The relationship between commercial refined vegetable oils stabilities and health implications: A systematic review and meta-analysis

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Abstract

Deep-frying is a popular food preparation method although oxidized oil may be a health hazard. Minor components in frying oil including antioxidants like tocopherols and tocotrienols, fatty acid composition, triacylglycerol (TAG), and vitamins serve to protect vegetable oil from thermal deterioration. The eating habits of three ethnicity in Malaysia due to influence from the West was briefly mentioned. The importance of fats and oils, as well as the characteristics of each plant oil, were also explained in this project paper. A total of 31 studies fulfilled our inclusion criteria. Studies with humans and animals were accepted and included in this Meta-analysis. The probability of occurrence of obesity, atherosclerosis, hypertension, Type 2 diabetes, and oxidative stress were checked. The overall weighted mean differences for palm oil (PO), canola oil (CNO), corn oil (CO), extra virgin olive oil (EVOO), sunflower oil (SFO), and soybean oil (SBO) were 0.18 [95% CI: 0.11, 0.25; $P < 0.00001$], 5.50 [95% CI: 4.12, 6.87; $P < 0.00001$], 0.62 [95% CI: -4.71, 5.95; $P = 0.82$], 1.13 [95% CI: 0.39, 1.87; $P = 0.003$], -3.79 [95% CI: -5.61, -1.97; $P < 0.00001$], 0.46 [95% CI:0.29, 0.64; $P < 0.00001$] respectively. In short, this study revealed that there was no strong relationship found between a heated and/or repeated heated vegetable oil with the adverse health complications included based on current meta-analysis.

Introduction

Fat and oils are important constituents of the human diet. Fats play a functional role in food either by making it more palatable or providing energy in domestic cooking and industrial production. The global demand of vegetable fats is constantly increase and it seemed as an necessity in the human (Khan et al., 2012) for optimal functioning other than proteins and carbohydrates. Fats are the major source of energy as there is 9 kcal per gram of fat consumed which is double the amount of energy content protein and carbohydrate provide (Marangoni et al., 2012). Besides, fats also facilitate the absorption of fat-soluble vitamins A, D, E, and K in the small intestine (Karunaratne et al., 2017).

Vegetable oils are obtained from plant seeds, nuts, and fruits. Vegetable oils are consist of triacylglycerol (TAG), free fatty acids (FFA), monoacylglycerol (MAG), diacylglycerol (DAG), and non-glyceridic nutrients (Zeng et al., 2012). In addition, minor constituents such as pigments, flavour compounds, hydrocarbon, sterols, phenols, and vitamins are present in vegetable oils (Lee et al., 2020). Edible oils such as canola oil, olive oil, and sunflower oil are high in monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) whereas coconut oil, cocoa oil, and palm oil are high in saturated fatty acids (Savva and Kafatos, 2016). These fatty acids are playing a vital role in human cellular metabolism as they act as energy storage and assisting cell division for growth (Cisbani and Bazinet, 2021).

Vegetable oil is particularly important in deep fat frying. Deep frying is very much preferred by the Malaysian

population. Deep frying is one of the most adapted household methods in food preparation. Deep frying can produce final food with flavors, fragrance aroma, crispy texture, and palatability. During the frying process, food is immersed in hot oil with temperatures between 150 – 190 , resulting in the heat transfer from oil to the food. Therefore, the choice of frying oil and its oxidative stability must be taken into serious consideration because of the amount of fats absorbed by the food materials (Jurid et al., 2020; Abiodun et al., 2020).

In this study, a meta-analysis approach was used to synthesis the results obtaind from previous study to disclose the relation between oxidation stability and health implications (atherosclerosis, hypertension, Type 2 diabetes, obesity, and oxidative stress) among palm oil (PO), canola oil (CNO), corn oil (CO), soybean oil (SBO), sunflower oil (SF) and extra virgin olive oil (EVOO).

Methods

This study focused on all published in-vivo and human studies regarding thermally degraded vegetable oils and their adverse effects which fulfilled all of the following criteria: (1) original data for dietary interventions using thermally oxidized palm oil (PO), corn oil (CO), canola oil (CNO), extra virgin olive oil (EVOO), sunflower oil (SFO) and soybean oil (SBO) (inclusive of diets with repeatedly heated plant oils as well); (2) Must include a control group of either a normal diet with unheated vegetable oils or a basal diet (fed with only rat chow); (3) the mean ± standard deviation values of weight gain, BMI (kg/m^2), adipose tissue, low-density lipoprotein (LDL) cholesterol, the thickness of artery wall, liver thiobarbituric acid reactive substances (TBARS) and homeostatic model assessment of insulin resistance (HOMA-IR) were reported. We excluded studies that used (1) any other vegetable oil that was not mentioned above; (2) a mixture of vegetable oil in the diet; (3) modified oil that chemically interesterified, enzymatically interesterified, or hydrogenated.

