UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE
PROGRAMA DE PÓS-GRADUAÇÃO DE CIÊNCIAS DA NUTRIÇÃO

Kathleen Krüger Peres

A implicação dos alimentos à saúde humana: Alimentos Ultraprocessados e Azeite de Oliva

Porto Alegre
2022

KATHLEEN KRÜGER PERES

A implicação dos alimentos à saúde humana:

Alimentos Ultraprocessados e Azeite de Oliva

Dissertação de Mestrado apresentada ao Programa de Pós-Graduação em Ciências da Nutrição, como requisito parcial para obtenção do título de Mestre.

Orientadora: Profª. Drª. Simone Morelo Dal Bosco

Porto Alegre

2022

Catalogação na Publicação

Peres, Kathleen Krüger
A implicação dos alimentos à saúde humana : alimentos ultraprocessados e azeite de oliva / Kathleen Krüger Peres. -- 2022.
111 p. : il., tab. ; 30 cm.

Dissertação (mestrado) -- Universidade Federal de Ciências da Saúde de Porto Alegre, Programa de Pós-Graduação em Ciências da Nutrição, 2022.

Orientador(a): Simone Morelo Dal Bosco.

1. Nutrição e Alimentos. 2. Revisões Sistemáticas. 3. Alimentos Ultraprocessados. 4. Azeite de Oliva. I. Título.

Sistema de Geração de Ficha Catalográfica da UFCSPA com os dados fornecidos pelo(a) autor(a).

AGRADECIMENTOS

Quando pensei em escrever os agradecimentos dessa dissertação um filme passou na minha cabeça. Lembro como se fosse a pouco tempo o meu sonho de estudar na UFCSPA, quando ia de Guaíba até Porto Alegre e atravessava o Túnel da Conceição e repetia dentro do carro aos meus pais: “vocês veem aquela faculdade? É ali que eu vou me formar!” E hoje, eu escrevo os agradecimentos da minha dissertação de mestrado aqui, mais uma vez no lugar em que tanto sonhei me profissionalizar. Os sonhos não acabaram, porquê um dia quero retornar com título de professora dessa universidade.

E se os sonhos existem, eles têm toda a estrutura para serem o que são, estrutura essa que veio de muito apoio da minha família. Eu jamais seria o que sou hoje sem o apoio dos meus pais (Evelize e Pyter) e dos meus avós (Elcira e Aureo). A eles eu devo toda a gratidão que não teria forças para demonstrar em palavras.

Nessa caminhada, com esse apoio, eu conheci pessoas incríveis e que sempre acreditaram em mim, em especial a minha orientadora e amiga Simone. Quando ela aceitou aquela aluna de nutrição de segundo semestre, cheia de energia a planejar um grupo de pesquisa, que iniciou: eu, Carine, Rafaella… e foi agregando todas que hoje estão trilhando o caminho da pesquisa, a qual eu tanto amo.

Além dessa pessoa incrível que eu tive a honra de conhecer e trabalhar junto, eu jamais deixaria de agradecer minhas outras professoras do PPG.

Fazer um mestrado em plena pandemia não foi nada fácil. Eu sempre tive dificuldades em estudar no formato on-line e acredito que todas nós, colegas e professoras, passamos um “bocado” de trabalho para nos adaptarmos.

Quando eu olho a Kathleen de 2020 eu reconheço o crescimento e que isso só foi estruturado pela participação de pessoas incríveis na minha vida, que me apoiaram, que acreditaram em mim e que proporcionaram toda a minha jornada mais leve.

Esse final de mestrado foi um pouco conturbado e por vezes pensei que não iria conseguir aguentar todas as coisas que estavam acontecendo na minha vida, mas, nunca eu pensei em desistir desse sonho, até porquê o sonho da docência ainda é muito grande e vivo dentro de mim.

Quem nunca me deixou desistir ou desanimar também tem papel nessa caminhada, minhas amigas (Karen, Natália, Bianca, Carine, Wal, vocês são parte da minha história e dessa jornada de vida), meu namorado (Pedro) que me ajudou muito nessa reta final e mais todas as pessoas maravilhosas que eu tenho na minha vida. Um agradecimento imenso, de coração.

E sem mais delongas, esse título de mestre também é de todos que participam da minha jornada. Eu amo vocês.

Muito obrigada!

“Sob os raios do Sol sigo um sonho meu”

SUMÁRIO

LISTA DE ABREVIATURAS E SIGLAS

ONU	Organização das Nações Unidas
OMS	Organização Mundial da Saúde
DCV	Doenças Cardiovasculares
EVOO	Azeite de Oliva Extravirgem
VOO	Azeite virgem
ROO	Azeite refinado
DCNT	Doenças Crônicas Não Transmissíveis
IMC	Índice de Massa Corporal
UPFs	Alimentos Ultraprocessados
AVC	Acidente Vascular Cerebral
EPIC	*European Prospective Investigation into Cancer and Nutrition*
ESFA	Autoridade Europeia de Segurança Alimentar
EUROLIVE	*European Study of the Antioxidant Effects of Olive Oil and its Phenolic Compounds on Lipid Oxidation*
PREDIMED	Estudo Multicêntrico *Prevención con Dieta Mediterranea*
PRISMA-P	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International prospective register of systematic reviews
MeSH	Medical Subject Headings
NOS	Newcastle-Ottawa Scale
HR	Risk ratio
GBD	Global Burden of Disease Study
NRF 9.3	A new category-specific nutrient rich food
HEI-2000	Healthy Eating Index
PCR	Proteína C Reativa
IL6	Interleucina 6
IL1	Interleucina 1
TNF-α	Fator de Necrose Tumoral Alfa
MCP-1	Monocyte chemotactic protein-1
sVCAM-1	Circulating Vascular Cell Adhesion Molecule-1
VCAM-1	Vascular Cell Adhesion Molecule 1

ICAM-1	Intercellular adhesion molecule-1
TBARS	Malondialdehyde and thiobarbituric acid reactive substances
PON-3	Paraoxonase-3 protein
ApoA1	Apo lipoproteína A1
ApoB	Apo lipoproteína B
MCP-1	Monocyte chemoattractant protein-1
FMD	Flow mediated dilatation
PAS	Pressão arterial sistólica
PAD	Pressão arterial diastólica
TG	Triglicerídeos - TG
CT	Colesterol Total - CT
LDL	Low Density Lipoproteins - LDL
HDL	High Density Lipoproteins - HDL
OO	Olive Oil - OO
ROO	Refined Olive Oil - ROO
EVOO	Extra virgin olive oil - EVOO
HPOO ou HP(E)VOO	High phenolic olive oil
LPOO or LP(E)VOO	Low phenolic olive oil
MOO	Mixed OO (ROO + virgin OO)
PUFAs	Ácidos graxos poliinsaturados
MUFAs	Ácidos graxos monoinsaturados

