The Association Between Type of Fat and the Risk of Developing Cardiovascular Diseases

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The Association Between Type of Fat and the Risk of Developing Cardiovascular Diseases

Dovid Leib Glassner

Dovid Leib Glassner graduated June 2018 with a Bachelor's of Science in Biology and is currently pursuing medical school.

Abstract
Objective: To determine the significance of various types of dietary fat in the progression of atherosclerosis leading to heart disease.
Methods: Study inclusion criteria constituted relevance to the discussion topic and peer reviewed literature. Age of the published material was taken into account as well, with greater preference being given to more recent research as the topic of nutrition and its relation to chronic disease remains an emerging science.
Results: This research review found an overall significant relationship between the type (monounsaturated, polyunsaturated, saturated and trans-fat) of dietary fat intake and the incidence of cardiovascular disease. While earlier research identified an increased risk of cardiovascular disease to be associated with an overall increased intake of dietary fat, newer studies recognized the increased risk to be associated more specifically with saturated and trans fatty acids. Substitution of other dietary fats in place of saturated fat in the diet also plays a role in cardiovascular disease. The studies reviewed here found a protective effect of polyunsaturated fatty acids when replacing saturated fat in the diet. On the other hand, replacing saturated fats with carbohydrates has no evidence of improved cardiovascular health. Studies looking at the implications of substituting saturated fat with monounsaturated fats remain inconclusive at this time. Aside from dietary fat intake, the progression of atherosclerosis leading to cardiovascular disease can be caused by oxidative stress such as in the case of hyperglycemia and diabetes.
Conclusions: As health care costs continue to rise in this country, preventive medicine plays an increasingly important role in the prevention and treatment of chronic disease. Research shows that decreasing the percentage of saturated fats in the diet and substituting these with healthier polyunsaturated fats, as well as minimizing oxidative stress in the body can decrease the incidence of cardiovascular disease, a leading cause of death in the United States.

Introduction
In February of 1980 the United States Department of Agriculture and Department of Health and Human Services jointly published the first set of Dietary Guidelines for Americans. During this time, health scientists were beginning to focus on the link between macronutrient intake and a correlated risk for chronic diseases. In these original guidelines, Americans were encouraged to keep their total fat intake levels below thirty percent of their diet, have less than ten percent of dietary fat come from saturated fat, and maintain a cholesterol intake that was under 300 mg per day (Canty, 2018).

The guidelines have been updated every five years since and have evolved based on accumulating scientific evidence, population patterns in health status, food consumption, and physical activity. The 2015 Dietary Guidelines have a stronger emphasis on healthy eating patterns and regular physical activity. However, there has been minimal change in the recommendations for fat intake for almost 40 years since the first set of guidelines. In 2015, the Dietary Guidelines for Americans recommended that fat be 20-35% of the diet with less than 10% coming from saturated fat and minimizing trans fats as much as possible. While the 2015 guidelines did not address cholesterol, the recommendations from 2010 remain the same as well (<300 mg/day) (U.S. Dept. of Health and Human Services, 2015).

Controlling fat intake has consistently been recommended to improve health for Americans with a specific focus on limiting saturated fat in the diet. However, heart disease, a form of cardiovascular disease, remains to be the leading cause of death for both men and women worldwide. Stroke, a complication of cardiovascular disease is the fifth leading cause of death in the United States. Dietary fat intake is a major modifiable risk factor in the development and progression of cardiovascular disease. (Center for Disease Control, 2017).

Methods
Studies reviewed in this paper were selected from journal databases, library catalogs, and Health and Nutrition Science professional websites. Papers were gathered from PubMed, CINAHL, Medline, and similar scientific search engines using advanced search phrases “PUFA,” “MUFA,” “dietary fat intake,” “trans-fat,” “oxidative stress,” and “CVD”.

The writer considered over 36 papers and over 20 papers were included in the final research review. Study inclusion criteria consisted of relevance to the discussion topic and peer-reviewed literature. Age of the published material was taken into account as well, with greater preference being given to more recent research as the topic of nutrition and its relation to chronic disease remains an emerging science.

