part of a wide-ranging and varied diet. The risk is that, if the emphasis is disproportionately on 1 nutrient, other dietary considerations will not attract the attention they deserve.

Should concentrating on the sugar content of fruit juice justify playing down the importance of other contributions? When 14 dietary factors were related to the burden from disease, the 6 factors most highly associated were diets high in sodium, low in vegetables, low in fruit, low in whole grains, and low in nuts and seeds.[120] The authors commented, "A policy focus on the sugar and fat components of diets might have a comparatively smaller effect than that of promotion of increased uptake of vegetables, fruit, whole grains, nuts and seeds."

When it comes to public health, it is only possible to make the best guess given the current state of knowledge. If it is assumed that the obvious molecular similarities between intact and juiced fruit result in a similar health benefit, the effect of a portion of fruit juice can be estimated from the data of Aune et al.[5] When 1 portion of fruit was eaten rather than none, all-cause mortality declined by 5.5%. Two portions of fruit a day reduced the risk by 11%, and three portions by 15.6%. The context of these findings is that an American survey found that only 12.2% of adults ate the recommended amount of fruit, whereas 9.3% met the recommendation for vegetables.[121] Clearly, an increase of 1 portion a day would benefit the health of the vast majority. Similarly, a survey by the European Union found that most Europeans do not meet the recommended level of intake. In fact, only 4 of 19 countries had an average intake that reached that level.[46] As an example, in the United Kingdom the average intake of fruit and vegetables, excluding the intake of juice, was 258 g/day, which amounts to 3.2 portions.[46] As judged by Aune et al[5] in their analysis, adding 1 portion to the existing average diet in the United Kingdom would decrease the risk of all-cause mortality by 3.9%.

Such findings should generate little surprise because, since 2003, the World Health Organization/Food and Agriculture Organization of the United Nations have advocated the consumption of fruit and vegetables to improve health. However, although it is an easy decision to recommend increased consumption, implementing such a recommendation has proved extremely difficult. There is considerable public resistance. Many countries have run public information campaigns, but their lack of impact can be judged by the current low levels of consumption. The critical question is, "How can this be increased?"

The reasons for not eating fruits and vegetables were discussed above. Essentially, there is the perception that it was often impractical and demanded time and effort. Many of the problems reflect the inherent nature of preparing and eating fruit and vegetables, problems that cannot be easily overcome. However, the convenience of fruit juice is an exception; it avoids most of the stated reasons for choosing not to consume.

Psychologically, a major factor is the feeling of self-efficacy—that is, the perception that you can succeed is basic to initiating and maintaining a behavior. Because consumption of juice is convenient and involves minimal effort, there is little reason to believe one could not drink juice. As such, the active encouragement to drink 1 portion of fruit juice a day stands a good chance of rapidly increasing fruit intake, when it is difficult to suggest alternative strategies. Given the association between increasing intake by only 1 portion and a decreased risk of death and disease,[5] there is the potential for a policy of actively encouraging drinking 1 portion of fruit juice a day to benefit health.

However, the decline in the consumption of fruit juice over recent years[35–37] is probably in part due to the emphasis on the sugar content, creating the perception that juice is unhealthy. A positive aura, emphasizing the bioactive molecules provided, will be needed to develop a perception that juice is a health food, rather than the current emphasis on its sugar content, which implies it is a junk food. Care would need to be taken to ensure that 100% fruit juice is consumed in moderate amounts and that it does not replace intact fruit. Although by no means solving the entire problem, a recommendation to consume juice offers a step in the right direction. Because it is convenient and avoids most of the reasons for not consuming, there is a good chance that dietary behavior will change.

Thus, the question is, "Should daily juice consumption be recommended in a world where it has proved very difficult to increase the intake of fruit and vegetables?" The argument is that the relatively attractive nature of juice and its convenience make it "low-hanging fruit." There is a second question: "Is there any alternative that has as good of a chance of increasing intake and therefore having such a large impact on health?" The conclusion will need to be considered separately for children and adults, and the debate will need to examine the consumption of polyphenols, carotenoids, and vitamin C. Any recommendation will need to be made in the context of the entire diet, such that the full range of foods consumed amounts to a balanced diet.