RESUMO

Introdução: Com base no estudo em alimentos tem-se como objeto de estudo dessa dissertação os alimentos ultraprocessados e o azeite de oliva. Os alimentos ultraprocessados são classificados de acordo com o grau de processamento e adição de ingredientes que são apenas a nível industrial. O processamento gera diversos alimentos com aditivos e conservantes, e o consumo desses alimentos pela população gera um potencial risco à saúde, associando principalmente ao maior risco de mortalidade. Em relação ao azeite de oliva e seus compostos fenólicos tem-se estudado os potenciais efeitos cardioprotetores de seu consumo na população, avaliando que sua composição pode atuar na saúde como um potencial protetor às doenças cardiovasculares e seus fatores de risco, como no nível de pressão arterial, teor de perfil lipídico e de marcadores inflamatórios que causam danos à saúde cardiovascular.

Objetivo: Relacionar dados sobre o consumo de alimentos ultraprocessados como fator de risco de mortalidade e também o consumo de azeite de oliva e sua composição como fator protetor de doenças cardiovasculares e seus fatores de risco.

Metodologia: Foram realizadas uma revisão sistemática e uma revisão de revisões sistemáticas, sendo o objetivo da revisão sistemática avaliar o consumo dos alimentos ultraprocessados e o risco de mortalidade, por meio da pesquisa científica através dos bancos de dados *PubMed*, *Scopus* e *Web of Science*. Foram sistematicamente pesquisados estudos que examinam a relação entre o consumo de alimentos ultraprocessados e o risco de mortalidade. A análise de evidências foi realizada usando uma ferramenta para avaliar o risco de viés e qualidade metodológica (NOS), e baseada no protocolo PRISMA e suas etapas, um total de cinco estudos foram incluídos. A revisão de revisões sistemáticas foi realizada por meio da busca sistemática de revisões nos bancos de dados científicos *PubMed, Web of Science* e *Cochrane Library.* Foram incluídos artigos que analisaram a relação entre o consumo de azeite de oliva e as doenças cardiovasculares, totalizando seis artigos. Utilizou-se ferramentas para avaliar o risco de viés (ROBIS), qualidade metodológica (AMSTAR-2) e qualificação da evidência (GRADE).

Conclusão: O efeito do consumo dos alimentos ultraprocessados gera um aumento de risco de mortalidade, e tal risco aumenta quanto maior é a ingestão desses alimentos, portanto o consumo desse grupo alimentício está associado a um maior risco de mortalidade da população. Já com relação ao efeito potencial cardioprotetor do azeite de oliva e de seus compostos fenólicos, demonstrou-se que quanto maior o teor de compostos fenólicos do azeite de oliva maior é a redução dos possíveis fatores de risco cardiovasculares, como a melhora do perfil lipídico, pressão arterial e marcadores inflamatórios.

Palavras Chave: Alimentos Ultraprocessados. Mortalidade. Revisões Sistemáticas. Azeite de Oliva. *genus Olea*. Fatores de Risco de Doenças Cardíacas.

ABSTRACT

Introduction: Based on the study of food, the objects of study of this dissertation are ultra-processed foods and olive oil. Ultra-processed foods are classified according to the degree of processing and addition of ingredients that are only at an industrial level. Food processing generates several foods with additives and preservatives, and the consumption of these foods by the population poses a potential health risk, mainly associated with a higher risk of mortality. In regard to olive oil and its phenolic compounds, the possible cardioprotective effects of its consumption in the population have been studied, evaluating that its composition can act in health as a potential protector against cardiovascular diseases and their risk factors, such as the level of blood pressure, lipid profile and inflammatory markers that damage cardiovascular health.

Objective: To relate data on ultra-processed foods consumption as a risk factor for mortality and the consumption of olive oil and its composition as a protective factor for cardiovascular diseases and their risk factors.

Methodology: A systematic review and a review of systematic reviews were carried out, with the objective of the systematic review to evaluate the ultra-processed foods consumption and the risk of mortality, through scientific research through the PubMed, Scopus, and Web of Science databases. We systematically searched for studies examining the relationship between ultra-processed food consumption and mortality risk. Evidence analysis was performed using a tool to assess the risk of bias and methodological quality (NOS), and based on the PRISMA protocol and its steps, a total of five studies were included. The review of systematic reviews was carried out through a systematic search of reviews in the scientific databases PubMed, Web of Science, and Cochrane Library. Articles that analyzed the relationship between olive oil consumption and cardiovascular disease were included, totaling six articles. Tools were used to assess the risk of bias (ROBIS), methodological quality (AMSTAR-2), and qualification of evidence (GRADE).

Conclusion: The effect of the consumption of ultra-processed foods generates an increased risk of mortality, and this risk increases the higher the intake of these foods, therefore, the consumption of this food group is associated with a higher risk of mortality in the population. Regarding the potential cardioprotective effect of olive oil and its phenolic compounds, it was demonstrated that the higher the content of phenolic compounds in olive oil, the more significant the reduction of possible cardiovascular risk factors, such as the improvement in the lipid profile, blood pressure, and inflammatory markers.

Keywords: Ultra-Processed Foods. Mortality. Systematic Reviews. Olive Oils. *genus Olea*. Cardiovascular Risks.

1 INTRODUÇÃO

O cenário da alimentação é preocupante e demonstra uma relação inadequada entre os alimentos e a saúde humana. Uma epidemia global de doenças crônicas relacionadas aos hábitos alimentares levou à experimentação do uso de alimentos como parte formal do atendimento e tratamento do paciente, visando utilizar esse alimento como forma de ação protetora e desempenhando um papel que por vezes seria do medicamento[1].

Uma em cada cinco mortes em todo o mundo é atribuível à alimentação abaixo do ideal, mais do que qualquer outro fator de risco, incluindo o tabaco[1]. A relação da saúde e os alimentos está descrita nas medidas de orientação das grandes agências de cuidado à saúde humana, como por exemplo, está presente nos Objetivos de Desenvolvimento Sustentável da Organização das Nações Unidas e também como metas da Organização Mundial da Saúde (OMS)[2].