To improve the writer and reader’s understanding of the relation between dietary fat intake and disease, noted textbooks in advanced biochemistry topics were referenced and included in the discussion section of this paper.

Discussion
Fat is an essential macronutrient required by the body. In 1927, the effects of fat deficiency on growth and development inspired researchers Evans and Burrs to dub fat “vitamin F”. Two years later, in 1929, Evans and Burrs found that a fat-free diet in weanling rats produced impaired growth, scaly skin, tail necrosis, increased mortality, and impaired fertility (Ross, et. al, 2014). These symptoms were reversed when provided with linoleic or linolenic acid and the term “essential fatty acids” was coined. Almost thirty years later, in 1958, Essential Fatty Acid Deficiency (EFAD) was first demonstrated in humans, when infants fed a milk-based diet lacking essential fatty acids (EFAs) showed severe skin symptoms alleviated by the addition of linoleic acid. Total Parenteral Nutrition Support, lacking fat-soluble vitamins, was
also shown to produce EFAD in a 6-year-old girl maintained on total parenteral nutrition for five months (Burr, 1981).

We require fat and fat-soluble vitamins for energy reserves, cell signaling, synthesis of hormones, and their structural role in cell membranes (Canty, 2018). The average intake of fat in this country has remained relatively consistent since the 1990s. The average American consumes 33% of his calories from fat and 10% from saturated fat. There were significant changes over the years in the consumption of monounsaturated fat (MUFA) (14.6% to 13%, p = 0.03) and polyunsaturated fat (PUFA) (6.9%-8.0%, p = <0.001) as well as the ratio of PUFAs to saturated fat (7.1%-8.1%, p = < 0.001) (fig. 1) (Vadiveloo, et. al. 2013).

Atherosclerosis is the narrowing of the arterial wall caused by a buildup of plaque. As the endothelial layer on the artery wall weakens, it becomes susceptible to plaque accumulation by a high concentration of Low-Density Lipoprotein (LDL)-cholesterol in the blood. As the plaque begins to build, monocytes and macrophages are attracted to the site of the plaque contributing to stenosis (Narrowing of the artery lumen). The layer of smooth muscle in the artery begins to grow a fibrous cap over the plaque. As the plaque continues to develop, this cap can rupture and form a blood clot that may cause a heart attack or a stroke (Escott-Stump, 2015, Mahan and Raymond, 2017).

Types of Fats
As part of the Strong Heart Study, researchers examined the association between dietary fat intake and coronary heart disease in 2,938 Indian American adults ages 45-79 for an average of 7 years. Over 400 participants experienced Coronary Heart Disease (CHD) during this time, including 138 fatalities. The researchers divided participants into two age group categories, 47-59 years and 60-79 years. Across both age groups, individuals who developed CHD were more likely male, hypertensive and with lower High-Density LipoProteins (HDL) levels and higher serum triglycerides. Amongst the older group, those that developed CHD had higher LDL levels as well. Amongst the younger group, an increasing rate of mortality due to CHD was seen with greater quartiles of total fat intake, specifically saturated and monounsaturated fat (Lee, et. Al. 1990). This study suggests that abnormal lipoprotein levels (low HDL, high LDL) are associated with an increased morbidity in adults. Additionally, total fat, rather than a specific type of fat, is associated with increased mortality from CHD.

The Seven Countries Study (Keys, et. al. 1984) investigated the intake of various fatty acids as well as dietary cholesterol in relation to serum cholesterol and 25-year mortality from coronary heart disease. The study was carried out from 1956-1964 and constituted 16 cohorts across seven countries to include over 12,000 men between the ages of 40-59 years. Dietary intake data was collected and standardized by one dietitian. In 1960 total lipids were measured (at that time there was no instrument available to measure trans-fat, omega-3 or omega-6 fatty acids). Data was collected and reported for saturated, monounsaturated and polyunsaturated fats. Later, in 1987, total lipids were isolated and cis and trans fats, as well as omega-3 fatty acids, were identified. The individual saturated fatty acids, namely lauric acid and myristic acid, were significantly related to cholesterol levels (p < 0.001). Moreover, the researchers identified a strong positive relationship between the intake of saturated fats and death rates from CHD (p <0.001) (fig. 2). It is worthwhile to note that a 25-year lapse in time from the collection of data to the analysis may have impacted the researchers’ findings.