Search strategy

The search was conducted through three different literature databases – PubMed, (http://www.ncbi.nlm.nih.gov/pubmed), CENTRAL (Central Register of Controlled Trials; http://www.cochranelibrary.com/) and EMBASE (https://www.embase.com/). Published articles were searched from 2000 to 2020 for randomized controlled feeding trials, cohort, and case-control studies. Several different combinations of keywords were used: frying oil, heated vegetable/plant oils, heated PO/CNO/CO/EVOO/SFO/SBO, thermally oxidized, repeatedly heated vegetable oil, obesity, weight gain, atherosclerosis, high blood pressure, hypertension, Type 2 diabetes, and oxidative stress in all animals and human studies. Besides that, reference lists of relevant articles were scanned to identify potential articles not included in the databases.

MeSH terms

MeSH (Medical Subject Headings) also known as controlled vocabulary was used to search for different articles under specific search terms for a wider and comprehensive search. The following terms were used: ("frying oil"), ("heated vegetable oil" OR "heated plant oil" AND "atherosclerosis"), ("heated vegetable oil" OR "heated plant oil" AND "obesity" OR "weight gain" OR "overweight"), ("heated vegetable oil" OR "heated plant oil" AND "Type 2 diabetes"), ("heated vegetable oil" OR "heated plant oil" AND "cardiovascular disease" OR "hypertension" OR "high blood pressure"), ("heated vegetable oil" OR "heated plant oil" AND "cancer" OR "oxidative stress" OR "oxidative stress biomarkers"), (repeatedly heated "palm oil" OR "canola oil", "corn oil", "extra virgin olive oil", "sunflower oil" and "soybean oil") in PubMed, Cochrane and EMBASE library.

Study selection

Titles and abstracts of all relevant searched papers were read and were eliminated if they do not fulfill our inclusion criteria. The study was excluded if it was from one of the following criteria: (1) The article is irrelevant to the purpose of the study. (2) The article is a review paper. (3) The article does not include the relevant vegetable oils. (4) The article does not have the relevant intervention. (5) The article does not have a relevant comparison group (control group). (6) The article does not discuss the outcome that is relevant

to this research. (7) The article uses a non-standard format or is not published online. (8) The article is not in English and cannot be translated. (9) The article is not included in the year range of 2000 – 2020. (10) The article is duplicated or replicated. Study papers were rejected if they fulfilled even only one clause of the scheme above and they were mentioned as the main reason for rejection.

Data extraction

Information including the name of authors, publication year, the population of the study, characteristics of the subjects (rat species, gender, age, and health condition), intervention period, drop-out rates, study designs, types of oils used for feeding, duration and temperature of thermally heated oil, physical and biochemical changes including weight gain, BMI (kg/m^2), adipose tissue, LDL cholesterol, the thickness of artery wall, liver TBARS, MDA, GSH/GSSG, and HOMA-IR, along with corresponding SE, SD, and 95% CI values were extracted.

Quality assessment

The risk of bias of each study was conducted using the Risk of Bias table in Review Manager 5.4.1 to critically judge the information within each article and to evaluate whether each study involved in meta-analysis meets the internal validity criteria. Standard criteria including sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) were used to assess the quality of each study. The risk of bias was classified into low, unclear, or high with explanations given for each criterion. Publication bias was also accessed using funnel plots.

Data synthesis and statistical analysis

The comparison tests were categorized into two groups: 1) Heated (vegetable oil) and 2) control group. Hence, there are six separate comparison tests for each respective oil to determine its summary effect estimate. Review Manager 5.4.1 was used to perform the statistical analyses with the extracted mean ± standard deviation and sample size as data inputs. A random-effect model was used as the studies were heterogeneous from each other in the scope of intervention, population and outcome, hence making it impossible to impose a fixed-effect model that pools all of the study findings to arrive at a summary estimate. The selected studies were very different by the results of adverse health effects caused by consuming thermally oxidized vegetable oil but other areas such as the type of oil used in interventions are sufficiently similar nonetheless. Weighted mean differences, the statistical significance of each included paper, and heterogeneity between studies were highlighted. Chi-square test was used to determine significant heterogeneity ($P < 0.1$). In addition to that, I^2 statistic was used to quantify heterogeneity through the percentage of total variation across studies attributable to heterogeneity rather than chance. Cut off points of percentage are such: >75% (high heterogeneity), 50 – 75% (moderate heterogeneity), and <50% (low heterogeneity).

Results

The study flow diagram of the literature search and screening as per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) is showed in Figure 1. A total of 2331 journals were identified when using keywords and various databases (Pubmed, Cochrane, Embase) to perform the literature search. In addition, 8 other journals were identified through a reference list of other related journals. After duplicates were removed, 2312 records were left to screen and we identified 2060 non-related journals that were not clinical trials, randomized controlled trials of humans and animals, unavailable full text, or other vegetable oils that were not relevant. The remaining 72 full-text articles were further accessed for eligibility through reading and 41 of them were removed due to the absence of control groups and unavailable data. In the end, a total of 31 articles fulfilled our criteria and was included in the meta-analysis. In this review, we observed 5 health complications which were obesity, atherosclerosis, hypertension, diabetes, and oxidative stress from consuming heated palm oil (HPO), heated corn oil (HCO), heated canola oil (HCNO), heated extra virgin olive oil (HEVOO), heated sunflower oil (HSFO), and heated soybean oil (HSBO). A total of 8 human studies and 23 in vivo studies involving rats and rabbits were included in this meta-analysis. For obesity, data were

