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The Effect of Palm Oil on Health Outcomes: A Protocol for Systematic Reviews and Meta-analyses of Controlled Clinical Trials

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ABSTRACT

Background: It is suggested that palm oil consumption might increase the likelihood of developing chronic diseases including cardiovascular disease. Previous studies that investigated the effect of palm oil intake on anthropometric measures, blood glucose control, inflammation, and oxidative stress markers were inconclusive. This is while previous systematic review and meta-analyses should be updated.

Objectives: The present study describes a protocol for a range of systematic reviews and meta-analyses to examine the effect of palm oil intake on body weight and fat, inflammatory markers, oxidative stress, liver enzymes, blood pressure, and blood glucose control indices.

Methods: ISI web of science, EMBASE, MEDLINE, Scopus, and Google Scholar will be searched using medical subject heading (MeSH) and non-MeSH keywords. Controlled clinical trials will be selected based on predefined eligibility criteria. The intra-study risk of bias will be checked by using the Cochrane collaboration's tool. Mean difference (MD) (the difference between mean change values in the intervention group/period and control group/period) and its corresponding standard deviation will be calculated to be used as effect size. A random-effects meta-analysis will be performed to pool the results. Subgroup analysis and meta-regression will be conducted to explore the possible sources of heterogeneity. Sensitivity analysis will be conducted by removing the studies one-by-one from the overall analyses. Publication bias will be assessed by inspecting funnel plots and using asymmetry tests.

Conclusion: The results of systematic reviews and meta-analyses might provide helpful data about the effects of palm oil consumption on different aspects of health among adults. The evidence provided by the results of systematic reviews can be useful for dietitians, clinicians, public health policy-makers, and the public.

Keywords: Palm oil; Body weight; Body composition; Blood pressure; Inflammation; Blood glucose control; Systematic review

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Introduction

Palm oil consists of saturated fatty acids such as palmitic (44.3%) and myristic acids (4.6%) and unsaturated fatty acids such as oleic (38.7%) and linoleic acids (10.5%) *[1]*. Furthermore, palm oil is rich in tocotrienol (600-1000 parts per million [PPM]), carotenes (500-700 PPM), phytosterols (300-620 PPM) and contains less amount coenzyme Q10 and polyphenols; as both harmful and

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beneficial components are found in palm oil, it is hard to decide about its health effects *[2]*. It is proposed that palm oil intake might increase low-density lipoprotein cholesterol, and risk of cardiovascular disease including mortality from ischemic heart disease *[3, 4]*; however the studies have led to conflicting results *[5-7]*. The increasing trend of palm oil production by allocating more farmland for this plant and also lower traffic for importing palm oil rather than other alternative oils have increased the concerns regarding its health effects, worldwide *[8]*.

Palm oil consumption has been particularly associated with increased cardiovascular disease (CVD) risk *[9]*. A systematic review in 2014 showed that the substitution of primary dietary fats with palm oil might increase serum low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (TC), and apolipoprotein B (Apo B); furthermore replacing unsaturated oils (MUFA and PUFA) with palm oil might increase TC, Apo B and HDL cholesterol *[10]*. However, several high-quality clinical trials have been conducted to examine the effect of palm oil consumption on cardiometabolic risk markers since 2014 *[11, 12]* and the available data should be updated. Moreover, the effect of palm oil intake on other cardiovascular diseases (CVD) risk factors like body weight and fat, inflammatory markers, oxidative stress markers, liver enzymes, blood pressure, and blood glucose indices have got less attention and are usually assessed as secondary outcomes in clinical trials *[13-16]*.

Several investigations have examined the effect of palm oil intake on anthropometric measures *[17, 18]*, blood glucose control *[19, 20]*, inflammation markers *[16, 21]* or even oxidative stress markers *[22]* and they have led to conflicting results; however, we are not aware of any systematic reviews and meta-analysis to summarize the data in this regard. For instance, although many studies showed no effects of palm oil on blood glucose control markers *[23-25]*, some studies reported that palm oil might increase serum insulin levels in comparison with partially hydrogenated soybean oil *[14]*. Also, inconsistent results were found when studies examined the effect of palm oil on anthropometric indices. In one study, palm oil showed decreasing effects on body weight after 5 weeks of intervention *[26]* and in another study olive oil showed increasing effects on body weight while palm oil had no effect on body weight *[15]*. A wide range of inflammation markers, oxidative stress markers, and blood glucose indices were also examined as secondary outcomes in different studies; however, results were not conclusive *[4, 16, 20, 27]*.