More recent studies support these findings as well, indicating that the source of dietary fat influences heart disease. A 20 year follow up of the Nurses’ Health Study looked at the association specific types of dietary fat intake as they relate to the risk of coronary heart disease. The study consisted of 78,778 US women who were without CVD or diabetes at the initiation of the study in 1980. At the follow up, 1,766 incidences of CHD were reported, 525 of which were fatal. Researchers found that intake of polyunsaturated fats was inversely associated with CHD (P = 0.004) (fig. 3). The results were substantial amongst women with an overweight BMI (>35 kg/m2). Trans-fat intake was associated with an increased risk of developing CHD (P=0.01), particularly in women under 65 years of age (Colditz, Hankinson, 2005).
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These findings are consistent with a 2006 cross-sectional study of 1,123 adults between the ages of 20 and 98 explaining the possible connection between the inverse relationships. The researchers looked at the relationship between fasting plasma polyunsaturated fatty acid (PUFA) levels and markers of inflammation. They found a statistically significant, negative correlation between the intake of PUFAs, specifically omega-3 and omega-6 fatty acids and plasma levels of pro-inflammatory markers (IL-6, TNF, IL-10, CRP). This study suggests that the anti-inflammatory properties of polyunsaturated fatty acids are associated with lowering plasma levels of pro-inflammatory markers that play a role in the progression of atherosclerosis (Ferruci, et. Al. 2006).

Replacing Saturated Fat in the Diet

Current guidelines from the HHS and USDA recommend <10% of calories come from saturated fat and the American Heart Association recommends no more than 5-6% of intake should come from saturated fat to decrease LDL cholesterol. However, there are fewer studies and recommendations discussing what the recommended replacement for saturated fat in the diet should be. A meta-analysis of eight randomized control trials that included over 1,000 incidences of CHD amongst 13,614 participants, found that increased PUFA intake in place of saturated fat in the diet reduced CHD events by 19% (Mozaffarian, et. Al. 2010). Consequently, it may be concluded that the effects of replacing saturated fat in the diet with monounsaturated fat are mixed. Future studies looking at the implication of replacing saturated fat with proteins and/or MUFAs would be beneficial.

Animal vs. Plant Fats

Emerging research looked at monounsaturated fatty acids to identify if the source of MUFAs had a relationship to its impact on heart disease. Researchers used data from the Nurses’ Health Study that included 63,000 women and data from the Health Professionals Follow-Up study that included 30,000 men. Both of these studies utilized food frequency questionnaires administered every four years to evaluate participants’ diets. When analyzed, participants with a higher intake of MUFAs from plant sources showed a 16% lower risk of death (from any cause) compared with those that had a lower intake. In contrast, participants with a higher intake of MUFAs coming from animal protein exhibited a 21% increase in risk of death related to any cause. Replacing dietary MUFAs from animal sources for the equivalent per gram in plant sources may lower the risk for death by heart disease or any cause of death between 24% and 26% (Roeder, 2018).

Similar findings have been reported for with saturated fat. It is thought that plant sources of saturated fat may, in fact, play less of a role in the morbidity and mortality from coronary heart disease than animal sources. These findings can be explained by a recent study looking at the structural implications of fatty acids. An animal source of saturated fatty acids is located mainly at the sn-2 position of the glycerol backbone as shown in figure 5 and affects the metabolism, functionality, and physiological effects of the saturated fatty acids (fig. 4) (Nettelton, et. al. 2017). The Multi-Ethnic Study of Atherosclerosis aimed to determine the association between SFA intake from varying food service and in the incidence of CVD. The study included 5,209 participants between the ages of 45–84 that were followed for a 20y Follow-up.

It is important to note that these studies measured the effects of replacing saturated fatty acids with PUFAs in the diet and therefore cannot ascertain whether the benefits were related to the decrease in saturated fatty acids or the increase in dietary PUFAs. It can be concluded that replacing saturated fats with PUFAs in the diet likely decreases the incidence of CHD while replacing saturated fat with carbohydrates does not. Consequently, it may be concluded that the effects of replacing saturated fat in the diet with monounsaturated fat are mixed.