CONCLUSION

The take-away message is that only a small proportion of the population achieves the 5-a-day recommendation for fruit and vegetable intake and it has proved difficult to increase consumption because of the practicalities, inconvenience, and the effort required when consuming whole fruit. Psychologically, believing that one can successfully carry out the behavior (self-efficacy) is fundamental to changing behavior. Because fruit juice avoids many of the reasons for not consuming intact fruit, it can promote self-efficacy and thus encourage consumption. This review does not suggest that fruit juice should replace intact fruit; in fact, the opposite is most likely, as, in practice, juice and intact fruit are consumed in different circumstances and are rarely alternatives. Because fruit juice offers a source of vitamin C, carotenoids, and polyphenols, increasing consumption has the potential to benefit health.

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REFERENCES

1. Gillespie D. *Sweet Poison*. Harmondsworth, UK: Penguin Books; 2008.
2. Lustig RH. *Fat Chance: The Bitter Truth about Sugar*. London: Fourth Estate Books; 2012:
3. World Health Organization. *Guideline: Sugars Intake for Adults and Children*. Geneva: World Health Organization; 2015.
4. Public Health England. Eatwell Guide. Available at: http://www.gov.uk/government/publications/the-eatwell-guide. Accessed June 1, 2018.
5. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. *Int J Epidemiol.* 2017;46:1029–1056.
6. Li Y, Zhang D, Pagán JA. Social norms and the consumption of fruits and vegetables across New York City neighborhoods. *J Urban Health.* 2016;93:244–255.
7. Anderson AS, Cox DN, McKellar S, et al. Take Five, a nutrition education intervention to increase fruit and vegetable intakes: impact on attitudes towards dietary change. *Br J Nutr.* 1998;80:133–140.
8. Hodder RK, Stacey FG, Wyse RJ, et al. Interventions for increasing fruit and vegetable consumption in children aged five years and under. *Cochrane Database Syst Rev*. 2017;9:CD008552.
9. Shaikh AR, Yaroch AL, Nebeling L, et al. Psychosocial predictors of fruit and vegetable consumption in adults: a review of the literature. *Am J Prev Med.* 2008;34:535–543.
10. Bandura A. Self-efficacy mechanism in human agency. *Am Psychol.* 1982;37:122–147.
11. Kreausukon P, Gellert P, Lippke S, et al. Planning and self-efficacy can increase fruit and vegetable consumption: a randomized controlled trial. *J Behav Med.* 2012;35:443–451.
12. McSpadden KE, Patrick H, Oh A, et al. The association between motivation and fruit and vegetable intake: the moderating role of social support. *Appetite.* 2016;96:87–94.