taken from either their weight gain, BMI (kg/m^2), and adipose tissue; meanwhile, for atherosclerosis, we extracted data from low-density lipoprotein (LDL) cholesterol and thickness of the artery wall as it is caused by an abnormally high concentration of LDL-cholesterol that deposits on the artery. Data of vasodilation and blood pressure were taken for hypertension while oxidative stress includes oxidative markers such as liver thiobarbituric acid reactive substances (TBARS), malondialdehyde (MDA), and the ratio of glutathione to oxidized glutathione (GSH/GSSG); and lastly, for diabetes, data of homeostatic model assessment of insulin resistance (HOMA-IR) was used. Table 1 shows the study design and baseline characteristics of these 31 studies.

Figure 2 shows the comparison between heated (inclusive of multiple reheating) palm oil and control on atherosclerosis, hypertension, and obesity only. Seven parts of data (from five reported journals) (Famurewa et al., 2017; Kamisah et al., 2016; Kamisah et al., 2015; Nkanu et al., 2018; Siti et al., 2017) were statistically significant at the study level and did not overlap the line of null effect. The results were also statistically significant at the meta-analysis level ($P < 0.00001$), therefore there were no health complications with the HPO consumption. This set of studies showed a high heterogeneity ($I^2 = 100\%$) with the random-effects model as the studies had different study designs. The overall mean difference was 0.18 (95% CI: 0.11, 0.25; $P < 0.00001$). Figure 3 shows the effect of HCNO on obesity and both studies (Bautista et al. 2014a and Bautista et al. 2014b) showed statistically significant and the overall effect estimate was statistically significant ($P < 0.00001$) which meant there was no adverse effect of HCNO on human health. The heterogeneity of this forest plot was high ($I^2 = 95\%$) and the total mean difference was 5.50 [95% CI: 4.12, 6.87]. Figure 4 shows the comparison between HCO and control of hypertension. The total mean difference was 0.62 [95% CI: -4.71, 5.95] with $P = 0.82$ (not significant). This set of studies had a low heterogeneity ($I^2 = 0\%$) as they were of the same paper. The comparison between HEVOO and control can be seen in Figure 5. Four studies (Battino et al., 2002; Rueda-Clausen et al., 2007; Sayon-Orea et al., 2013) which were Battino et al. 2002, Rueda-Clausen et al. 2005[a]; 2005[b]and Sayon-Orea et al. 2013, respectively were statistically significant on the right side of the forest plot. The overall effect was also statistically significant ($P = 0.003$) which meant HEVOO was not cause any adverse effects mentioned above. The mean difference was 1.13 [95% CI: 0.39, 1.87] with a relatively high heterogeneity of $I^2 = 96\%$. Figure 6 shows a comparison of HSFO and control of obesity and oxidative stress. Three out of five studies (Aruna et al., 2005; Garrido-Polonio et al., 2004; Srivastava e al., 2010) were statistically significant which were Aruna et al. 2005, Garrido-Polonio et al. 2004a, and Srivastava et al. 2010. The overall effect estimate was statistically significant ($P < 0.00001$) on the left side of the forest plot which meant the effects of consuming HSFO include obesity and oxidative stress. This analysis had a relatively high heterogeneity ($I^2 = 99\%$) and the mean difference is -3.79 [95% CI: -5.61, -1.97]. The comparison between HSBO and control is shown in Figure 7 above with 9 statistically significant studies including (Rueda-Clausen et al., 2007, Das et al., 2017; Leong et al., 2010; Yen et al., 2010) Adam et al. 2009b, Awney 2001, Chiang et al. 2011, Chuang et al. 2013, Leong et al. 2010b; 2010c; 2010d, Rueda-Clausen et al. 2005a and Yen et al. 2010. The heterogeneity was relatively high for this set as well ($I^2 = 98\%$) as they included various study designs and intervention method and the mean difference was 0.46 [95% CI:0.29, 0.64]. However, the overall effect was statistically significant ($P < 0.00001$) which means HSBO will not cause any health implications.

Discussion

Results of this meta-analysis showed an inconclusive association between deteriorated vegetable oils and adverse health effects. Other plant oils such as PO, CNO, CO, EVOO, and SBO did not display any form of health complications except for SFO which was found to have a positive association with obesity and oxidative stress biomarkers. One of the studies in Figure 2; Famuwera et al. (2017) displayed a considerable change in the plasma lipid profile of rats especially in the serum LDL-C level followed by chronic consumption of a 15 %-oxidized palm oil diet that was prepared through continuously heating for 5 days at 180 , 10 min every day. The mean difference of -0.80 between the intervention and control group proved that heated PO was concordant with the elevated levels of serum LDL-C. Changes in lipid serums TC, TG, LDL-C, and VLDL-C in rats have been related to the increase in the risk of cardiovascular diseases including atherosclerosis, hypertension, and neurodegeneration for decades. Nkanu et al. (2017) had the second-largest weight (11.7