Future studies looking at the implication of replacing saturated fat with proteins and/or MUFAs would be beneficial.
decade from 2000. Diet was assessed using a food frequency questionnaire and over 300 cases of CVD were assessed during follow up valuations.

After adjusting for confounding factors, researchers concluded that a higher intake of saturated fat from dairy sources was associated with a lower risk of CVD (95% CI for +5 grams per day and 5% of energy intake from dairy sources of saturated fat). In contrast, meat saturated fat was associated with an increased risk of developing CVD with the same increase in grams per day and % energy intake (fig. 5).

Substituting 2% of energy intake from meat sources of saturated fat with dairy sources of saturated fat was associated with a 25% decreased risk of CVD (Otto, et al. 2012). This particular study found no association between CVD and intake of plant or butter saturated fats, however, intakes recorded in the Food Frequency Questionnaires were narrow.

**Processed Fat: Trans Fat**

Since in 2006, food manufacturers have been required to list trans-fat on all food labels. Trans fats (trans unsaturated fatty acids) are artificially produced solid fats. Liquid vegetable oils are heated with catalysts in a process called hydrogenation, which breaks double bonds in unsaturated fats and adds hydrogens, thereby solidifying the fat, making it a solid at room temperature.

The current dietary guidelines for healthy Americans recommend keeping trans-fat intake “as low as possible” (<10% of total calories). These recommendations are based on studies that have found that trans fats increase LDL-cholesterol levels in the blood while decreasing healthy levels of HDL-cholesterol. One early study demonstrated this by providing 34 adult women and 25 adult men with three diets that each study subject followed for three consecutive weeks. All three diets were mixed, and 25 adult men with three diets that each study subject fol

![Figure 5: Dietary Source of Saturated Fat May Affect CVD Risk Source: Canty, D. Advanced Nutrition: Protein, Fats and Carbohydrates. Spring 2018.](image-url)

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**Do PUFAs Have any Faults in Relation to Disease?**

Lipid peroxidation is the oxidative deterioration of lipids possessing double bonds by interaction with a reactive oxygen species (ROS). Given their higher content of double bonds, PUFAs are more susceptible to oxidation than SFAs and even MUFAs. Antioxidants, such as vitamin E and vitamin C, in our diets and in our bodies, serve to detoxify the oxidative damage caused by ROS. In a healthy individual, the generation of reactive oxygen species is in normal balance with antioxidant activity. However, increasing amounts of oxidative damage and/or decreasing amounts of antioxidants leads to oxidative stress in which elevated levels of ROSs can lead to oxidative damaging of proteins, carbohydrates and DNA molecules.

Oxidative stress has been linked to disease states such as atherosclerosis and certain cancers. The question remains whether the disease state causes the increased lipid peroxidation and oxidative stress or if the oxidative damage leads to the disease state (Ross, et al. 2014).

**Coconut Oil: Celebrity Status Threatened**

The American Heart Association published a 2018 Presidential
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Advisory that had much of the health community involved in a conversation regarding saturated fats and their role in oxidative damage and chronic disease. The AHA's advisory mentioned a New York Times piece highlighting a recent health survey in the United States which found that 73% of Americans classified coconut oil as a “health food” compared to 37% of nutritionists. The AHA contributes the positive perception of coconut oil in its relation to health promotion and disease prevention to a result of good marketing by the coconut oil industry (Sacks et al., 2017). Statistics from the USDA reveal that coconut oil consumption increased from 2013 to 2014 by 9.55% and then dropped in 2014 and 2015 to 6.23% and 13.47% respectively. This information sheds some light on the increased promotion of coconut oil as a health food by the coconut oil industry and the belief of Americans, that it is a health food. However, coconut oil's nutrition profile did not change during this time. It remains to be 82% saturated fat, and like all densely saturated fats, plays a role in cardiovascular disease.