Com base nos artigos científicos pode-se então caracterizar os alimentos, sua composição e as possíveis implicações desses à saúde humana, pois é através dos hábitos alimentares que se pode manter a população saudável e também com menores riscos de futuros adoecimentos[3].

Tendo em vista a prática alimentar apresentada pelo reduzido consumo de alimentos *in natura* e maior aumento de produtos prontos para o consumo[4], vimos que o impacto dos alimentos ultraprocessados em várias doenças relacionadas ao estilo de vida já foi estudado, incluindo diabetes mellitus, síndrome metabólica, doenças cardiovasculares (DCV), dislipidemia, hipertensão e câncer[5-8].

Tais alimentos são determinados através do nível de processamento, conforme a classificação NOVA. Esses contêm substâncias predominantemente industriais e pouco ou nenhum alimento integral, sendo produzidos por grandes indústrias, nas quais as etapas e técnicas de processamento ocorrem pela adição de diversos ingredientes, como: sal, açúcar, óleos, gorduras e além de substâncias cujo uso é apenas em nível industrial[9-10]. Sabendo o possível efeito prejudicial com relação ao consumo de ultraprocessados, associa-se tal padrão alimentar ao aumento dos riscos de adoecimento e de doenças crônicas não transmissíveis, sendo tais doenças possíveis geradoras do risco aumentado de mortalidade na população adulta[11].

Em contrapartida à resposta metabólica prejudicial do consumo de determinados alimentos, pode-se realizar a utilização desses como forma de atuar na prevenção de doenças, um exemplo importante abordado pela literatura científica é o consumo do azeite de oliva como possível alimento cardioprotetor. As propriedades de saúde do azeite de oliva, em especial o azeite de oliva extra-virgem (EVOO) são atribuídas à sua predominante concentração de ácidos graxos monoinsaturados e também a presença de uma variedade de compostos fenólicos, como exemplo o ácido oleico, oleuropeína e hidroxitirosol[12,13].

A classificação dos azeites de oliva se deve através de seu processo de obtenção, tais como: Azeite virgem (VOO), azeite extravirgem (EVOO), azeite refinado (ROO), azeite, azeite de bagaço de azeitona e azeite lampante (EEC Regulation 1513/2001; *EU Regulation* No. 29/2012 *and EU Regulation* 1348/2013).

Com o consumo de uma alimentação rica em antioxidantes e compostos fenólicos podemos atuar na prevenção de doenças que hoje sabemos ser prejudiciais à sociedade, por essa razão o estudo do azeite de oliva como alimento protetor e promotor de saúde é necessária, além disso devido ao número de estudos sobre o assunto e o aumento de pesquisas sobre o consumo de azeite de oliva e seus efeitos cardiovasculares, a realização de uma *overview* que sumarize e avalie a qualidade dessa evidência é útil para a recomendação posterior de tal alimento.

O objetivo dessa dissertação foi relacionar dados sobre o consumo de alimentos ultraprocessados como fator de risco de mortalidade e também o consumo de azeite de oliva e sua composição como fator protetor de doenças cardiovasculares e seus fatores de risco.

2 REFERENCIAL TEÓRICO

A alimentação é um instinto primitivo do ser humano, principalmente devido a suas necessidades fisiológicas.

> A alimentação é, após a respiração e a ingestão de água, a mais básica das necessidades humanas; Mas como "não só de pão vive o homem", a alimentação, além de uma necessidade biológica, é um complexo sistema simbólico de significados sociais, sexuais, políticos, religiosos, éticos, estéticos etc" (Carneiro H. Comida e Sociedade Uma História da Alimentação. Elsevier; 1ª edição. 7 abril 2003)

Por essa razão os hábitos alimentares e padrões alimentares podem ser considerados indicadores e determinantes das possíveis intercorrências de saúde na população humana[14].

> "Em praticamente todas as culturas, os alimentos sempre foram relacionados com a saúde, não apenas porque a sua abundância ou escassez colocam em questão a sobrevivência humana, mas também porque o tipo de dieta e a explicação médica para a sua utilização sempre influenciaram a atitude diante da comida, considerando a sua adequação a certas idades, gênero, constituições físicas ou enfermidades presentes." (Carneiro HS. Comida e Sociedade: significados sociais na história da alimentação. História: Questões & Debates, Curitiba, n. 42, p. 71-80, 2005. Editora UFPR)

Durante anos as preocupações com relação aos hábitos alimentares vêm sendo pauta na história da saúde, um exemplo a ser recrutato, Pedro Escudero, médico, recomendou já em 1934, que para a alimentação ser saudável deveria apresentar o hábito de ser qualitativamente completa e quantitativamente suficiente, com sua composição apropriada[15].

Essas preocupações em relação à alimentação estiveram centradas na história pelo elevado consumo de alimentos com alto teor de açúcar, sódio e gordura, devido ao elevado consumo desses alimentos, aliado a fatores como sedentarismo e estresse, já estavam sendo relacionados à incidência de Doenças Crônicas Não Transmissíveis (DCNT), responsáveis por elevadas taxas de mortalidade da população nos últimos anos[16].

De acordo com as tendências mundiais de alimentação, a Organização Mundial da Saúde (OMS) planejou recomendações por meio da Estratégia Global para Alimentação Saudável, Atividade Física e Saúde, a fim de evitar e prevenir o adoecimento da população[17].

Os hábitos alimentares são então conhecidos por serem possíveis fatores preditivos de vários resultados de saúde, pois a composição da alimentação de acordo com tal padrão poderá ter influência nos desfechos de saúde, como por exemplo no Índice de Massa Corporal (IMC)[14], no funcionamento do metabolismo[18], função imunológica[19], na saúde cardiovascular[20], bem como até mesmo preditor de possíveis erros de replicação celular que podem ser diagnosticados como câncer[21].

Com base nesta evidência da relação entre hábitos alimentares e resultados de saúde humana, precisa-se encarar a alimentação como a futura ação da saúde primária para a promoção de saúde e também prevenção de doenças que possuem em sua fisiopatologia base alimentar, sendo ela um fator de risco ou de promoção[22].

Em tal perspectiva, é fundamental o aspecto de tomada de consciência para as práticas alimentares saudáveis, sendo essas: as escolhas alimentares, preparo das refeições e dos alimentos em suas diversas formas, o consumo dos alimentos e das refeições. Esses fatores são necessários pois demandam atenção e dedicação constantes para que sejam ensinadas. Com a realização de pesquisas e além dessas práticas de ações de educação alimentar e nutricional, a fim de entregar à sociedade uma autonomia e promover o autocuidado na base dos hábitos alimentares e assim praticar uma alimentação saudável e adequada[23].