%) also reported a 104 % increase in serum LDL-c when thermally HPO was incorporated into the diet. However, its point estimate of effect was situated on the right, which favoured the control group. It was important to note that the latter study has a longer intervention duration of 16 weeks as opposed to the former study with only 28 days. Furthermore, Nkanu et al. (2017) had a larger weight as it offers more vital information therefore being closer to the underlying true effect. Other studies that were not mentioned were either situated on the line of null effect hence being statistically insignificant or contribute 0 % weight to the pooled effect estimate. Based on the test of the overall effect, this comparison was statistically significant as atherosclerosis, obesity, and hypertension were not interrelated with consumption of HPO. There was insufficient evidence to prove the impact of HPO on obesity and weight gain. Odia et al. (2015) recently has proven that fresh palm oil consumption can prevent the heart and blood vessels from the plague, ischemic injuries, and a reduced risk for cardiovascular diseases. However, this suggestion was in opposition to a meta-analysis relating palm oil consumption with heightened LDL-cholesterol (Sun et al., 2015). The rationale of functional alteration in blood vessels can be due to the depletion of antioxidants in oxidized oil.

The was one study that managed to fulfill all inclusion criteria by using CNO as the sample. According to Bautista et al. (2014), CNO was heated for one frying cycle and ten frying cycles at 190 . After 10 weeks of follow-up, Wistar rats were found to have a noticeable increase in adipose tissue as well as early signs of endothelial dysfunction induced by toxic compounds such as peroxynitrite the consumption of repeatedly heated oil (1 and 10 frying cycles). Dyslipidemia including hypertriglyceridemia and hypoalphalipoproteinemia are often related to the increase in abdominal adipose tissue due to the appearance of an abnormal amount of lipids in the blood (Eringa et al., 2013). Interestingly, the caloric consumption of repeatedly heated CNO was higher than fresh CNO because raw oil was less desirable than HCNO due to the absence of organoleptic characteristics. Despite that, the point effect of estimate and overall effect estimate (5.50[95% CI:4.12, 6.87]) favours the control group and suggested that consumption of HCNO in the diet had no deleterious effect on weight ($P < 0.00001$). A recent reported SR-MA revealed that body fat markers or related anthropometric measures were not significantly affected ($P > 0.05$) by consumption of CNO. The findings suggested that a modest decrease in body weight indeed as the PUFAs present in CO can regulate proliferation, differentiation, and apoptosis of adipocytes, causing an alteration in genes that increases fat oxidation and reduces fat deposition (Buckley and Howe, 2010).

Data of vasodilation response were taken from (Das et al., 2017) to investigate the adverse effects of corn oil in one, five, and ten frying cycles. Vasodilation is the widening of blood vessels as a result of the relaxation of the blood vessel muscular walls. Vasodilation is a relaxation mechanism in smooth muscle cells of arteries that increases blood flow. Vasodilation is proportional to blood pressure; as the arteries and arterioles dilate, an immediate decrease in blood pressure will be imposed (Wieling et al., 2016). The percentage of vasodilation was significantly lower in the aortic rings of 1 frying cycle of HCO (88.49%+-7.91), 5 frying cycles of HCO (68.15%+-3.70), and 10 frying cycles of HCO (63.44%+-6.91) when compared to the control (105.54% +-9.76) and fresh CO (101.54%+-3.72) groups ($P < 0.05$). In addition to that, the percentage of vasodilation was significantly lower in 5 and 10 frying cycles of HCO compared to 1 frying cycles of HCO ($P < 0.05$). Based on previous studies, oxidative stress and vascular inflammation which was involved in cardiovascular diseases including hypertension was observed in HCO (Korkmaz et al., 2013). A reported study postulated that atherosclerotic lesion scores for fatty plaques, fatty streaks, and fibrous plaque scores were significantly higher in rabbits that were treated with HCO. Rabbits were also found negative in terms of weight gain as HCO had higher unsaturation (Deen et al., 2021), therefore, more likely to be oxidized and less palatable, causing a reduction in feeding efficiency (Idris et al., 2018). However, Figure 4 shows none of the studies were statistically significant as the point effect of the estimate were on the line of no effect and could be confirmed by the test of overall effect ($P = 0.82$). We observed a lack of clinical trials that incorporates corn oil into diets which indicates a need for more research papers in order to truly establish the effects of CO on human health. The physicochemical properties of CO are superior in terms of bioactive compounds and oxidative stability, it is highly refined and high in inflammatory n -6 fatty acids which outweighs its beneficial effects.