A recent review looked at seven interventional studies comparing coconut oil with unsaturated fats in the diet and their individual influences on lipid profiles of study participants. All seven trials resulted in higher total cholesterol for those receiving coconut oil intervention, all of which were statistically significant. Six out of the seven studies found a statistically significant increase of LDL cholesterol for the intervention group. HDL levels were statistically significantly raised in five studies for those receiving the coconut oil intervention (Eyres et al., 2016). The AHA warns consumers that the HDL improvements seen with diet or drug treatment cannot be directly linked to changes in CVD occurrences and therefore encourages Americans to look at the LDL changes as affected by various fats alone in regard to their role in CVD (Sacks et al., 2017).

Atherosclerosis: Other Players
As the walls of the arteries get thicker, narrowing the lumen due to plaque buildup, patients with atherosclerosis experience worsening symptoms of CVD, including hypertension (Nelms et al., 2016). During the initial stages of plaque buildup, the endothelial cells of the luminal lining, which provide the barrier between the lumen and the vascular wall, may experience dysfunction and contribute to increased plaque and blood pressure. Certain stimuli can trigger the dysfunction of the endothelial cells, deeming these stimuli proatherogenic. Diabetes and oxidative stress are amongst the major players that contribute to the eventual loss of functionality of the endothelial cells, along with dyslipidemia, abnormally elevated cholesterol or fats (lipids) in the blood (Chistiakov, et al., 2015).

Glucosamine, often used in the management of osteoarthritis, has anti-inflammatory effects by contributing to a redox state in an oxidative environment. In an attempt to take advantage of its properties, glucosamine supplements consisting of 300 mg were given to 20 individuals daily for 30 days and arteriosclerosis and CVD were compared to 19 controls. Flow-mediated vasodilation was monitored in all participants at the start and for the duration of the four-week trial. At the end of four weeks, parameters such as blood pressure, blood glucose, and lipid levels were measured. No significant changes were found in these clinical markers prior to or following the study between the two groups. However, glucosamine supplementation significantly improved flow-mediated vasodilation (P = 0.02) highlighting the role that oxidative stress independently plays in atherosclerosis and cardiovascular disease (Katoh et al., 2017).

This is similar to what is seen in the strong correlation between diabetes, specifically type 2, and incidence of CVD. The American Heart Association considers diabetes to be one of the seven top causes of cardiovascular disease. More than 68% of people over the age of 65 with diabetes will die from a form of heart disease. Adults with diabetes are twice to four times as likely to die of heart disease than adults of the same age without diabetes (American Heart Association, 2018).

Oxidative stress has been shown to contribute to atherosclerotic buildup in animal models. Elevated blood glucose in type 2 diabetic patients allows for glucose persisting in the bloodstream to become damaged, increases the amount and rate at which reactive oxygen species (ROS) accumulate. ROS are potent oxidants that, without adequate antioxidant activity, can proliferate and cause oxidative damage in individuals leading to the dysfunction and apoptosis of endothelial cells, worsening atherosclerosis and hypertension leading to worsening cardiovascular complications (Jay et al., 2006).

A double-blinded crossover study looked at the role that antioxidants could play in lowering levels of ROS and oxidative stress and mortality risk due to CVD in diabetes over the age of 55. Exclusion criteria included uncontrolled hypertension and history of a myocardial infarction and/or stroke within the last month. Participants were randomized to receive either a vitamin E (a potent Anti-oxidant) supplement or a placebo pill. At the end of eight weeks, researchers measured forearm blood flow and found that vitamin E supplementation significantly improved blood flow (P <0.01), demonstrating improved cardiovascular profiles in diabetic patients receiving antioxidant supplementation (Alshiek et al., 2017).

Implications
The Lifestyle Heart Trial suggests a correlation between a lifestyle change in patients with atherosclerosis and regression in their artery lesions. Forty-one participants with atherosclerosis were randomized to an experimental group (n=22) and control group (n=19). Angiographies were conducted at baseline and again at a one-year follow-up. During the year the experimental group was given a low-fat, vegetarian diet with less than 10% of calories coming from fat and a ratio of PUFAs to saturated
fat of less than 1. The experimental group was also required to participate in aerobic exercise and attend weekly support group meetings. Following one year, blood serum was collected and analyzed from all 22 participants. The results showed an average percentage diameter stenosis decrease from 16.9% to 16.5% amongst the experimental group. The control group who continued with their usual diet and lifestyle showed stenosis progression from 15.5% to 18.5%. The average percentage regression in the diameter stenosis of the control group was 82% (18 out of 22). In the experimental group, total cholesterol was lowered by 24.3% and LDL concentration by 37.4%. This study shows that a lifestyle change in patients with coronary heart disease can lead to significant regression in arterial stenosis (Ornish, et. al. 1990). Changes in lipid profiles and angina pectoris are displayed in the tables (ref., tables 1 and 2).