The aim of the present study is to describe a protocol for a range of systematic reviews and meta-analyses to examine the effect of palm oil consumption in comparison with other edible oils on body weight and composition [body mass index (BMI), waist circumference, waist/hip ratio (WHR), body fat, lean body mass, visceral fat], cardiovascular disease risk factors [lipid profile, lipoprotein a, apolipoprotein B, apolipoprotein A1, homocysteine, plasminogen activator inhibitor-1 (PAI-1), fibrinogen, cholesteryl ester transfer protein (CETP), and blood pressure], blood sugar indices [quicki, insulin, homeostatic model assessment for insulin resistance (HOMA-IR), HbA1c, and fasting blood glucose], inflammatory markers [interleukin 1(IL1), IL6, TNF alpha, paraoxonase, and thrombin], oxidative stress markers [malonedialdehyde (MDA), Glutathione peroxidase (GSH), and thiobarbituric acid reactive substance (TBARS)], and liver enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST)] in adults (aged 18 years and more).

Materials and Methods

The present study is reported based on preferred reporting items for systematic reviews and meta-analyses protocols (PRISMA-P) *[28]* and the study protocol is registered in the prospective register of

systematic reviews (PROSPERO) [registration code: CRD42020140481

Study eligibility

Participants

The studies conducted on adult participants with normal conditions or chronic disease (including abnormal lipid profile, increased blood glucose, obesity/overweight, and liver disorders) will be included. The studies on pregnant women will be excluded.

Intervention

The eligible studies should have at least one arm with palm oil intervention. To investigate the pure effects of palm oil, other different co-interventions like drugs and exercise will be excluded; however, if co-interventions in all groups be the same, the study will be included. The duration of the studies should be more than 2 weeks. Other resemble oils such as palm kernel oil, red palm oil, and processed palm oils which lead to change in palm oil composition will not be considered. The studies that examine palm oil with less than 5 g/day and also other extracts of palm oil will be excluded.

Comparisons

Only trials with placebo groups or those administered other types of oil will be included. The studies will be excluded if the difference between the intervention and control groups/periods be more than palm oil.

Outcomes

Body weight and composition [body mass index (BMI), waist circumference, waist/hip ratio (WHR), body fat, lean body mass and visceral fat] will be recorded as primary outcomes. Data on cardiovascular disease risk factors [lipid profile, lipoprotein a, apolipoprotein B, apolipoprotein A1, homocysteine, plasminogen activator inhibitor-1 (PAI-1), fibrinogen, cholesteryl ester transfer protein (CETP), and blood pressure], blood glucose control markers [quicki, insulin, HOMA-IR, HbA1c, fasting blood glucose (FBG)] inflammatory markers [interleukin 1(IL1), IL6, TNF alpha, paraoxonase, thrombin], and stress oxidative markers [malonedialdehyde (MDA), Glutathione peroxidase (GSH) and thiobarbituric acid reactive substance (TBARS)], and liver enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST)] will be extracted as secondary outcomes.

Types of studies

All RCTs both parallel and cross-over with at least two arms/periods will be included in the study.

Search strategy

The present study will search the ISI web of science, EMBASE, MEDLINE, Scopus, and Google Scholar using medical subject heading (MeSH) and non-MeSH keywords. The search strategies used to find the related papers in different databases are provided in the **Supplementary Table 1**. After finalizing the search two independent authors will select the related studies according to eligibility criteria. For the first step, the titles/abstracts will be screened and all potential publications will be selected. The researchers will find full-texts in the second step and then select the related studies. Final lists of included studies from the two authors will be combined with a clear reason for exclusion. The third reviewer will be consulted in case of disagreement. The reference lists of related articles will also be checked to find other potentially related articles.

Data collection and analysis

Selection of studies

The summary of the search, selection, and inclusion of studies will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) diagram.

Data extraction and management

Two reviewers will extract data separately and will double-check for final confirmation. One pre-prepared form will be used for data extraction. Three types of

data will be extracted including participant characteristics, intervention details, and outcome measures.

1. **Participant characteristics**

Age, sex, number of male and female participants, number of participants in the control and intervention periods, and the health condition of study participants.

2. **Intervention details**

The intervention duration, number of arms, amount of oils used for intervention, and funding source.

3. **Outcome measures**

Baseline and post-intervention levels for the outcome variables, changes from baseline, P-values for comparison between groups/periods and P-value for within-group/period changes, and possible adverse effects.