Olive oil consists of 85 % of the types of fats consumed in the Mediterranean diet whose consumption is

related to a lowered risk of cardiovascular diseases, cancer, and Alzheimer's disease. An in vivo study by (Ghorbel et al., 2015) suggested the protective effects of EVOO on hepatoxicity due to the decrease in liver damage induced by aluminum and acrylamide. Furthermore, a 40 % ($P < 0.05$) relative risk reduction and nonsignificant 18 % risk reduction in Type 2 Diabetes was discovered through the intervention group that consumed a Mediterranean diet that was supplemented with EVOO compared to the control diet group. The forest plot in Figure 4 ($P = 0.003$) was in agreement with both studies above. The susceptibility of cells is influenced by the composition of fatty acids as it is able to alter the cell membrane's fatty acids. Cells enriched with MUFAs present in EVOO have been shown to be less vulnerable to damage caused by oxidation. Furthermore, MUFAs in EVOO is associated with a lowered risk of coronary heart disease and thereby inducing a desirable effect on health. In investigating the relationship between consumption of foods fried by olive oil and incidence of weight change and obesity in a Mediterranean prospective cohort study, subjects who used olive oil for frying purposes gained slightly lesser weight and showed the lesser risk of obesity compared to other oil types. However, the effects were minor, as explained by the mean difference of 0.50[95% CI: 0.31, 0.69]. As food items are being fried in high heat, it absorbs a large amount of oil and becoming a major nutritional critical point by increasing the fat content and calories. However, it is an additive, leading to people consuming them in large amount at one sitting unknowingly. EVOO has reported to only suffered from a loss of tocopherol and phenolic compound from a sixty minutes frying procedure but not a fatty acid pattern change. One of the statistically significant studies which its point estimate of effect favours the control group suggested that TBARS increased, not from the fatty acid composition change but through the loss of antioxidants and a heightened number of toxic compounds. Even so, a stable source of oil like EVOO is also susceptible to crucial oxidative modifications that will impose health effects on both structure and function of organs. Despite the accessibility of an array of epidemiological and experimental evidence tying the benefits of consumption of EVOO in limiting certain pathologies, the toxicological hazards related to thermally oxidized EVOO is still severely lacking.

The composition of SFO consists of approximately 86 % of polyunsaturated and monosaturated fatty acids causing a significantly lower thermal stability. It is especially susceptible to heat, air, and light which accelerates SFO oxidation. SFO was reported to lose up to 76 % of tocopherols and reached > 25 % of total polar compounds (TPC) during a frying process (Wiege et al., 2020; Juarez et al., 2011). Thermal alterations were prevalent in HSFO including more than 10 % increase of polymeric and dimerized triacylglycerols. Among the listed vegetable oils, only HSFO proved to cause obesity and oxidative stress ($P < 0.0001$). Food efficiency ratio was lower in diets with fresh SFO than HSFO, as the palatability was acceptable when the TPC was between 25 – 30 %. Not only that, polyaromatic hydrocarbons (PAHs) are known as one of the carcinogenic compounds with mutagenic properties that are formed and accumulated during thermal deterioration. Other toxic components formed during the heating of oil such as MDA and TBARS are reliable lipid peroxidation markers in rats. GSH is known as one of the scavengers of reactive oxygen species (ROS) and the GSH/GSSG ratio is included as one of the oxidative stress markers in this comparison as it is directly proportional to biological redox status (Zitka et al., 2012; Pawelczyk et al., 2017). A consumption of a meal rich in lipids or carbohydrates that increases the susceptibility of oxidative damage that is caused by the imbalance of ROS and antioxidant system is known as the postprandial oxidative state. A randomized crossover human study that has the second largest weight on this comparison table (17.4%) explained that the increased ingestion of ROS from deep-fried breakfast causes a significant damage to molecules in the organism, leading to inflammation process and initiation of atherosclerosis through the oxidation of LDL, vasoconstriction and thrombogenicity. Unfortunately, this was the only study that has its horizontal line of 95 % CI crossing the line of no effect, suggesting the difference between the control and intervention group was not statistically significant. Due to the small number of studies included in this meta-regression, this interpretation was still tentative, yet it further insinuates that HSFO can cause overweight and oxidative stress.

The UC Riverside Research team postulated that SBO was related to obesity, diabetes, and impose adverse effects on neurological conditions such as autism, Alzheimer's diseases, and depression. Both of the modified and non-modified SBO had a similar effect on the brain pronounced on the hypothalamus. With the research

on male rats, the oxytocin levels were found to be reduced after the ingestion of SBO (Deol et al., 2020). Besides, the intervention group of mice fed with HSBO was found a significantly lower liver α-tocopherol, but the liver TBARS levels were significantly higher than the groups consuming fresh SBO. This finding was following several reported studies suggesting oxidized frying oil to compromise antioxidant status in tissues (Liao et al., 2005). Peroxisome proliferator-activated receptor (PPAR)-α is a type of nuclear receptor that is activated by ligand transcriptional factor. PPAR-α oversees regulating the expression of genes in organisms taking part in fatty acid β-oxidation and plays a vital role in energy homeostasis. PPAR-α agonists have demonstrated their anti-inflammatory and anti-thrombotic actions in previous research that prevents atherosclerosis events to worsen through altering its metabolic risk factors, reducing atherosclerotic plaque formation and the probability of coronary heart disease (CHD), especially in metabolic syndrome (Van Ruth et al., 2010). The study with a mean difference of 5.30[95% CI: 2.77, 7.83] showed that ingestion of HSBO by maternal mice not only affects hepatic PPAR-α activity but carries on to its offspring in adulthood as well. In addition, a significant and steady increase ($P < 0.05$) in blood pressure was observed since from the first month until the end of intervention duration in rats fed with 5 and 10 frying cycles of HSBO samples by 20 % and 33 %, respectively, compared to the control group. In contrast, this increment was not observed in the control group and fresh SBO group. This result was in agreement with a study by (Leong et al., 2008) suggesting an increase in blood pressure was in conjunction with prolonged consumption of heated vegetable oil.