No âmbito das ações de educação alimentar e nutricional, uma prática fundamental para atuarmos como promotores de saúde é o ensino da classificação de alimentos segundo seu grau de processamento e classificação, como o Guia Alimentar para a População Brasileira nos demonstra[24].

Além de práticas de educação nutricional, o conhecimento da composição dos alimentos e seus possíveis benefícios à saúde podem ser aplicados para auxiliar no tratamento e prevenção de doenças. Entender a aplicabilidade e o potencial dos antioxidantes presentes em compostos vegetais que podem ser do interesse humano devido às suas propriedades. Os compostos fenólicos estão amplamente presentes nas plantas e são conhecidos por sua função antioxidante[25]. Sendo assim, o entendimento sobre os alimentos e suas propriedades são necessárias para o futuro da saúde de nossa população mundial.

2.1 Referencial Teórico - Artigo 1

Uma análise dos alimentos pode ser realizada através do seu processamento, o qual é definido como todos os métodos e técnicas usados pelas indústrias de alimentos, bebidas e indústrias associadas para transformar alimentos frescos inteiros em produtos alimentícios.

Tendo em vista o Guia Alimentar para População Brasileira e sua versão mais atualizada publicada em 2014[24] e também o trabalho de Monteiro *et al* (2010), a classificação dos alimentos foi dividida em três grupos de acordo com a extensão e finalidade do processamento utilizado em sua produção[26]:

• Grupo 1: alimentos não processados (*in natura*) e minimamente processados

O primeiro grupo inclui alimentos não processados, também chamados de alimentos *in natura* e os minimamente processados. Alimentos não processados não passam por nenhum método de mudança em sua composição ou em suas características, sendo aqueles que possuem base em sua forma natural. Já os alimentos minimamente processados estão incluídos em uma categoria a qual foram realizados processos mínimos, sendo eles principalmente físicos, como corte, higienização, entre outros. Tais processos são aplicados a alimentos *in natura* com o objetivo de preservá-los e torná-los mais disponíveis e acessíveis, e muitas vezes mais seguros e palatáveis. A esses processos incluem limpeza, porcionamento, remoção de frações não comestíveis, ralar, flocar, espremer, engarrafar, secagem, resfriamento, congelamento, pasteurização, fermentação, redução de gordura, embalagem a vácuo e gás e embalagem simples.

Podem ser utilizados pelo produtor primário, empacotador, distribuidor ou varejista, bem como pelos fabricantes, para eventual venda ao consumidor.

São exemplos de alimentos do Grupo 1: carne fresca e leite, grãos, legumes, nozes, frutas e vegetais e raízes e tubérculos vendidos como tal são geralmente minimamente processados de várias maneiras.

• Grupo 2: ingredientes culinários ou alimentos processados

Os alimentos processados ou ingredientes culinários possuem outras atuações industriais em sua formação. Esses alimentos passam por processos diferentes daqueles utilizados para obter alimentos minimamente processados ou *in natura*, pois alteram a natureza dos alimentos originais. Nesse grupo inclui-se substâncias extraídas e purificadas de alimentos não processados ou minimamente processados para a produção de ingredientes culinários e/ou da indústria alimentícia.

Os processos empregados podem ser físicos e também químicos, como por exemplo: pressão, moagem, refino, hidrogenação e hidrólise, e uso de enzimas e aditivos. Os alimentos do grupo 2 não são comestíveis ou palatáveis por si só, e têm maior densidade energética e menor densidade de nutrientes em comparação com os alimentos integrais dos quais foram extraídos. São utilizados em residências ou restaurantes, no preparo e cozimento de pratos compostos por alimentos *in natura* ou minimamente processados (grupo 1), e também no desenvolvimento industrial de produtos ultraprocessados (grupo 3). Os alimentos do Grupo 2 incluem ingredientes comuns da indústria de alimentos, como amidos, farinhas, óleos e gorduras, sal, açúcar e adoçantes, além de também ingredientes industriais, como xarope de milho rico em frutose, lactose e proteínas de leite e soja.

• Grupo 3: Alimentos ultraprocessados (UPFs)

O terceiro grupo envolve produtos alimentícios ultraprocessados prontos para consumo ou prontos para aquecer com pouca ou nenhuma necessidade de preparação, a não ser tais citadas. Os produtos alimentícios do grupo 3 são resultado do processamento de diversos gêneros alimentícios, incluindo ingredientes do grupo 2 e alimentos básicos não processados ou minimamente processados do grupo 1.

Os processos utilizados na produção de produtos do grupo 3 incluem salga, adoçamento, cozimento, fritura, fritura, cura, defumação, decapagem, enlatamento, e também frequentemente o uso de conservantes e aditivos cosméticos, adição de vitaminas sintéticas e minerais, e tipos sofisticados de embalagens. O processamento industrial do grupo 3 foi inicialmente projetado para criar produtos com maior prazo de validade, acessíveis ao consumo, convenientes à rotina e também atraentes em sua forma prontos para consumir. Esse grupo alimentício também foi formulado para reduzir a deterioração microbiana, possuindo uma longa vida útil para o consumo, além disso sua possibilidade de serem transportados por longas distâncias e para serem extremamente palatáveis. Essa última característica pode atuar muitas vezes, como formadores de hábitos alimentares na população.

Nessa categoria de alimentos inclui-se guloseimas, bebidas adoçadas adicionadas ou não de adoçantes artificiais, pós para refrescos, embutidos e outros produtos derivados de carne e gordura animal, produtos congelados prontos para aquecer, produtos desidratados (como misturas para bolo, sopas em pó, macarrão instantâneo e temperos prontos), e uma infinidade de novos produtos que chegam ao mercado todos os anos[24,26].

