Seed Oils and Health:

Examining and Evaluating the Evidence

Understanding dietary fat and fatty acids

Dietary fat accounts for approximately one-third of all calories consumed by Americans whereas protein and carbohydrate, the other two macronutrients, typically comprise approximately ~15% and 55%, respectively (**Figure 1**). Dietary fat provides 9 calories per gram whereas protein and carbohydrate each provide 4 calories per gram. For this reason, fat and foods high in fat, are calorically dense (i.e., higher energy density).

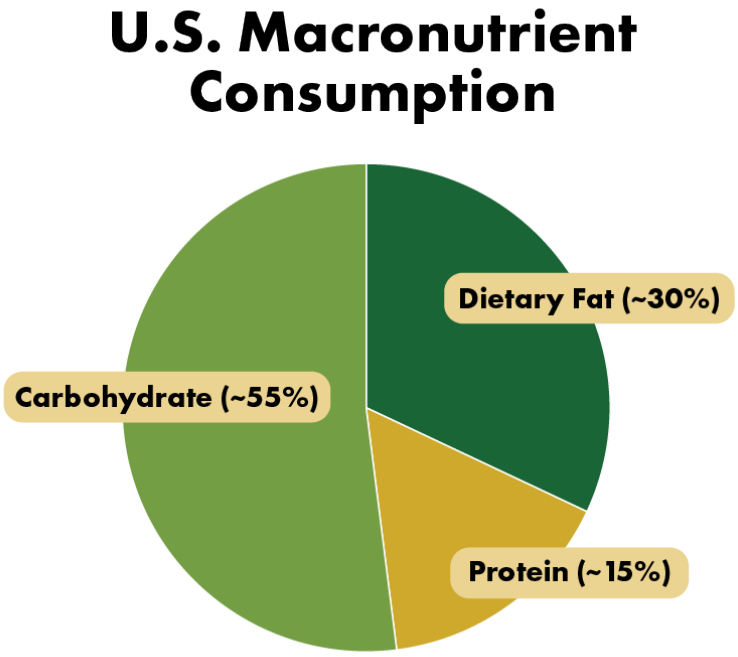


Figure 1

Dietary fat is comprised of different types of individual fatty acids as shown in **Table 1**. The two main classes of fatty acids are saturated and unsaturated fatty acids. In saturated fats, each carbon atom is attached to four hydrogen atoms whereas unsaturated fatty acids contain at least one carbon-carbon double bond, which means that the carbons are not saturated with hydrogen atoms (**Figure 2**). Unsaturated fatty acids are further subdivided into mono- (one double bond) and poly- (>1 double bond) unsaturated fatty acids.

Fats containing multiple double bonds are more susceptible to oxygen during storage (or becoming oxidized), than monounsaturated fats and saturated fats. For this reason, oils in high polyunsaturated fats should be stored away from light and heat and should be purchased in amounts that can be consumed within several months rather than longer periods of time. As discussed below, the susceptibility of seed oils (also known as vegetable oils) to oxidation doesn't infer that when they are consumed they cause oxidative stress*in humans because we have mechanisms in place to combat oxidation. Simply put, humans are not a bottle of seed oil.

Monounsaturated fats are commonly referred to as omega-9 fatty acids because the first double bond occurs at carbon 9 from the methyl end whereas polyunsaturated fatty acids are commonly classified as either omega-3 or omega-6 fatty acids because the first double bond occurs at carbon 3 and 6, respectively. In addition to the degree of saturation, fatty acids are of different chain lengths, that is, they contain different numbers of carbon atoms.

There are two essential fatty acids, the omega-6 polyunsaturated fatty acid, linoleic acid, and the omega-3 polyunsaturated fatty acid, alpha-linolenic acid. These two fatty acids are classified as essential because they are required for our survival but cannot be endogenously synthesized, that is, made by our body. Therefore, they must come from the foods we eat. Linoleic acid and alpha-linolenic acid account for most of the omega-6 and omega-3

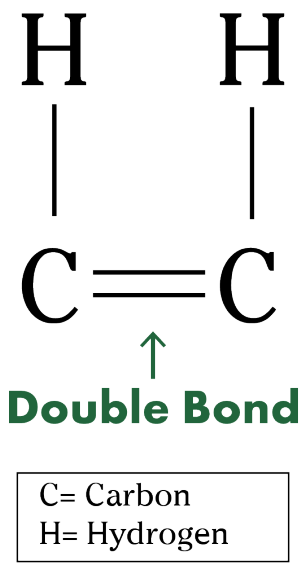


Figure 2

content of the diet, respectively.