Deep frying induces flavours which is described as fruity, nutty, buttery, burnt, and grassy. These flavour notes depend on the type of oil and the number of frying times, but it is not affected by the frying temperature. The subtle taste of these aromas is due to the oxidation of linoleic acid present. When the oxidation increase, a fishy odor can be generated and desirable notes degraded. This, the oil is deteriorated and not suitable for consumption. A palatable and desirable fried flavour is commonly produced at the optimal concentration of oxygen, as poor and weak flavour is produced when there is low concentration of oxygen and vice versa, off flavours are produced in high levels of oxygen which agrees with studies included in this meta-regression as well as previously reported studies (Burenjargal and Totani, 2008; Totani and Ojiri, 2007). Volatile compounds from linoleic or linolenic acids such as dienal, alkenals, lactones, and hydrocarbons contributes to the fried flavour compounds. Antioxidant mechanisms present in vegetable oils including tocopherol and tocotrienols are retained in refined vegetable oils with a modest loss of 30 % of antioxidants during the deodorization phase. However, these antioxidant contents dissociate rapidly and completely during oil oxidation and become less effective during high temperatures. In addition, carotenes are unable to exhibit protective effects on oils in the absence of other antioxidants. Carotene works synergistically together with tocotrienols as it is able to regenerate carotenes from its radicals. This effect has been observed during the frying of potato slices at 163 . Lignan compounds were found to be much more effective during deep-fat frying (Fan and Eskin, 2015). Free fatty acid (FFA) is another factor that increases the vulnerability of oil to oxidation. The amount of unsaturation in FFA influences the oxidative stability of oil tremendously rather than its chain length. Significant effects have been seen on the thermo-oxidative degeneration in plant oils that concedes with a recent study done by (Sayyad, 2015) that claimed the frying performance of SFO was determined by the content of linoleic acid rather than the composition of tocopherol.

Conclusion

This Systematic Review and Meta-Analysis has achieved its objective to investigate the relation of oxidative stability of different vegetable oil as well as the subsequent risk of developing adverse health implications by drawing together data from multiple studies. Results were found to be robust in several meta-analyses with significant value ($P < 0.05$) stratified on study characteristics and inspected the relationship between heated vegetable oils and induced diseases through a controlled inclusion of studies. These findings thus underscore the absence of mentioned diseases or disorders regarding chronic consumption of a diet with repeatedly heated cooking oils except in SFO. The clinical significance of results from meta-regressions should be acknowledged as it debunked the conception of ingestion of all types of thermally heated oils in diet will cause Alzheimer's disease, obesity, Type 2 Diabetes, events of cardiovascular disease and eventually metabolic syndrome.

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Conflict of interests

None to declare.

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Table 1: Characteristics of included studies

Name	Type of oil	Subject
Adam et al. 2009a	PO	30 female Sprague–Dawley rats
Adam et al. 2009b (46)		
Famurewa et al. 2017a		20 male Wistar strain rats
Famurewa et al. 2017b (10)		
Kamisah et al. 2015(12)		32 Sprague–Dawley rats
Kamisah et al. 2016 (11)		
Nkanu et al. 2017a		30 male Wistar rats
Nkanu et al. 2017b (13)		
Nurul Iman et al. 2013 (47)		32 male Sprague-Dawley rats
Siti et al. 2017a (14)		56 male Sprague Dawley rats
Siti et al. 2017b		
Tan et al. 2012a		24 adult male Sprague-Dawley rats
Tan et al. 2012b (48)		
Bautista et al. 2014a	CNO	48 male Wistar rats
Bautista et al. 2014b (26)		
Das et al. 2017a	CO	30 male Sprague-Dawley rats
Das et al. 2017b		
Das et al. 2017c (21)		
Alonso and Martínez-González 2004 (49)	EVOO	5573 humans included
Battino et al. 2002 (15)		16 male Wistar rats
Farnetti 2011 (50)		12 obese, 5 lean women
Rueda-Clausen et al. 2007a		10 healthy young men
Rueda-Clausen et al. 2007b (16)		
Salas-Salvado et al. 2011a		418 nondiabetic humans
Salas-Salvado et al. 2011b (51)		
Salas-Salvado et al. 2014a		3541 patients
Salas-Salvado et al. 2014b (52)		
Sayon-Orea et al. 2013 (17)		9850 men and women