13. Deci EL, Koestner R, Ryan RM. A meta-analytic review of experiments examining the effects of extrinsic rewards on intrinsic motivation. *Psychol Bull*. 1999;125:627–668.
14. Teixeira PJ, Patrick H, Mata J. Why we eat what we eat: the role of autonomous motivation in eating behaviour regulation. *Nutr Bull*. 2011;36:102–107.
15. Deci EL, Ryan RM. Self-determination theory: a macrotheory of human motivation, development, and health. *Can Psychol*. 2008;49:182–185.
16. Action on Sugar. Children's Fruit Juice Survey—Media Coverage. 2017. Available at: http://www.actiononsugar.org/news-centre/sugar-in-the-news/all-media-coverage/childrens-fruit-juice-survey---media-coverage.html. Accessed December 28, 2017.
17. Jebb S. Fruit juice should not be part of your five a day, says government adviser. *Guardian*. January 12, 2014. Available at: https://www.theguardian.com/science/2014/jan/12/remove-fruit-juice-sugar-five-a-guidance-government-health-adviser. Accessed December 28th, 2017.
18. Mourao DM, Bressan J, Campbell WW, et al. Effects of food form on appetite and energy intake in lean and obese young adults. *Int J Obes (Lond)*. 2007;31:1688–1695.
19. Hagele FA, Buesing F, Nas A, et al. High orange juice consumption with or in-between three meals a day differently affects energy balance in healthy subjects. *Nutr Diabet*. 2018;8:19.
20. Benton D, Young HA. Reducing calorie intake may not help you lose body weight. *Perspect Psychol Sci*. 2017;12:703–714.
21. Malik VS, Pan A, Willett WC, et al. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *Am J Clin Nutr*. 2013;98:1084–1102.
22. Heyman MB, Abrams SA. Fruit juice in infants, children, and adolescents: current recommendations. *Pediatrics*. 2017;139:e20170967.
23. Frantsve-Hawley J, Bader JD, Welsh JA, et al. A systematic review of the association between consumption of sugar-containing beverages and excess weight gain among children under age 12. *J Pub Health Dentist*. 2017;77:S43–S66.
24. Auerbach BJ, Wolf FM, Hikida A, et al. Fruit juice and change in BMI: a meta-analysis. *Pediatrics*. 2017;139:e20162454.
25. Mozaffarian D, Hao T, Rimm EB, et al. Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med*. 2011;364:2392–2404.
26. Pereira A, Fulgoni V. Consumption of 100% fruit juice and risk of obesity and metabolic syndrome: findings from the National Health and Nutrition Examination Survey 1999–2004. *J Am Coll Nutr*. 2010;29:625–629.
27. Wang Y, Lloyd B, Yang M, et al. Impact of orange juice consumption on macronutrient and energy intakes and body composition in the US population. *Public Health Nutr*. 2012;15:2220–2227.
28. Yu ZM, DeClercq V, Cui Y, et al. Fruit and vegetable intake and body adiposity among populations in Eastern Canada: the Atlantic Partnership for Tomorrow's Health Study. *BMJ Open*. 2018;8:e018060.
29. Celis-Morales C, Livingstone KM, Affleck A, et al. Correlates of overall and central obesity in adults from seven European countries: findings from the Food4Me Study. *Eur J Clin Nutr*. 2018;72:207–219.
30. Auerbach BJ, Littman A, Krieger J, et al. Association of 100% fruit juice consumption and 3-year weight change among postmenopausal women in the Women's Health Initiative. *Prev Med*. 2018;109:8–10.
31. Hebden L, O'Leary F, Rangan A, et al. Fruit consumption and adiposity status in adults: a systematic review of current evidence. *Crit Rev Food Sci Nutr*. 2017;57:2526–2540.