Figura 1: Ilustração sobre os alimentos e sua classificação

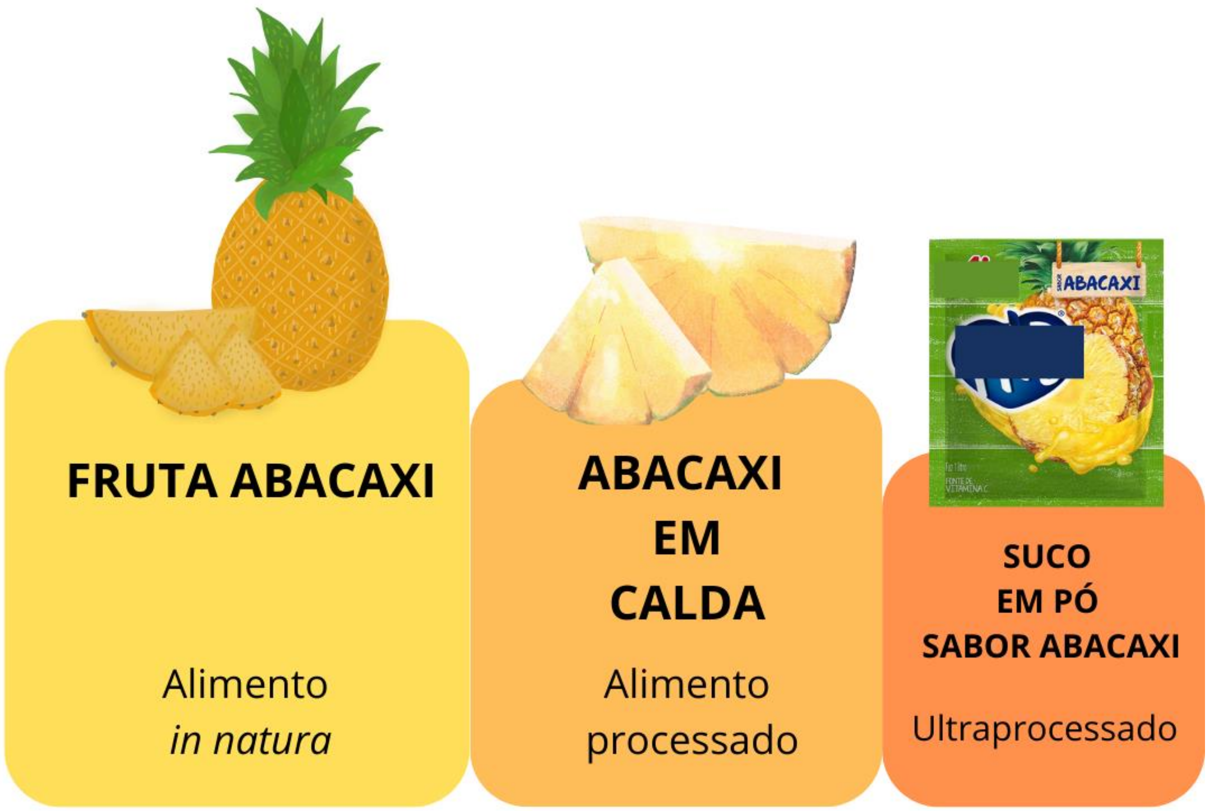


Figura 1 - Adaptado pela autora de: Brasil, 2014 (24)

Com a propagação desses produtos UPFs na sociedade, percebeu-se que houve uma relação do seu consumo com a saúde humana, sendo essa relação inversamente proporcional ao consumo[27].

Além disso, a relação com a qualidade da dieta e o consumo de UPFs também pode ser associada a diversos fatores de risco para doenças relacionadas à alimentação, tais doenças ocorrem através da contribuição dos hábitos alimentares, sendo esses fatores determinantes para presença ou não dessas comorbidades, distúrbios ou condições de saúde[27,28].

Evidências demonstram o impacto da ingestão de alimentos UPFs em várias doenças relacionadas ao estilo de vida associada a um risco aumentado de desenvolvimento de diabetes mellitus tipo II, doenças cardiovasculares (DCV), dislipidemia, hipertensão e câncer[29,30,31]

O possível adoecimento da população relacionado ao consumo de alimentos ultraprocessados pode-se dar devido a própria composição alimentícia, pois tais alimentos possuem formulações industriais fabricadas a partir de substâncias derivadas de alimentos in natura e acrescidos de aditivos, para tornarem-se mais palatáveis são ricos em açúcares, sal e gorduras, caracterizando em produtos de alta densidade energética que aumentam o aporte calórico da dieta. Além disso, esses alimentos contém pequenas quantidades de fibras, proteínas, micronutrientes e fitoquímicos, e presença de gorduras trans e saturadas em excesso, que podem ser prejudiciais à saúde. Por essa razão e composição, tais alimentos podem ser responsáveis por diversas comorbidades atuais, que contribuem para o adoecimento da população e problemas de saúde[21,32], o qual pode gerar aumento do risco de mortalidade da população adulta, sendo precoce ou não.

A associação entre ingestão de UPFs e risco de mortalidade foi averiguada, e uma possibilidade de avaliar a mortalidade da população através de estudos científicos são por meio de trabalhos de coorte, os quais possuem um acompanhamento da população e também o possível adoecimento, sendo a mortalidade avaliada como incidência, buscando estabelecer na literatura o consumo de UPFs e os seus possíveis danos à saúde humana[33].

O consumo dietético desses alimentos acarreta em riscos nutricionais e de saúde, o trabalho do grupo GBD 2017 DIET COLLABORATORS[1] apresentou que no ano de 2017 onze milhões de mortes foram associadas a dieta e a qualidade da alimentação, sendo 3 milhões à alta ingestão de sódio, micronutriente intimamente ligado a composição dos UPFs.

Demais estudos demonstraram a interação do consumo de UPFs e o maior risco de mortalidade populacional, No trabalho de Rico-Campá *et al*, o risco de mortalidade por todas as causas foi avaliado de acordo com o consumo de UPFs diário, os achados significativos representaram o consumo de >4 porções de UPFs associado ao risco de mortalidade de 62% maior do que quando consumido em menos porções[34].

Tendo em vista o risco de mortalidade, podemos relacioná-lo aos dados da Organização Mundial da Saúde no ano 2021[35], em que 71% das causas de mortes em todo o mundo foram por doenças cardiovasculares, câncer e diabetes miellitus[35], além disso os dados trazem o aumento do risco de morte associado a doenças crônicas não transmissíveis e a dieta, corroborando a ideia de que as doenças crônicas não transmissíveis tão prevalentes tem relação com a qualidade da dieta, bem como no perfil nutricional de quem as consome[36]. Os dados sobre mortalidade podem estar associados ao aumento das mudanças dos hábitos alimentares, aliado ao crescimento da incidência das doenças crônicas em idades mais jovens, como mostra o estudo de Lin *et al*[37], além disso há perspectiva de aumento de consumo desses alimentos pela população mais jovem[38], sendo assim essencial a análise dos riscos desse consumo à saúde humana.