Name	Type of oil	Subject
Skowron et al. 2018 (53)		32 male rabbits
Sutherland et al. 2002 (54)		16 healthy men
Aruna et al. 2005 (18)	SFO	Male Wistar rats
Garrido-Polonio et al. 2004a		18 male Wistar rats
Garrido-Polonio et al. 2004b (19)		
Perez-Herrera et al. 2013(55)		20 obese people
Srivastava et al. 2010 (20)		50 male Wistar rats
Adam et al. 2008a	SBO	24 healthy and mature female Sprague-Dawley rats
Adam et al. 2008b		
Adam et al. 2008c		
Adam et al. 2008d (56)		
Adam et al. 2009a		30 female Sprague Dawley rats
Adam et al. 2009b (57)		
Awney 2011 (58)		24 male Sprague-Dawley weanling rats
Chiang et al. 2011 (59)		24 male C57BL/6J mice
Chuang et al. 2013 (60)		40 female and male C57BL/6JNarl mice
Leong et al. 2010a		42 adult male Sprague-Dawley rats
Leong et al. 2010b		
Leong et al. 2010c		
Leong et al. 2010d (22)		
Ng et al. 2012a		24 male Sprague-Dawley rats
Ng et al. 2012b (61)		
Rueda-Clausen et al. 2007a		10 healthy young men
Rueda-Clausen et al. 2007b (16)		
Yen et al. 2010 (23)		16 spontaneously hypertensive rats and 16 normotensive Wistar m