32. Rampersaud GC, Valim MF. 100% citrus juice: nutritional contribution, dietary benefits, and association with anthropometric measures. *Crit Rev Food Sci Nutr*. 2017;57:129–140.
33. Bellisle F, Hebel P, Fourniret A, et al. Consumption of 100% pure fruit juice and dietary quality in French adults: analysis of a Nationally Representative Survey in the context of the WHO recommended limitation of free sugars. *Nutrients*. 2018;10:459.
34. Ozen AE, Bibiloni, MD, Pons A, et al. Fluid intake from beverages across age groups: a systematic review. *J Hum Nutr Diet*. 2015;28:417–442.
35. Fruit Juice Focus. AIJN Juice Report. 2017. Available at: http://www.fruitjuicefocus.com/aijn-juice-report-2017-highlights/. Accessed June18, 2018.
36. . Australian Food News. Soft drink and fruit juice consumption declining in Australia. Available at: http://www.ausfoodnews.com.au/2013/04/03/soft-drink-and-fruit-juice-consumption-declining-in-australia.html. Accessed June 18, 2018.
37. Ramsey L. Americans are eating less of one fruit, and it could signal a bigger problem in our diets. Available at: http://uk.businessinsider.com/us-food-commodity-consumption-report-2016-3? r=US&IR=T. Accessed June 18, 2018.
38. Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *Am J Clin Nutr*. 2004;79:537–543.
39. Wang D, Sievenpiper JL, de Souza RJ, et al. Effect of fructose on postprandial triglycerides: a systematic review and meta-analysis of controlled feeding trials. *Atherosclerosis*. 2014;232:125–133.
40. Dolan LC, Potter SM, Burdock GA. Evidence-based review on the effect of normal dietary consumption of fructose on development of hyperlipidemia and obesity in healthy, normal weight individuals. *Crit Rev Food Sci Nutr*. 2010;50:53–84.
41. Sun SZ, Empie MW. Fructose metabolism in humans—what isotopic tracer studies tell us. *Nutr Metab (Lond)*. 2012;9:89.
42. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. *BMJ*. 2013;346:e7492.
43. Sievenpiper JL, de Souza RJ, Mirrahimi A, et al. Effect of fructose on body weight in controlled feeding trials: a systematic review and meta-analysis. *Ann Intern Med*. 2012;156:291–304.
44. Welsh JA, Sharma AJ, Grellinger L, et al. Consumption of added sugars is decreasing in the United States. *Am J Clin Nutr*. 2011;94:726–734.
45. Stephen AM, Champ MM, Cloran SJ, et al. Dietary fibre in Europe: current state of knowledge on definitions, sources, recommendations, intakes and relationships to health. *Nutr Res Rev*. 2017;30:149–190.
46. EFSA Panel on Dietetic Products, Nutrition, and Allergies. Scientific opinion on dietary reference values for carbohydrates and dietary fibre. *EFSA J*. 2010;8:1462.
47. US Department of Agriculture, Agricultural Research Service. Dietary fiber: usual intakes from food and water, 2003–2006, compared to adequate intakes. Available at: www.ars.usda.gov/Services/docs.htm? docid=22659. Accessed December 28, 2017.
48. *US Department of Agriculture, US Department of Health and Human Services*. Dietary Guidelines for Americans, 7th ed. Washington, DC: Government Printing Office; 2010.
49. Fuller S, Beck E, Salman H, et al. New horizons for the study of dietary fiber and health: a review. *Plant Foods Hum Nutr*. 2016;71:1–12.
50. Kim Y, Je Y. Dietary fiber intake and total mortality: a meta-analysis of prospective cohort studies. *Am J Epidemiol*. 2014;180:565–573.