2.2 Referencial Teórico - Artigo 2

O azeite de oliva pode ser classificado através de seu processo de produção, tais como: Azeite virgem (VOO), azeite extravirgem(EVOO), azeite refinado (ROO), azeite, azeite de bagaço de azeitona e azeite lampante (EEC Regulation 1513/2001; EU Regulation No. 29/2012 and EU Regulation 1348/2013).

A composição química do azeite varia de acordo com a tecnologia de extração que é aplicada para obter o azeite dos frutos da oliveira (figura 2). A extração do azeite depende do processo de esmagamento das azeitonas, frutos das oliveiras, e da separação do azeite da polpa do fruto sob pressão elevada. Outros processos de formação do azeite pode ser através de extrudado, pós-prensado, re-prensado com ou sem o uso de água quente, tal azeite obtido por este tipo de processo é geralmente caracterizado por uma intensidade de cor mais forte, aroma mais fraco e maior teor de ácidos graxos livres em sua composição[39 - 41].

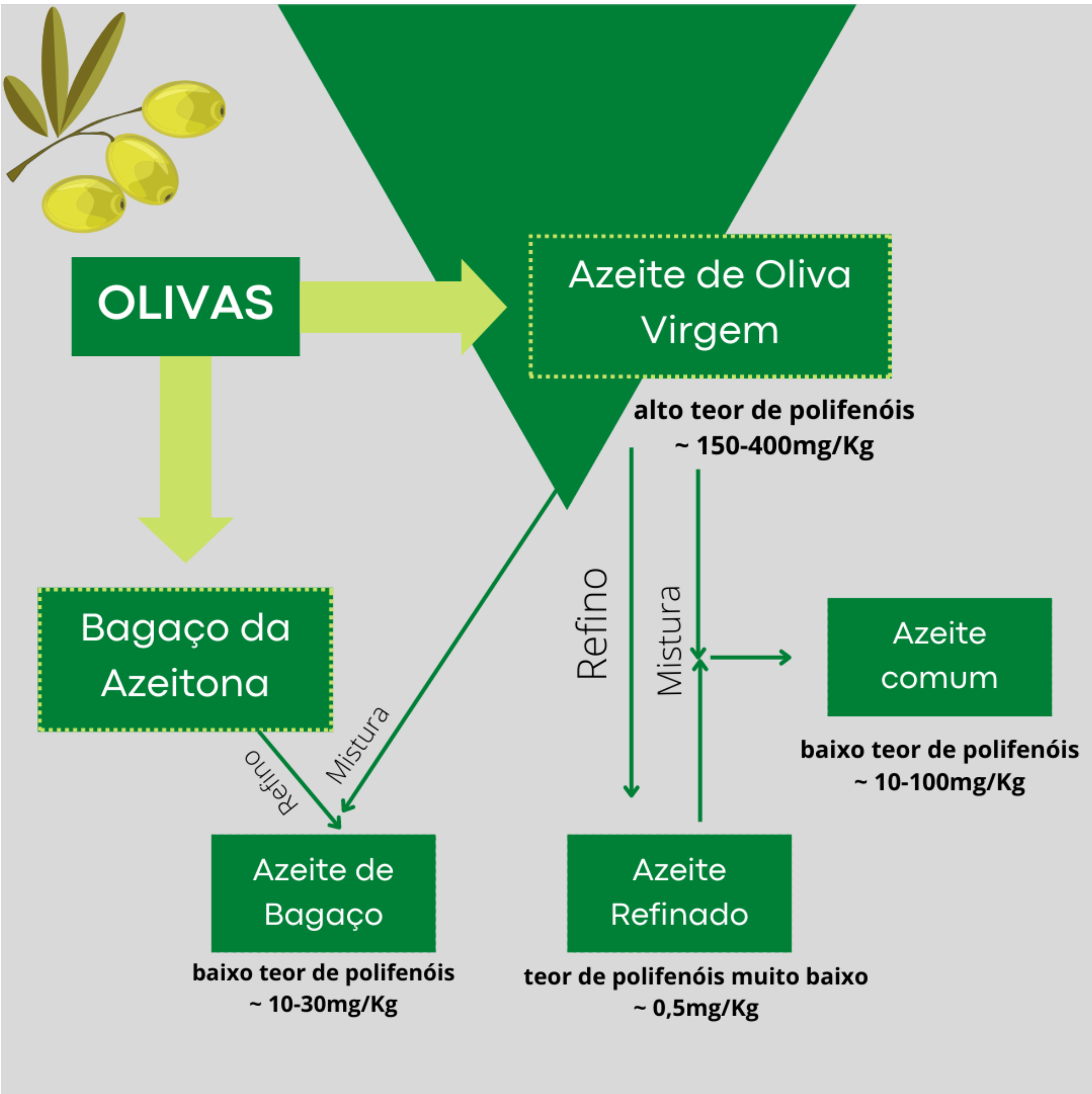


Figura 2 - Adaptado pela autora de: Gorzynik-Debicka M *et al* 2018. (41)

Para azeites os quais a extração foi realizada por processos químicos, esses só podem ser consumidos após um refino, sendo esse processo uma purificação do azeite obtido através de utilização química, pois o refino atua na purificação removendo qualquer solvente e/ou impurezas que ainda estão presentes. Porém, o azeite refinado é possui menor teor de vitaminas, compostos fenólicos, fitoesteróis e outros ingredientes naturais de baixo peso molecular, pois o processo acaba atuando na remoção desses ingredientes[42].

Outro tipo de azeite é o azeite extravirgem, que em seu processo de extração não demanda de produtos químicos, filtração ou refinos, sendo altamente mais puro, com alto teor de compostos fenólicos[43]. O azeite extravirgem (EVOO), é obtido por extração mecânica do fruto da azeitona, sem uso de calor ou solventes, as propriedades de saúde do EVOO são amplamente atribuídas à sua alta concentração de ácidos graxos monoinsaturados, assim como à presença de uma variedade de compostos fenólicos, sendo essa composição conhecida na literatura por seus beneficios em vários marcadores de saúde, como nas doenças crônicas e cardiometabólicas[13,44,45].

Os teores de compostos fenólicos podem variar devido ao processo de obtenção do azeite, sendo o teor característico de cada tipo de azeite de oliva de acordo com o processo tecnológico de produção de azeite[41].