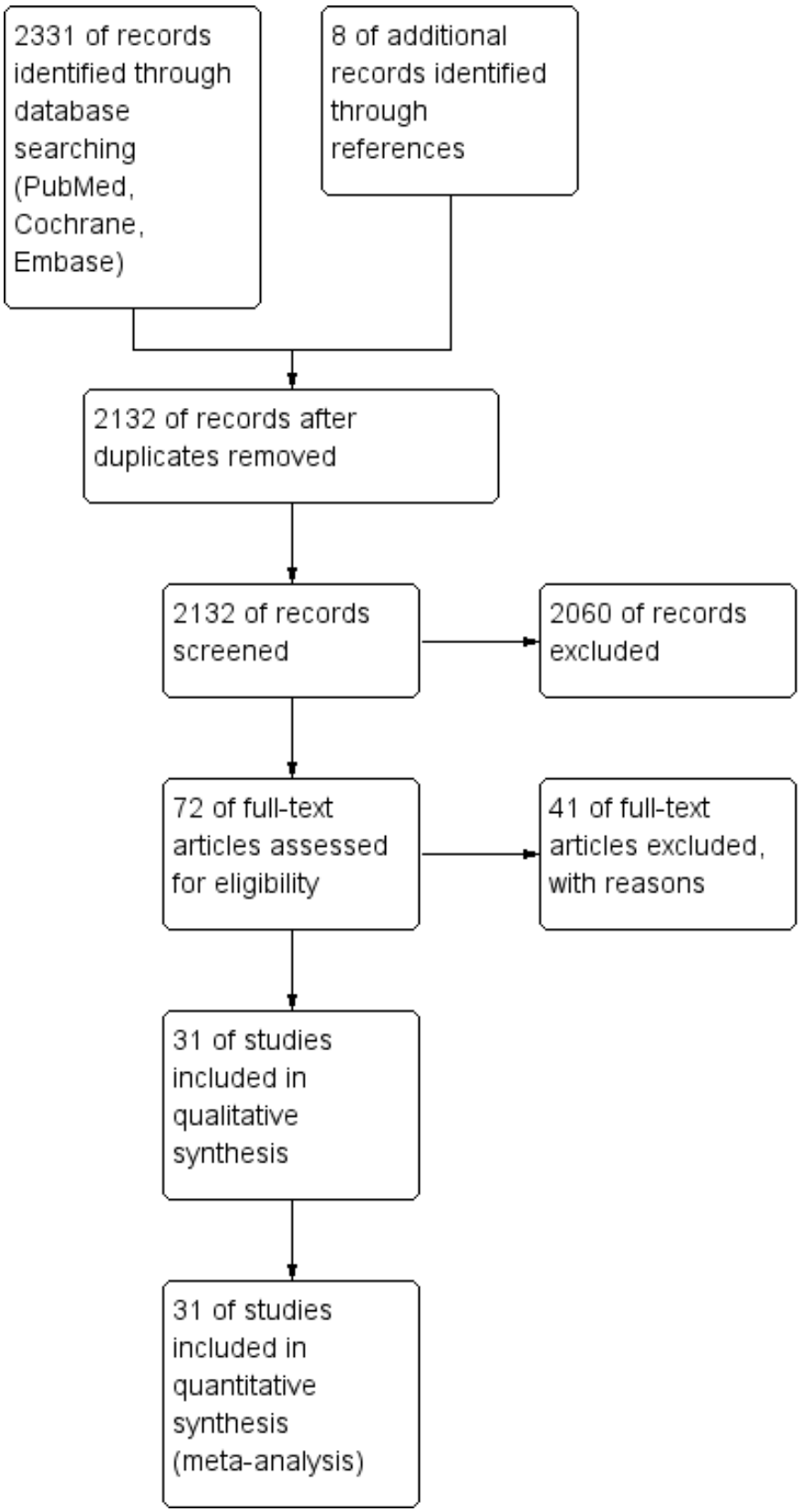

Figure 1: Study flow diagram of Meta-Analysis

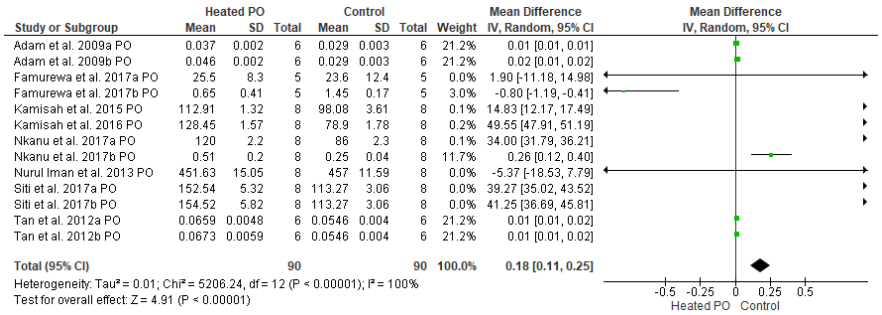

Figure 2: Forest plot showing adverse effects of HPO vs control consisting of atherosclerosis, hypertension, and obesity only.

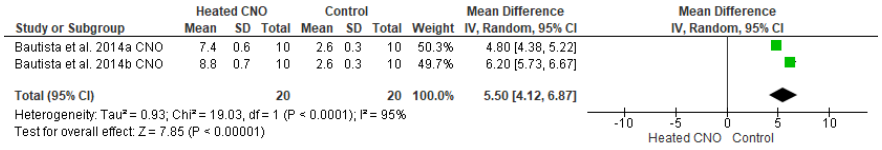

Figure 3: Forest plot showing adverse effects of HCNO vs control consisting obesity only.

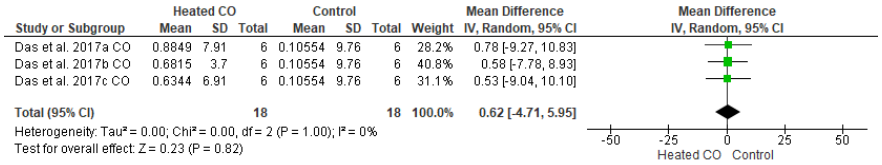

Figure 4: Forest plot showing adverse effects of HCO vs control consisting of hypertension only.

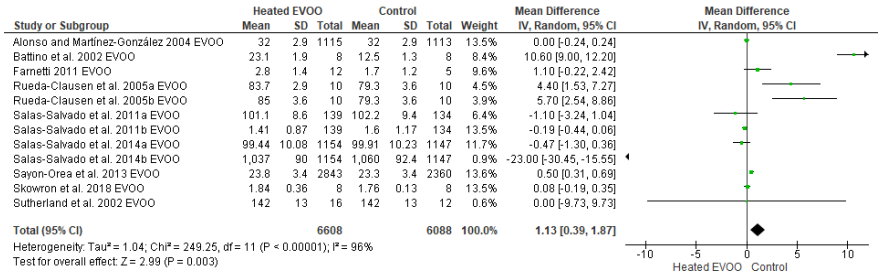

Figure 5: Forest plot showing adverse effects of HEVOO vs control consisting of atherosclerosis, hypertension, obesity, diabetes, and oxidative stress.

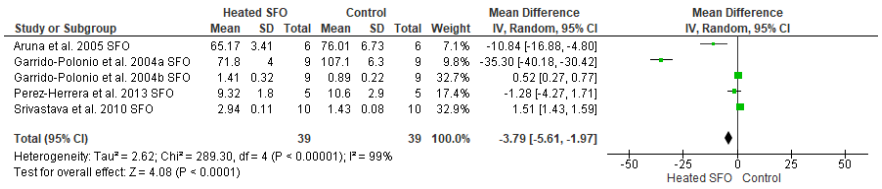

Figure 6: Forest plot showing adverse effects of HSFO vs control consisting of obesity and oxidative stress only.

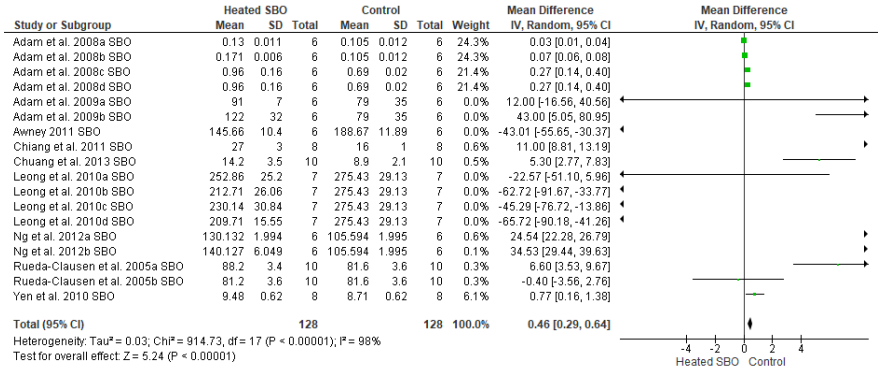

Figure 7: Forest plot showing adverse effects of HSBO vs control consisting of atherosclerosis, hypertension, oxidative stress and obesity only.