51. Byrd-Bredbenner C, Ferruzzi MG, Fulgoni VL, et al. Satisfying America's fruit gap: summary of an expert roundtable on the role of 100% fruit juice. *J Food Sci*. 2017;82:1523–1534.
52. Gibson S, Ruxton CHS. Fruit juice consumption is associated with intakes of whole fruit and vegetables, as well as non-milk extrinsic sugars: a secondary analysis of the National Diet and Nutrition Survey. *Proc Nutr Soc*. 2016;75:E259.
53. Francou A, Hebel P, Braesco V, et al. Consumption patterns of fruit and vegetable juices and dietary nutrient density among French children and adults. *Nutrients*. 2015;7:6073–6087.
54. Gil-Izquierdo A, Gil MI, Ferreres F. Effect of processing techniques at industrial scale on orange juice antioxidant and beneficial health compounds. *J Agric Food Chem*. 2002;50:5107–5114.
55. Wern KH, Haron H, Keng CB. Comparison of total phenolic contents (TPC) and antioxidant activities of fresh fruit juices, commercial 100% fruit juices and fruit drinks. *Sains Malaysiana*. 2016;45:1319–1327.
56. Abountiolas M, Nunes CN. Polyphenols, ascorbic acid and antioxidant capacity of commercial nutritional drinks, fruit juices, smoothies and teas. *Int J Food Sci Technol*. 2018;53:188–198.
57. Crowe-White K, Parrott JS, Stote KS, et al. Metabolic impact of 100% fruit juice consumption on antioxidant/oxidant status and lipid profiles of adults: an evidence-based review. *Crit Rev Food Sci Nutr*. 2017;57:152–162.
58. Franke AA, Cooney RV, Henning SM, et al. Bioavailability and antioxidant effects of orange juice components in humans. *J Agric Food Chem*. 2005;53:5170–5178.
59. Silveira JQ, Dourado G, Cesar TB. Red-fleshed sweet orange juice improves the risk factors for metabolic syndrome. *Int J Food Sci Nutr*. 2015;66:830–836.
60. Bates B, Lennox A, Prentice A, et al. Results from Years 1–4 (Combined) of the Rolling Programme (2008/2009–2011/12). London: National Diet and Nutrition Survey, Public Health England; 2017.
61. Hampl JS, Taylor CA, Johnston CS. Vitamin C deficiency and depletion in the United States: the third National Health and Nutrition Examination Survey, 1988 to 1994. *Am J Public Health*. 2004;94:870–875.
62. Juraschek SP, Guallar E, Appel LJ, et al. Effects of vitamin C supplementation on blood pressure: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2012;95:1079–1088.
63. Osganian SK, Stampfer MJ, Rimm E, et al. Vitamin C and risk of coronary heart disease in women. *J Am Coll Cardiol*. 2003;42:246–252.
64. Loria CM, Klag MJ, Caulfield LE, et al. Vitamin C status and mortality in US adults. *Am J Clin Nutr*. 2000;72:139–145.
65. Ashor AW, Lara J, Mathers JC, et al. Effect of vitamin C on endothelial function in health and disease: a systematic review and meta-analysis of randomised controlled trials. *Atherosclerosis*. 2014;235:9–20
66. Ashor AW, Werner AD, Lara J, et al. Effects of vitamin C supplementation on glycaemic control: a systematic review and meta-analysis of randomised controlled trials. *Eur J Clin Nutr*. 2017;71:1371–1380.
67. Mosdol A, Erens B, Brunner EJ. Estimated prevalence and predictors of vitamin C deficiency within UK's low-income population. *J Public Health*. 2008;30:456–460.
68. Agarwal S, Reider C, Brooks JR, Fulgoni VL. Comparison of prevalence of inadequate nutrient intake based on body weight status of adults in the United States: an analysis of NHANES 2001–2008. *J Am Coll Nutr*. 2015;34:126–134.