O azeite consiste principalmente em triacilglicerídeos, esses são um grupo diversificado de ésteres de glicerol com diferentes tipos de ácidos graxos em sua formação química. O ácido graxo predominante presente nos triglicerídeos dos azeites de oliva é o ácido oleico monoinsaturado (até 83% p/p). Também podemos encontrar na composição os: ácido palmítico, ácido linoleico, ácido esteárico e ácido palmitoleico que compõem o restante dos triglicerídeos do azeite. Além disso na composição do azeite há uma infinidade de microconstituintes lipofílicos ou anfifílicos presentes no azeite virgem, entre eles, fitoesteróis, esqualeno, tocoferóis, compostos fenólicos, derivados do ácido terpênico, eentre outros. Os compostos fenólicos são conhecidos na composição por ácidos fenólicos ou álcoois, derivados de oleuropeína, lignanas e flavonóides[46,47,48].

2.2.1 Compostos Antioxidantes e Fenóis

Os compostos fenólicos são compostos orgânicos naturais, sintéticos ou semisintéticos com vários grupos fenólicos na estrutura, sendo a sua composição química predominantemente caracterizada pela presença de um ou mais anéis aromáticos com grupos hidroxila ligados à sua formação[49,50].

As pesquisas vêm apresentando uma crescente evidência dos papéis benéficos dos compostos fenólicos vegetais na saúde do corpo humano. Essas estruturas são compostos bioativos naturais com estruturas químicas variadas, sendo o maior grupo de substâncias químicas no reino vegetal, suas fontes são, predominantemente frutas, legumes, nozes e sementes, raízes, cascas, folhas de diferentes plantas, ervas, produtos integrais, chás, o café e também vinho tinto.

Esses compostos apresentam poderosas propriedades antioxidantes e anti-inflamatórias que as tornam agentes importantes na saúde humana, derivados de produtos e alimentos naturais, além de serem eficientes e podem ser encontrados em uma alimentação saudável e balanceada[51-53].

Os compostos fenólicos foram estudados por sua capacidade em reduzir a morbidade e/ou retardar a progressão de doenças cardiovasculares, neurodegenerativas e cancerígenas. O mecanismo de ação desses compostos está fortemente relacionado à sua atividade antioxidante, além de serem conhecidos pela redução do nível de espécies reativas de oxigênio no corpo humano, os radicais livres que a própria atividade bioquímica corporal produz. Existem também a avaliação das propriedades químicas desses compostos como os efeitos anti-inflamatórios, antialérgicos, antiaterogênicos, antitrombóticos e antimutagênicos[54].

A ingestão diária de compostos fenólicos varia de 0,1 a 1,0 g por dia sendo a principal fonte alimentar frutas e vegetais, além de ervas, especiarias, temperos, café, chás ou vinho[55].

Nesse trabalho o foco será destinado as propriedades dos compostos fenólicos do azeite de oliva, que são especialmente interessantes no que diz respeito aos seus efeitos benéficos bem estabelecidos na saúde humana e no metabolismo, bem como a popularidade do azeite em muitas dietas diferentes, e especificamente na cozinha mediterrânea.

O termo "dieta mediterrânea" refere-se ao padrão da dieta comum na década de 1960, nos países que produziam olivas ao redor do Mar Mediterrâneo. Tal padrão alimentar demonstrou curiosidade, o Seven Countries Study apresentou em sua pesquisa que a mortalidade por doenças coronarianas na área do Mediterrâneo era 2 a 3 vezes menor do que no norte da Europa e nos Estados Unidos.[56,57]

O padrão alimentar mediterrâneo consiste em consumo de peixes, gorduras monoinsaturadas, azeite de oliva, frutas, legumes, grãos integrais, legumes, nozes e consumo moderado de álcool[58]. Com isso, sabemos que a dieta mediterrânea é rica em diversos micronutrientes e azeite de oliva, em sua predominância os azeites de oliva ricos em compostos fenólicos, esses podem ser os possíveis atuantes na regulação das doenças como as doenças cardiovasculares[59].

2.2.2 Compostos fenólicos presentes no Azeite de oliva

A composição de compostos fenólicos do azeite de oliva é conhecida pelos compostos fenólicos representados por álcoois fenólicos como hidroxitirosol (3,4-

dihidroxifeniletanol: 3,4-DHPEA) e tirosol (p -hidroxifeniletanol: p-HPEA), e seus secoiridóides derivados 3,4-DHPEA-EA (oleuropeína aglicona), p-HPEA-EA (ligstrosídeo aglicona), 3,4-DHPEA-EDA, p-HPEA-EDA (oleocantal) e oleuropeína.

Além de tais compostos, o ácido oleico e o hidroxitirosol estão presentes em maior quantidade no EVOO, e em menor teor a oleuropeína é também encontrada.

O hidroxitirosol (HT) que é abundante nas azeitonas (*Olea europea* L.) e, consequentemente, nos azeites que passaram por processos de extração sem uso de substâncias químicas, como no EVOO. Suas propriedades benéficas para a saúde humana estão relacionadas à capacidade da molécula de antioxidante de eliminar radicais livres e espécies reativas de oxigênio ou nitrogênio, bem como ativar outros sistemas antioxidantes endógenos no corpo[41].

A oleuropeína pertence a um grupo de derivados cumarínicos, secoiridóides. Tal composto possui uma propriedade importante para a saúde cardiovascular, atuando na redução da agregação plaquetária. Além disso, é também um dos principais compostos fenólicos que atua na inibição de proliferação endotelial. O uso de oleuropeína como tratamento oral resulta em uma diminuição do número de vasos sanguíneos, provando fortes propriedades antiangiogênicas. Os compostos fenólicos (oleuropeína, ácido protocatecuico) presentes no EVOO também demonstraram inibir a oxidação de LDL mediada por macrófagos do sistema imune. Além do uso do azeite de oliva, os extratos de folhas e frutos de oliveira contendo oleuropeína protegem a linha de células β pancreáticas, que são responsáveis pela produção de insulina (INS-1) contra o efeito deletério das citocinas inflamatórias[60,61].

2.2.3 Efeitos Cardioprotetores do Azeite de Oliva e seus Compostos Fenólicos

As doenças cardiovasculares (DCV) são a ameaça mais importante para a saúde da população no século XXI[62]. Dados presentes em pesquisas da OMS, 17,9 milhões de pessoas morrem anualmente por doenças cardiovasculares, o que representa 31% de todas as mortes, mais pessoas morrem a cada ano de doenças cardiovasculares - principalmente doenças isquêmicas do coração e acidentes vasculares cerebrais (AVC) - do que por qualquer outra causa ou doença. Vários fatores de risco têm sido associados a doenças cardiovasculares, incluindo hipertensão, diabetes tipo 2, dislipidemia e obesidade, todos os fatores que podem ser incluídos como fatores de risco modificáveis pela dieta[63]. Com o objetivo de reduzir o índice das doenças cardiovasculares, a OMS promoveu a Iniciativa HEARTS nas Américas em 2016. A OMS coordena a iniciativa HEARTS atuando em 1.400 unidades de saúde em 22 países em todos os continentes das Américas[64].