As shown in **Table 1**, soybean oil contains approximately 16% saturated fat, 22% monounsaturated fat, and 62% polyunsaturated fat (1). Lard contains nearly equal amounts of saturated and monounsaturated fat (2). In general, animal fats tend to be predominantly saturated fat, whereas fats from plants such as seed oils tend to be predominantly unsaturated fats. There will be variations in the fatty acid composition of different fats due to differences in varieties and growing conditions. Animal fats are solid whereas plant fats are liquid at room temperature.

Table 1. Fatty acid content of selected oils and fats (g/100 g) listed in order of total PUFA content*

			Total poly-unsaturated				*Total Saturated*	
Oil or fat	**Nutrient Database Number**	**Total poly-unsaturated**	**Linoleic acid**	**alpha-linolenic acid**	**Mono-unsaturated**	**Total Saturated**	**Palmitic acid**	**Stearic acid**
Grapeseed	4517	69.9	69.6	0.1	16.1	9.6	6.7	2.7
Soybean	4044	57.7	51.0	6.8	22.8	15.6	10.5	4.4
Corn	4518	54.7	53.5	1.2	27.6	12.9	10.6	1.9
Cottonseed	4502	51.9	55.5	0.2	17.8	25.9	22.7	2.3
Sesame	4058	41.7	41.3	0.3	39.7	14.2	8.9	4.8
Rice bran	4037	35.0	33.4	1.6	39.3	19.7	16.9	1.6
Sunflower[1]	4642	29.0	28.9	<0.1	57.3	9.0	4.2	3.6
Canola	4582	28.1	19.0	9.1	63.3	7.4	4.3	2.1
Peanut	4042	19.9	19.6	0.0	57.1	16.2	9.5	2.2
Avocado	4581	13.5	12.5	1.0	70.6	11.6	10.9	0.7
Safflower[2]	4511	12.8	12.7	0.1	75.2	7.5	4.9	1.9
Olive	4053	10.5	9.8	0.9	73.0	13.8	11.3	2.0
Lard	4002	11.2	10.2	1.0	45.1	39.2	23.8	13.5
Palm	4055	9.3	9.1	0.2	37.0	49.3	43.5	4.3
Tallow	4001	4.0	3.1	0.6	41.8	49.8	24.9	18.9
Butter	1001	3.0	2.7	0.3	21.0	51.4	21.7	10.0

**USDA FoodData Central, Standard Release Database. https://fdc.nal.usda.gov/*
[1]Mid-oleic (most commonly used sunflower oil) [2]High oleic (primary safflower oil of commerce)

Origins of the seed oil controversy

Until recently, there was little debate about the merits of seed oils because their consumption is endorsed by health agencies around the world. It has been and is widely accepted that these oils are beneficial to health.

It is universally agreed that replacing saturated fat in the diet with mono- and polyunsaturated fat lowers blood cholesterol levels, particularly LDL-cholesterol, elevated levels of which are an important cardiovascular disease risk factor. The U.S. Food and Drug Administration has approved Qualified Health Claims for soybean, canola and corn oil due to their unsaturated fat content. Replacing saturated fat with these unsaturated fat options and not increasing your total number of calories per day may reduce the risk of heart disease.

Nevertheless, in recent years, claims have been made that linoleic acid, and oils high in this fatty acid, which includes most seed oils, are harmful to health. Claims are based on several assertions but, most notable is that linoleic acid causes inflammation and oxidative stress, two processes involved in the etiology of most chronic diseases (3 4). Evidence cited in support of these claims includes the increase in the prevalence of obesity and diabetes which coincides with the increased popularity of seed oils. (As discussed below, results from ecological studies are not useful for establishing cause and effect relationships). Claims that seed oils are a modern addition to the diet and require extensive processing to be produced also figure prominently in discussions by those recommending the avoidance of seed oils.

The following information is intended to briefly address concerns and questions related to seed oils.

1. What is the recommended intake of linoleic acid?

The Acceptable Macronutrient Distribution Range (AMDR) for linoleic acid established by the Institute of Medicine (now known as the National Academy of Medicine) two decades ago is 5 to 10% of energy (5). The AMDR matches the recommendation of the American Heart Association issued in 2009 (6).