Dealing with missing data

In case of insufficient or missing data, the authors of the eligible articles will be contacted at least twice, one week apart. When they cannot be contacted, the available data will be analyzed alone and then the effects of missing data will be reported in the results and will be discussed by comparing their results with systematic reviews' results.

Assessment of risk of bias

Two reviewers (SB and SHA) will independently assess the risk of bias for the selected studies using the Cochrane Collaboration 'Risk of bias' assessment tool that evaluates sequence generation, allocation concealment, blinding, incomplete outcome data, loss to follow-up, and selective outcome reporting *[29]*. For each domain, the following method will be used to evaluate appropriate judgment of the risk of bias: "low risk", "high risk", or "unclear". The overall quality of the studies will be classified as low risk (low risk for all domains), high risk (high risk for at least one domain), and unclear risk (unclear for at least one domain). Any disagreements will be resolved by discussion.

Data analysis

Mean difference (MD) and its corresponding standard error (SE) will be calculated by using the mean changes and their standard deviations reported/calculated for the intervention and control groups/periods. Then MDs extracted from each study will be used as effect size for meta-analysis. The meta-analyses will be performed using random-effects meta-analysis which takes the between-study heterogeneity into account. Stata software, version 11.2 (Stata Corp, College Station, TX) will be used to analyze the data. P values less than 0.05 will be considered as statistically significant.

Assessment of heterogeneity

Q statistic and I^2 statistic measures will be used for the evaluation of heterogeneity between studies. P values < 0.05 for Cochran's Q test and I^2 higher than 25% will be considered as significant heterogeneity (29).

Subgroup analysis and Sensitivity analysis

Subgroup analyses will be performed to evaluate if intervention, individuals' health status, and other trial characteristics explain the possible heterogeneity between studies. Additionally, sensitivity analyses will also be performed through excluding studies one-by-one from meta-analysis.

Publication bias

Publication bias of the included studies will be evaluated using Begg's funnel plots and Egger's and Begg's asymmetry tests. If publication bias becomes evident, Duval and Tweedie's trim and fill analysis will be conducted to explore the effect of bias correction on the overall effects (28).

Discussion

The effect of palm oil consumption on different aspects of health have been previously investigated in observational studies and clinical trials *[30-32]*. Reviews on both animal and human studies have claimed the protective effect of palm oil on ischemic heart disease, the favorable effects on normal

reproduction in females and males, and the management of diabetes *[30, 33]* On the other hand, previous systematic reviews and meta-analyses have proposed that palm oil might adversely affect lipid profile (10). Furthermore, we are not aware of any study trying to investigate the effect of palm oil on weight, blood pressure, glycemic indexes, and inflammatory markers. However, these conclusions can be biased by the confounding factors in studies, the sample size of study participants, and differences in the design of included studies *[34, 35]*. An updated systematic review and meta-analysis based on randomized clinical trials might be more valuable to understand the effects of palm oil on health conditions that will be useful to provide recommendations or guidelines for implementation in practice.

The aim of this study is to provide a protocol for systematic reviews and meta-analyses to evaluate the effect of palm oil consumption on body weight, waist circumference, blood pressure, glycemic indexes, and inflammatory markers by gathering all recent publications and to assess its effect on the aforementioned measures. We anticipate that these systematic revies will provide helpful information about the effects of palm oil consumption on different aspects of health in adults. This evidence can be useful to dietitians, clinicians, public health policy-makers, patients, and healthy people.

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Author's contribution

MM conceived the study. SB and MM designed the search strategy. SB and SA wrote the first draft of the manuscript. SB revised the manuscript. All authors read and approved the final version of the manuscript.

Conflict of interest

There is no conflict of interest between authors.

References

[1] Mukherjee S, Mitra A. **Health effects of palm oil**. *Journal of human Ecology*. 2009;26:197-203

[2] May CY, Nesaretnam K. **Research advancements in palm oil nutrition**. *European journal of lipid science and technology*. 2014;116:1301-15

[3] Sun Y, Neelakantan N, Wu Y, Lote-Oke R, Pan A, van Dam RM. **Palm Oil Consumption Increases LDL Cholesterol Compared with Vegetable Oils Low in Saturated Fat in a Meta-Analysis of Clinical Trials**. *The Journal of nutrition*. 2015;145:1549-5810.3945/jn.115.210575.