69. Massenti R, Perrone A, Livrea MA, et al. Regular consumption of fresh orange juice increases human skin carotenoid content. *Int J Food Sci Nutr*. 2015;66:718–721.
70. Leoncini E, Nedovic D, Panic N, et al. Carotenoid intake from natural sources and head and neck cancer: a systematic review and meta-analysis of epidemiological studies. *Cancer Epidemiol Biomarkers Prev*. 2015;24:1003–1011.
71. Aune D, Chan DS, Vieira AR, et al. Dietary compared with blood concentrations of carotenoids and breast cancer risk: a systematic review and meta-analysis of prospective studies. *Am J Clin Nutr*. 2012;96:356–373.
72. Zhou Y, Wang T, Meng Q, et al. Association of carotenoids with risk of gastric cancer: a meta-analysis. *Clin Nutr*. 2016;35:109–116.
73. Chen F, Hu J, Liu P, et al. Carotenoid intake and risk of non-Hodgkin lymphoma: a systematic review and dose-response meta-analysis of observational studies. *Ann Hematol*. 2017;96:957–965.
74. Panic N, Nedovic D, Pastorino R, et al. Carotenoid intake from natural sources and colorectal cancer: a systematic review and meta-analysis of epidemiological studies. *Eur J Cancer Prev*. 2017;26:27–37.
75. Takeda A, Nyssen OP, Syed A, et al. Vitamin A and carotenoids and the risk of Parkinson's disease: a systematic review and meta-analysis. *Neuroepidemiology* 2014;42:25–38.
76. Rowles J, Ranard KM, Smith JW, et al. Increased dietary and circulating lycopene are associated with reduced prostate cancer risk: a systematic review and meta-analysis. *Prostate Cancer Prostatic Dis*. 2017;20:361–367.
77. Song B, Liu K, Gao Y, et al. Lycopene and risk of cardiovascular diseases: a meta-analysis of observational studies. *Mol Nutr Food Res*. 2017;61:1601009.
78. Schwarz S, Obermuller-Jevic UC, Ute C, et al. Lycopene inhibits disease progression in patients with benign prostate hyperplasia. *J Nutr*. 2008;38:49–53.
79. Gann PH, Deaton RJ, Rueter EE, et al. A phase II randomized trial of lycopene-rich tomato extract among men with high-grade prostatic intraepithelial neoplasia. *Nutr Cancer*. 2015;67:1104–1112.
80. van Breemen RB, Sharifi R, Viana M, et al. Antioxidant effects of lycopene in African American men with prostate cancer or benign prostate hyperplasia: a randomized, controlled trial. *Cancer Prev Res (Phila)*. 2011;4:711–718.
81. Bradford Hill A. The environment and disease: association or causation? *Proc R Soc Med*. 1965;58:295–300.
82. Levy J, Bosin E, Feldman B, et al. Lycopene is a more potent inhibitor of human cancer cell proliferation than either α or ß-carotene. *Nutr Cancer*. 1995;24:257–266.
83. Silveira JQ, Cesar TB, Manthey JA, et al. Pharmacokinetics of flavanone glycosides after ingestion of single doses of fresh-squeezed orange juice versus commercially processed orange juice in healthy humans. *J Agric Food Chem*. 2014;62:12576–12584.
84. Manach C, Williamson G, Morand C, et al. Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *Am J Clin Nutr*. 2005;81:230S–242S.
85. Grosso G, Micek A, Godos J, et al. Dietary flavonoid and lignan intake and mortality in prospective cohort studies: systematic review and dose-response meta-analysis. *Am J Epidemiol*. 2017A;185:1304–1316.
86. Grosso G, Godos J, Lamuela-Raventos R, et al. A comprehensive meta-analysis on dietary flavonoid and lignan intake and cancer risk: level of evidence and limitations. *Mol Nutr Food Res*. 2017;61:1600930.
87. Bo Y, Sun J, Wang M, et al. Dietary flavonoid intake and the risk of digestive tract cancers: a systematic review and meta-analysis. *Sci Rep*. 2016;6:24836.
88. Wedick NM, Pan A, Cassidy A, et al. Dietary flavonoid intakes and risk of type 2 diabetes in US men and women. *Am J Clin Nutr*. 2012;95:925–933.
89. Knekt P, Kumpulainen J, Jarvinen R, et al. Flavonoid intake and risk of chronic diseases. *Am J Clin Nutr*. 2002;76:560–568.
90. Xu H, Luo J, Huang J, et al. Flavonoids intake and risk of type 2 diabetes mellitus: a meta-analysis of prospective cohort studies. *Medicine*. 2018;97:e0686.
91. Somerville VS, Braakhuis AJ, Hopkins WG. Effect of flavonoids on upper respiratory tract infections and immune function: a systematic review and meta-analysis. *Adv Nutr*. 2016;7:488–497.
92. Kause D, Roupas P. Dietary interventions as a neuroprotective therapy for the delay of the onset of cognitive decline in older adults: evaluation of the evidence. *Funct Foods Health Dis*. 2017;7:743–757.
93. Duffey K, Gordon-Larsen P, Steffen LM, et al. Drinking caloric beverages increases the risk of adverse cardiometabolic outcomes in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr*. 2010;92:954–959.
94. Lynn A, Hamadeh H, Leung WC, et al. Effects of pomegranate juice supplementation on pulse wave velocity and blood pressure in healthy young and middle-aged men and women. *Plant Foods Hum Nutr*. 2012;67:309–314.