2. How much linoleic acid do Americans consume?

Americans consume approximately 8% of their calories from linoleic acid which is in line with recommendations. Little change in linoleic acid intake has occurred over the past 20 years (7).

3. Are seed oils a modern addition to the diet?

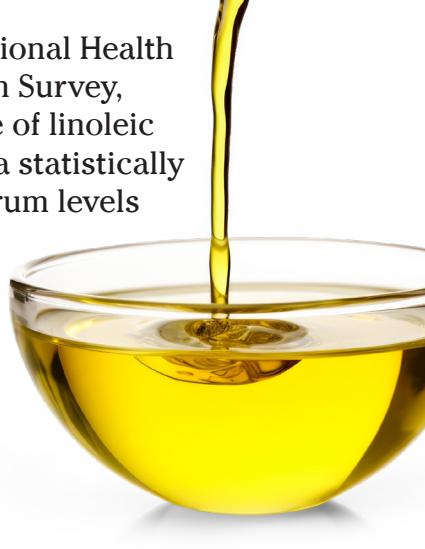
No. Sesame seed oil (8) and sunflower seed oil (9) have been consumed for many centuries. Olive oil (10) and palm oil (11) also have a multi-century-long history of consumption, but these oils are derived from fruits, not seeds. In the United States, seed oils markedly increased in popularity beginning in the 1960s with the rise in the consumption of soybean oil (12). From that point on, a gradual shift away from animal sources of fat to plant sources of fat occurred, and with it, came a marked increase in the intake of linoleic acid.

4. Does linoleic acid increase inflammation?

No. The authors of a narrative review that evaluated 15 randomized controlled trials (13) published in 2012 and a meta-analysis of 30 (14) randomized controlled trials published in 2017 concluded that linoleic acid does not increase inflammation. Additionally, a meta-analysis of 83 randomized controlled trials published in 2021 found that supplementation with polyunsaturated fatty acids has little or no effect on the prevention or treatment of inflammatory bowel disease and long-term inflammatory status (15).

Furthermore, several epidemiologic studies show that linoleic intake or markers of intake, are not associated with inflammation (16), or are inversely related to inflammation, that is, linoleic acid is associated with reduced inflammation (17-20).

For example, a cross-sectional analysis of 17,689 participants in the US National Health and Nutrition Examination Survey, showed that higher intake of linoleic acid was associated with a statistically significant decrease in serum levels of a key marker of overall inflammation (19). It is relevant to add that there is evidence that saturated fat increases inflammation (21) – something that is not often mentioned.



5. What caused thinking about linoleic acid and inflammation to change?

Concerns about inflammation assume that the linoleic acid we ingest is converted in our bodies to another fatty acid (arachidonic acid) from which pro-inflammatory compounds are produced. However, over the past 15 years, it has become abundantly clear that endogenous conversion of linoleic acid to arachidonic acid is negligible (22). The body tightly controls levels of arachidonic acid. Also, compounds produced from arachidonic acid are now known to have both pro- and anti-inflammatory effects.(23) Arachidonic acid is found in animal products, not seed oils.

6. Has the dietary omega-6 to omega-3 fatty acid ratio increased over the past several decades?

Yes. According to an analysis of over 17,000 participants of the National Health and Nutrition Examination Survey (years 2009-2016), the US dietary omega-6 to omega-3 fatty acid ratio is approximately 10:1 (24). Estimates are that around 1900, the US ratio was 5- 6:1 (12). These ratios are much higher than the estimates of the ratio of hunter-gatherers, which may have been as low as 2:1 (25).

7. Is the dietary omega-6 to omega-3 fatty acid ratio still considered a metric of overall diet quality?

No. At one point, a common perspective within the nutrition community was that a low omega-6 to omega-3 fatty acid ratio was desirable although the optimal ratio was debatable (26). However, the current consensus among health agencies is that this ratio is uninformative because both types of fatty acids are beneficial (see reference for further information) (27). The emphasis is now placed on making sure enough of each type of fatty acid is consumed (28).

Although higher amounts of linoleic acid can decrease the endogenous synthesis of longer-chain omega-3 fatty acids (which are beneficial) this synthesis is quite limited, even when linoleic acid intake is very low. To address the need for long-chain omega-3 fatty acids, it is best to directly consume these fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The best sources are cold-water fish such as salmon and mackerel. For those who do not consume cold water fish or do not want to use fish oil supplements, supplements derived from algae are widely available.