### Conclusions and Recommendations
The Dietary Guidelines for Americans published every five years is a set of evidence-based guidelines to promote healthy nutrition habits and prevent nutrition-related disease in the American population. These guidelines are constantly evolving based on the latest research findings and available science. Despite its regular updates, the DGA has remained relatively consistent in its recommendation for the dietary consumption of fats.

Recent National Health and Nutrition Examination Survey data shows Americans are consuming 33% of their calories in the form of fat. This paper reviewed the literature on types of fats and their individual relationship to the progression of cardiovascular disease, the cause for one-third of all deaths in this country.

Indeed, the type of fat a person is consuming impacts his or her risk of cardiovascular disease. Higher amounts of saturated fat in the diet have been found to be associated with increased

<table>
<thead>
<tr>
<th>Mean (SD) at Baseline</th>
<th>Mean (SD) at 12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Experimental Group</strong> (n=20-22)</td>
<td><strong>Control Group</strong> (n=17-19)</td>
</tr>
<tr>
<td><strong>Serum Lipids (mmol/l)</strong></td>
<td></td>
</tr>
<tr>
<td>- Total chol</td>
<td>5.88 (1.29)</td>
</tr>
<tr>
<td>- LDL</td>
<td>3.92 (1.25)</td>
</tr>
<tr>
<td>- HDL</td>
<td>1.00 (0.26)</td>
</tr>
<tr>
<td>- Triglycerides</td>
<td>2.38 (1.26)</td>
</tr>
<tr>
<td><strong>Lipid Ratios</strong></td>
<td></td>
</tr>
<tr>
<td>- Total/HDL</td>
<td>6.33 (2.14)</td>
</tr>
<tr>
<td>- LDL/HDL</td>
<td>4.18 (1.53)</td>
</tr>
<tr>
<td><strong>Blood Pressure (mm Hg)</strong></td>
<td></td>
</tr>
<tr>
<td>- Systolic</td>
<td>134 (13)</td>
</tr>
<tr>
<td>- Diastolic</td>
<td>83 (8)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>91.1 (15.5)</td>
</tr>
</tbody>
</table>

**Table 1: Changes in Risk Factors** Source: Ornish, D. 1990

<table>
<thead>
<tr>
<th>Chest pain</th>
<th>Mean (SD) at baseline</th>
<th>Mean (SD) at 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Experimental Group</strong> (n=20)</td>
<td><strong>Control Group</strong> (n=17)</td>
<td><strong>Experimental Group</strong> (n=20)</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>5-10 (14-1)</td>
<td>2-35 (3-77)</td>
</tr>
<tr>
<td><strong>Duration (min)</strong></td>
<td>2-73 (4-69)</td>
<td>3-47 (7-95)</td>
</tr>
<tr>
<td><strong>Severity</strong></td>
<td>2-3 (1-6)</td>
<td>1-8 (1-1)</td>
</tr>
</tbody>
</table>

**Table 2: Changes in Angina Pectoris** Source: Ornish, D. 1990
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risk of CVD. Replacing saturated fat with carbohydrates has not been found to improve lipid profiles or CVD risk factor biomarkers. On the other hand, replacing saturated fat with unsaturated fats, specifically PUFAs, have been associated with lowering an individual’s risk of developing CVD. The data on MUFAs remains inconclusive at this time.

The research suggests that health care professionals should encourage their patients and clients, especially those at risk for cardiovascular disease, to consume a diet lower in saturated fat and to mindfully replace those items with wholesome, real foods, and fats in PUFAs content while remaining wary of processed carbohydrates. As part of a healthy diet, consumers should also consume adequate foods high in antioxidants to provide a buffer for the potentially oxidizing effect of a diet higher in PUFAs.

References
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