95. Morand C, Dubray C, Milenkovic D, et al. Hesperidin contributes to the vascular protective effects of orange juice: a randomized crossover study in healthy volunteers. *Am J Clin Nutr*. 2011;93:73–80.
96. Park YK, Kim J-S, Kang M-H. Concord grape juice supplementation reduces blood pressure in Korean hypertensive men: double-blind, placebo controlled intervention trial. *Biofactors* 2004;22:145–147.
97. Amagase H, Nance DM. A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized *Lycium barbarum* (Goji) juice, GoChi. *J Altern Complement Med*. 2008;14:403–412.
98. Basu A, Betts NM, Oritz J, et al. Low-energy cranberry juice decreases lipid oxidation and increases plasma antioxidant capacity in women with metabolic syndrome. *Nutr Res*. 2011;31:190–196.
99. Dohadwala MM, Hamburg NM, Holbrook M, et al. Effects of Concord grape juice on ambulatory blood pressure in prehypertension and stage 1 hypertension. *Am J Clin Nutr*. 2010;92:1052–1059.
100. Ruel G, Lapointe A, Pomerleau S, et al. Evidence that cranberry juice may improve augmentation index in overweight men. *Nutr Res*. 2013;33:41–49.
101. Buscemi S, Rosafio G, Arcoleo G, et al. Effects of red orange juice intake on endothelial function and inflammatory markers in adult subjects with increased cardiovascular risk. *Am J Clin Nutr*. 2012;95:1089–1095.
102. Aptekmann NP, Cesar TB. Orange juice improved lipid profile and blood lactate of overweight middle-aged women subjected to aerobic training. *Maturitas* 2010;67:343–347.
103. Mulero J, Bernabe J, Cerda B, et al. Variations on cardiovascular risk factors in metabolic syndrome after consume of a citrus-based juice. *Clin Nutr*. 2012;31:372–377.
104. Xi B, Li S, Liu Z, et al. Intake of fruit juice and incidence of type 2 diabetes: a systematic review and meta-analysis. *PLoS One*. 2014;9:e93471.
105. Imamura F, O'Connor L, Ye Z, et al. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. *BMJ*. 2015;351:h3576.
106. Palmer JR, Boggs DA, Krishnan S, et al. Sugar-sweetened beverages and incidence of type 2 diabetes mellitus in African American women. *Arch Intern Med*. 2008;168:1487–1492.
107. Eshak ES, Iso H, Mizoue T, et al. Soft drink, 100% fruit juice, and vegetable juice intakes and risk of diabetes mellitus. *Clin Nutr*. 2013;32:300–308.
108. Fagherazzi G, Vilier A, Saes Sartorelli D, et al. Consumption of artificially and sugar-sweetened beverages and incident type 2 diabetes in the Etude Epidemiologique aupres des femmes de la Mutuelle Generale de l'Education Nationale-European Prospective Investigation into Cancer and Nutrition cohort. *Am J Clin Nutr*. 2013;97:517–523.
109. Murphy MM, Barrett EC, Bresnahan KA, et al. 100% Fruit juice and measures of glucose control and insulin sensitivity: a systematic review and meta-analysis of randomised controlled trials. *J Nutr Sci*. 2017;6:e59.
110. Kuzma JN, Schmidt KA, Kratz M. Prevention of metabolic diseases: fruits (including fruit sugars) vs. vegetables. *Curr Opin Clin Nutr Metabol Care*. 2017;20:286–293.
111. Norat T, Aune D, Chan D, et al. Fruits and vegetables: updating the epidemiologic evidence for the WCRF/AICR lifestyle recommendations for cancer prevention. *Cancer Treat Res*. 2014;159:35–50.
112. Clere N, Faure S, Martinez MC, et al. Anticancer properties of flavonoids: roles in various stages of carcinogenesis. *Cardiovasc Hematol Agents Med Chem*. 2011;9:62–77.
113. Cirmi S, Maugeri A, Ferlazzo N, et al. Anticancer potential of citrus juices and their extracts: a systematic review of both preclinical and clinical studies. *Front Pharmacol*. 2017;8:UNSP 420.
114. Aguilera Y, Martin-Cabrejas MA, de Mejia EG. Phenolic compounds as part of the Mediterranean diet: their role in the prevention of chronic diseases. *Phytochem Rev*. 2016;15:405–423.
115. Choi HK, Curhan G. Soft drinks, fructose consumption, and the risk of gout in men: prospective cohort study. *BMJ* 2008;336:309–312.
116. Chiu JL, Sievenpiper RJ, de Souza AI, et al. Effect of fructose on markers of non-alcoholic fatty liver disease (NAFLD): a systematic review and meta-analysis of controlled feeding trials. *Eur J Clin Nutr*. 2014;68:416–423.
117. US Department of Agriculture, US Department of Health and Human Services. Dietary Guidelines for Americans, 2015-2020, 8th ed. December 2015. Available at https://health.gov/dietaryguidelines/2015/guidelines/. Accessed August 7, 2019.
118. Leenders M, Boshuizan HC, Ferrari P, et al. Fruit and vegetable intake and cause-specific mortality in the EPIC study. *Eur J Epidemiol*. 2014;29:639–652.
119. Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ*. 2014;349:g4490.
120. Risk Factors Collaborators. Global, regional, and national comparative risk assessment of behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388:1659–1724.
121. Lee-Kwan SH, Moore LV, Blanck HM, et al. Disparities in state-specific adult fruit and vegetable consumption—United States, 2015. *Mmwr Morb Mortal Wkly Rep*. 2017;66:1241–1247.