8. Does linoleic acid intake increase oxidative stress?

No. Oxidative stress* refers to the balance between the endogenous production of compounds that cause oxidation and the natural antioxidant defenses that our body possesses (29). The lack of effect of linoleic acid on markers of oxidative status is illustrated by four randomized controlled trials that lasted 4–12 weeks and compared the effects of soybean oil with fats lower in linoleic acid. Only one of the four showed an increase in a marker of oxidative status, but given that an in vitro test, that is, a test not conducted in a living organism, was used to measure oxidation, and that soybean oil lowered levels of cholesterol, the overall health effect is likely beneficial (30).

In two trials, no effects on a range of oxidation markers were observed (31 32) and in one trial a measure of antioxidant compacity improved (33). In addition, in a two-year trial in which Indian participants with stable coronary artery disease were given either coconut oil, which is very low in linoleic acid, or sunflower oil, which is high in linoleic acid, to use for cooking, no differences in oxidative stress were noted between groups (34).

9. What impact does linoleic acid intake have on the risk of cardiovascular disease?

Evidence from multiple meta-analyses of prospective cohort studies consistently shows that higher polyunsaturated fat intake (primarily LA) and higher circulating (serum or plasma) linoleic acid levels are associated with lower risk of cardiovascular disease (CVD) (35-38). For example, a systematic review and meta-analysis of 18 prospective cohort studies found that a high intake of polyunsaturated fat was associated with a 13% reduced risk of CVD mortality and that for each 5% increase in energy intake from linoleic acid there was a 7% lower risk of CVD mortality (39).

In addition, and most importantly, a meta-analysis conducted by the American Heart Association (AHA) of four longer-term randomized controlled trials found that the risk of coronary heart disease or coronary events was reduced by 29% in response to higher intakes of linoleic acid (38). *(Note: Several trials commonly cited by those that recommend avoiding seed oils were evaluated by the AHA but were not included in the meta-analysis because of serious experimental design weaknesses and limitations. The AHA only included high-quality studies in its analysis).*

10. What impact does linoleic acid intake have on the risk of diabetes?

Several researchers have found blood or tissue levels of linoleic acid are positively associated with insulin sensitivity (40-46) and with reduced risk for developing insulin resistance as well as type

2 diabetes (45, 47, 48). Especially notable is a pooled analysis of individual-level data for 39,740 adults from 20 prospective cohort studies which found that higher proportions of linoleic acid biomarkers as percentages of total fatty acid were associated with a more than one-third reduced risk of developing type 2 diabetes (49).

In agreement, a pooled analysis of over 200,000 US men and women involved in three cohorts who were followed for approximately three decades showed that linoleic acid intake was significantly inversely related to risk of developing type 2 diabetes (50). Additionally, the results of a meta-analysis of 102 randomized controlled trials that included 239 dietary intervention arms involving 4,220 adults found that replacing 5% of calories from saturated fat with polyunsaturated fat significantly lowered blood glucose, hemoglobin A1c (a measure of longer-term glycemic control) C-peptide, and insulin resistance (50).

11. Does seed oil consumption increase the risk of obesity?

No. Obesity is a chronic disease of multifactorial origin that involves genetic as well as environmental determinants. Recent research with anti-obesity medications, such as GLP-1 receptor agonists, highlights the role of hormones in the development of appetite regulation and overweight/obesity. The prevalence of obesity has increased markedly over the past several decades in this country, and more recently, in many other high-income countries. However, some studies suggest that linoleic acid intake leads to elevated resting metabolic rate (i.e., an increase in the number of calories you burn as your body performs basic life-sustaining functions) (51 52), which conflicts with concerns that seed oils increase the risk of developing obesity, although not all studies show this is the case.

Also, some evidence indicates polyunsaturated fat decreases liver fat accumulation (47 53-56). Fatty liver is one of the main complications of obesity, as is diabetes, the risk of which is decreased in response to linoleic acid intake (50).

12. What impact does linoleic acid intake have on cancer risk?

The relationship between linoleic acid intake and cancer has been studied to a much lesser degree than CVD and type 2 diabetes. Nevertheless, a large, recently published prospective cohort of 253,138 UK Biobank participants examined the relationship between plasma levels of linoleic acid and cancer at 19 different sites. During the average follow-up period of 12.9 years, 29,838 participants were diagnosed with cancer. Plasma levels of linoleic acid were inversely associated with risk of 14 different cancers while in another four, there was no relationship (57).