[4] Chen BK, Seligman B, Farquhar JW, Goldhaber-Fiebert JD. **Multi-Country analysis of palm oil consumption and cardiovascular disease mortality for countries at different stages of economic development: 1980-1997**. *Globalization and health*. 2011;7:4510.1186/1744-8603-7-45.

[5] Bester D, Esterhuyse AJ, Truter EJ, van Rooyen J. **Cardiovascular effects of edible oils: a comparison between four popular edible oils**. *Nutrition research reviews*. 2010; 23: 334-4810. 1017/ s0954422410000223.

[6] May CY, Nesaretnam K. **Research advancements in palm oil nutrition**. *European journal of lipid science and technology : EJLST*. 2014;116:1301-1510.1002/ ejlt.201400076.

[7] Odia OJ, Ofori S, Maduka O. **Palm oil and the heart: A review**. *World journal of cardiology*. 2015;7:144-910.4330/wjc.v7.i3.144.

[8] Carter C, Finley W, Fry J, Jackson D, Willis L. **Palm oil markets and future supply**. *European Journal of Lipid Science and Technology*. 2007;109:307-14

[9] Bautista LE, Herran OF, Serrano C. **Effects of palm oil and dietary cholesterol on plasma lipoproteins: results from a dietary crossover trial in free-living subjects**. *European journal of clinical nutrition*. 2001;55:748-5410.1038/sj.ejcn.1601218.

[10] Fattore E, Bosetti C, Brighenti F, Agostoni C, Fattore G. **Palm oil and blood lipid–related markers of cardiovascular disease: a systematic review and meta-analysis of dietary intervention trials**. *The American journal of clinical nutrition*. 2014;99:1331-50

[11] Ng YT, Voon PT, Ng TKW, Lee VKM, Mat Sahri M, Mohd Esa N, et al. **Interesterified Palm Olein**

(IEPalm) and Interesterified Stearic Acid-Rich Fat Blend (IEStear) Have No Adverse Effects on Insulin Resistance: A Randomized Control Trial. *Nutrients*. 2018;1010.3390/nu10081112.

[12] Cheng C, Wang D, Xia H, Wang F, Yang X, Pan D, et al. **A comparative study of the effects of palm olein, cocoa butter and extra virgin olive oil on lipid profile, including low-density lipoprotein subfractions in young healthy Chinese people**. *International journal of food sciences and nutrition*. 2019;70:355-6610.1080/09637486.2018.1504009.

[13] Alias IZ, Jr., Mdisa Z, Abdulkadir K, Ali O. **The effect of increased consumption of edible palm oil on the nutritional status, lipid profiles and lipid peroxidation among malaysian aboriginestc**. *Malaysian journal of nutrition*. 2002;8:137-56

[14] Vega-López S, Ausman LM, Jalbert SM, Erkkilä AT, Lichtenstein AH. **Palm and partially hydrogenated soybean oils adversely alter lipoprotein profiles compared with soybean and canola oils in moderately hyperlipidemic subjects**. *American Journal of Clinical Nutrition*. 2006;84:54-62

[15] Tholstrup T, Hjerpsted J, Raff M. **Palm olein increases plasma cholesterol moderately compared with olive oil in healthy individuals**. *American Journal of Clinical Nutrition*. 2011;94:1426-3210.3945/ajcn.111.018846.

[16] Karupaiah T, Chuah KA, Chinna K, Matsuoka R, Masuda Y, Sundram K, et al. **Comparing effects of soybean oil- and palm olein-based mayonnaise consumption on the plasma lipid and lipoprotein profiles in human subjects: a double-blind randomized controlled trial with cross-over design**. *Lipids in Health and Disease*. 2016;1510.1186/s12944-016-0301-9.

[17] Sun G, Xia H, Yang Y, Ma S, Zhou H, Shu G, et al. **Effects of palm olein and olive oil on serum lipids in a Chinese population: A randomized, double-blind, cross-over trial**. *Asia Pacific Journal of Clinical Nutrition*. 2018;27:572-8010.6133/apjcn.032017.12.

[18] Sundram K, French MA, Clandinin MT. **Exchanging partially hydrogenated fat for palmitic acid in the diet increases LDL-cholesterol and endogenous cholesterol synthesis in normocholesterolemic women**. *European Journal of Nutrition*. 2003;42:188-9410.1007/s00394-003-0411-9.

[19] Vega-Lopez S, Ausman LM, Jalbert SM, Erkkila AT, Lichtenstein AH. **Palm and partially hydrogenated soybean oils adversely alter lipoprotein profiles compared with soybean and canola oils in moderately hyperlipidemic subjects**. *Am J Clin Nutr*. 2006;84:54-6210.1093/ajcn/84.1.54.