13. Are seed oils highly processed?

Yes. Seed oils do undergo considerable processing although seed oils are not classified by the Nova food classification system as ultra-processed. Extraction of oil from seeds is accomplished using pressure or solvents such as hexane. The residual hexane levels in oils are magnitude of orders below safety thresholds established by regulatory bodies. Decreasing the non-oil components while maintaining the inherent fatty acid composition and preserving the inherent antioxidant properties of the seed oil serves as the basis for subsequent common preparation steps of degumming, refining, bleaching (meaning color removal, not bleach addition), and deodorization.

Claims are made that the processing results in harmful substances being added and created. However, the critical issue is not what happens to the oil, but what happens when it is consumed. The totality of the evidence clearly indicates that seed oil consumption promotes overall health.

Evaluating Research

The marked increased consumption of seed oils beginning in the 1960s (12) correlates with the increase in the prevalence of obesity (58). This type of ecological correlation, while intriguing, is not a basis for concluding that seed oil consumption contributes to the obesity epidemic. During roughly that same period, death due to cardiovascular disease (CVD) dramatically decreased (59). Did seed oils contribute to the decreased mortality? Perhaps, but along with the increased seed oil consumption was a decrease in smoking rates (60), a major CVD risk factor (61), and improvements in medical treatment of CVD (62).

Ecological observations or studies are limited because inferences about individuals are made based on aggregate data from groups, leading to potential confounding variables and difficulty controlling for individual-level factors. For example, perhaps people who consume larger amounts of seed oils also smoke more and exercise less. Nevertheless, the results of ecological studies often form the basis for generating hypotheses, as do ***animal studies*** (**Figure 3**, hierarchy of evidence). But for reaching meaningful conclusions more robust designs are needed; most notable are prospective epidemiologic studies and randomized controlled trials. These types of studies have been extensively used to evaluate the relationship between seed oils and health outcomes.

Randomized controlled trials are considered to be the only type of study that allow conclusions about causality to be made because the act of randomization balances participant characteristics between or among groups allowing attribution of any differences in an outcome to the study intervention (63). However, because chronic diseases typically take decades to develop and compliance with dietary interventions often wanes with time, randomized controlled trials investigating the effect of a dietary intervention on chronic disease risk usually focus on changes in markers of disease risk, rather than the disease outcome per se. Thus, blood pressure and blood lipid levels (e.g., cholesterol) are assessed, rather than coronary events such as heart attacks, and bone turnover (formation and resorption) and bone mineral density are assessed, rather than fractures. Nevertheless, in many cases it is infeasible to conduct randomized controlled trials to examine certain dietary hypotheses which is why prospective cohort studies are considered so valuable (64).

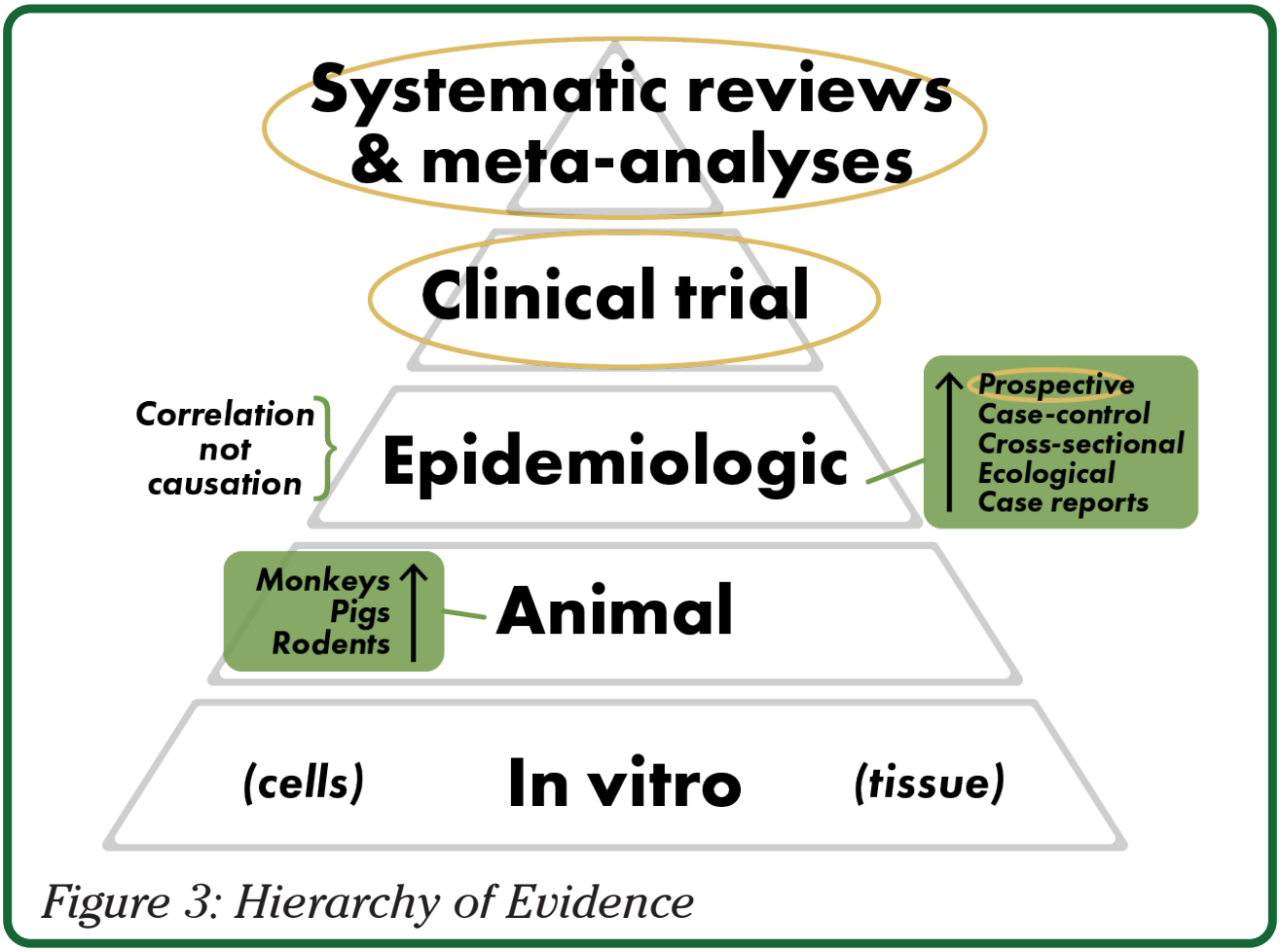


Figure 3: Hierarchy of Evidence

Prospective cohort studies form the basis for much of our understanding of diet-health relationships and are extensively relied upon to develop dietary guidelines. For this type of study, a group of people (cohort) who do not have the outcome of interest at study enrollment is followed for a period during which data on the exposure to factors(s) of interest is collected. Outcomes are then tracked, to investigate associations between exposures and outcomes. These types of studies often follow thousands of individuals for many years and even decades.

Despite their utility, prospective cohort studies, like all epidemiologic studies, are not able to establish causality. Because participants are not randomized there may be factors (confounding variables) unaccounted for that are responsible for observed associations. Researchers go to great lengths to take these factors into account, that is to statistically adjust for them, but it is not possible to know with certainty that a study has avoided all residual confounding. Having said this, there is a set of criteria (Bradford Hill criteria) that can be useful in establishing epidemiologic evidence of a causal relationship between a presumed cause and an observed effect that has been widely used in public health research (65).

When evaluating the veracity of a hypothesis, it is critical to not only consider study type and quality, but also to make sure conclusions are based on the totality of the evidence. For most dietary hypotheses, an enormous amount of relevant research has been conducted. For various reasons, outliers – studies that produce results inconsistent with the greater body of work – are usually present. By selectively citing the literature (i.e., cherry-picking), one can construct a heavily referenced document that supports a given hypothesis but does not accurately reflect the consensus. Consequently, although narrative reviews of the literature are routinely published and can contribute to the literature, they carry much less weight among scientists than systematic reviews and meta-analyses and are not included in the hierarchy of evidence (**Figure 3**).

Systematic reviews are conducted to avoid unintentionally omitting studies. Formal procedures to identify studies are employed and presented along with the results when the research is published. In this way, determining that the totality of the evidence has been considered with confidence is possible. Because it is unlikely that any single study is sufficiently robust to form the basis for a conclusion, the results of multiple similarly designed studies are often combined and statistically analyzed (i.e., meta-analyzed) to integrate the findings. It is common for systematic reviews and meta-analyses of prospective cohort studies, and of randomized controlled trials, to be conducted.

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