[20] Teng KT, Nagapan G, Cheng HM, Nesaretnam K. **Palm Olein and Olive Oil Cause a Higher Increase in Postprandial Lipemia Compared with Lard but Had No Effect on Plasma Glucose, Insulin and Adipocytokines**. *Lipids*. 2011;46:381-810.1007/s11745-010-3516-y.

[21] Wood R, Kubena K, Tseng S, Martin G, Crook R. **Effect of palm oil, margarine, butter, and sunflower oil on the serum lipids and lipoproteins of normocholesterolemic middle-aged men**. *The Journal of Nutritional Biochemistry*. 1993;4:286-9710.1016/0955-2863(93)90099-I.

[22] Temme EH, Mensink RP, Hornstra G. **Comparison of the effects of diets enriched in lauric, palmitic, or oleic acids on serum lipids and lipoproteins in healthy women and men**. *Am J Clin Nutr*. 1996;63:897-90310.1093/ajcn/63.6.897.

[23] Cheng C, Wang D, Xia H, Wang F, Yang X, Pan D, et al. **A comparative study of the effects of palm olein, cocoa butter and extra virgin olive oil on lipid profile, including low-density lipoprotein subfractions in young healthy Chinese people**. *International journal of food sciences and nutrition*. 201810.1080/09637486.2018.1504009.

[24] Heber D, Ashley JM, Solares ME, Wang HJ, Alfinslater RB. **THE EFFECTS OF A PALM-OIL ENRICHED DIET ON PLASMA-LIPIDS AND LIPOPROTEINS IN HEALTHY-YOUNG MEN**. *Nutrition Research*. 1992;12:S53-S910.1016/s0271-5317(05)80450-6.

[25] Lv C, Wang Y, Zhou C, Ma W, Yang Y, Xiao R, et al. **Effects of dietary palm olein on the cardiovascular risk factors in healthy young adults**. *Food and Nutrition Research*. 2018;6210.29219/fnr.v62.1353.

[26] Marzuki A, Arshad F, Razak TA, Jaarin K. **Influence of dietary fat on plasma lipid profiles of Malaysian adolescents**. *American Journal of Clinical Nutrition*. 1991;53:1010S-4S10.1093/ajcn/53.4.1010S.

[27] Voon PT, Ng TK, Lee VK, Nesaretnam K. **Diets high in palmitic acid (16:0), lauric and myristic acids (12:0 + 14:0), or oleic acid (18:1) do not alter postprandial or fasting plasma homocysteine and inflammatory markers in healthy Malaysian adults**. *Am J Clin Nutr*. 2011;94:1451-710.3945/ajcn.111.020107.

[28] Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. **Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement**. *Systematic reviews*. 2015;4:1

[29] Higgins JP, Green S. **Cochrane handbook for systematic reviews of interventions**: *John Wiley & Sons*; 2011

[30] Obahiagbon F. **A review: aspects of the African oil palm (Elaeis guineesis jacq.) and the implications of its bioactives in human health**. *American Journal of Biochemistry and Molecular Biology*. 2012;2:106-19

[31] Cheng C, Wang D, Xia H, Wang F, Yang X, Pan D, et al. **A comparative study of the effects of palm olein,**

cocoa butter and extra virgin olive oil on lipid profile, including low-density lipoprotein subfractions in young healthy Chinese people. *International journal of food sciences and nutrition*. 2019;70:355-66

[32] Scholtz SC, Pieters M, Oosthuizen W, Jerling JC, Bosman MJ, Vorster HH. **The effect of red palm olein and refined palm olein on lipids and haemostatic factors in hyperfibrinogenaemic subjects**. *Thrombosis research*. 2004;113:13-25

[33] Loganathan R, Subramaniam KM, Radhakrishnan AK, Choo Y-M, Teng K-T. **Health-promoting effects of red palm oil: evidence from animal and human studies**. *Nutrition reviews*. 2017;75:98-113

[34] Flegal KM. **Evaluating epidemiologic evidence of the effects of food and nutrient exposures**. *The American journal of clinical nutrition*. 1999;69:1339S-44S

[35] Li G, Zhang Y, Mbuagbaw L, Holbrook A, Levine MA, Thabane L. **Effect of green tea supplementation on blood pressure among overweight and obese adults: a protocol for a systematic review**. *BMJ open*. 2014;4:e004971