Estilos de vida e dietas saudáveis em idades mais jovens são fatores-chave para uma vida livre de doenças crônicas em idades mais avançadas. Conclui-se que a prevenção de DCV por meio de dieta e estilo de vida é uma prioridade de saúde pública, as DCV podem ser geradas através de determinadas disfunções de pressão arterial e perfil lipídico, aumento dos marcadores inflamatórios, entre outros fatores que podem gerar no organismo o potencial risco cardiovascular[65].

Os países do sul da Europa onde a dieta tradicional é predominantemente a dieta mediterrânea têm as menores taxas de incidência de doença coronariana, apesar de uma alta prevalência de fatores de risco cardiovascular clássicos[66,67].

Uma relação inversa entre a ingestão de azeite de oliva, mortalidade e incidência de doença cardíaca coronária foi relatada nas coortes *European Prospective Investigation into Cancer and Nutrition* (EPIC)[68-71].

No trabalho de Guasch-Ferré *et al* foi relatado que a ingestão de azeite – especificamente extra-virgem – no contexto de uma alimentação com padrão mediterrâneo foi associado a uma redução no risco de DCV e mortalidade em indivíduos idosos com alto risco cardiovascular[72].

Uma meta-análise de 32 estudos de coorte mostrou que o consumo de azeite de oliva estava associado a um risco reduzido de mortalidade por todas as causas, eventos cardiovasculares e acidente vascular cerebral ao comparar o tercil superior ao inferior de consumo[73].

O efeito cardioprotetor dos hábitos alimentares já é bem conhecido e estudado, o estudo de George et al (2019)[74] apresentou diversos estudos epidemiológicos e ensaios clínicos que demonstram o padrão alimentar da dieta mediterrânea atua na função cardioprotetora[75-77], ensaios clínicos e estudos em animais demonstram que o EVOO pode ser um alimento potencialmente protetor na redução das DCV, sendo nos desfechos de pressão arterial, marcadores inflamatórios e perfil lipídico[78-80].

Com relação ao EVOO rico em compostos fenólicos, uma meta-análise de 69 estudos experimentais demonstrou efeitos moderados na redução da pressão arterial sistólica, porém sem efeitos na pressão arterial diastólica. A redução dessa após a ingestão de EVOO foi descrita em pacientes hipertensos e com doenças cardíacas coronárias prévias[81].

A Autoridade Europeia de Segurança Alimentar (EFSA) declarou em 2011 que "o consumo de compostos fenólicos do azeite contribui para a proteção dos lipídios do sangue contra danos oxidativos" em uma dose diária de 5 mg de hidroxitirosol e seus derivados (por exemplo, complexo oleuropeína e tirosol)[82], tal declaração foi decorrente ao estudo "European Study of the Antioxidant Effects of Olive Oil and its Phenolic Compounds on Lipid Oxidation" (EUROLIVE), ensaio clínico chave na pesquisa de compostos fenólicos nos EVOO e a relação à saúde humana, demonstrando então o papel cardioprotetor do hidroxitirosol[83].

O estudo multicêntrico *Prevencion con Dieta Mediterranea* (PREDIMED), realizado na Espanha, demonstrou que após 4,8 anos de observação, houve um menor risco cardiovascular e menor incidência de eventos cardiovasculares no grupo atribuído à dieta mediterrânea com consumo de EVOO[84].

Os marcadores inflamatórios relacionados às doenças cardiovasculares são potenciais preditores de doenças endoteliais[85]. As doenças crônicas possuem potencial elevado na produção e síntese de citocinas pró-inflamatórias como IL-1, TNF-α e ambas atuam na saúde endotelial, aumentando o mecanismo de agregação plaquetária e lipídica nas paredes arteriais, aumentando o potencial de aterogênese, assim causando eventos cardiovasculares futuros[86,87].

Os mecanismos pelos quais os compostos fenólicos do EVOO podem exercer um efeito anti-inflamatório, especificamente nas doenças cardiovasculares, envolvem sua capacidade de: (1) atividade antioxidante; (2) modificação da cascata de sinalização e da rede de transcrição (bloqueio da sinalização e expressão do fator nuclear kappa B); (3) diminuição da adesão de células imunes (linfócitos T e monócitos) ao endotélio; e (4) melhora da disfunção endotelial[88].

Em estudos in vitro, a oleuropeína e o hidroxitirosol demonstraram exercer vários efeitos protetores em um modelo de aterosclerose inibindo a ativação endotelial e a adesão de células endoteliais. Demonstrou-se que a hidroxitirosol aumenta a expressão de genes envolvidos no efluxo de colesterol e, em células endoteliais expostas a estímulos inflamatórios ou com espécies reativas de oxigênio, de enzimas antioxidantes[89,90].

O grupo do estudo de Casas *et al* demonstrou os efeitos da suplementação de uma dieta mediterrânea com EVOO nas concentrações plasmáticas de moléculas inflamatórias e na estabilidade da placa aterosclerótica. Os participantes foram avaliados em três momentos: no início do estudo, após 3 anos e após 5 anos. Em contraste com o grupo controle, houveram reduções significativas em IL-6, IL-8, MCP-1, MIP-1β, IL-1β, IL-5, IL-7, IL-12p70, IL-18, TNF- α e IFN-γ em 3 e 5 anos, em comparação com a linha de base[91].

O consumo de azeite de oliva rico em compostos fenólicos parece modular favoravelmente a inflamação, o que contribui para o desenvolvimento e progressão das doenças cardiovasculares. Ensaios clínicos realizados em indivíduos com risco para o desenvolvimento de doenças cardiovasculares mostram efeitos positivos da ingestão diária de diferentes quantidades de azeite de oliva sobre marcadores inflamatórios. Em humanos, esses efeitos foram observados em nível celular (células imunes) e em marcadores inflamatórios. A suplementação dietética com azeite de oliva está associada a mudanças nos padrões alimentares como um todo, o que pode melhorar o perfil inflamatório dos indivíduos, também é importante considerar que os padrões alimentares, como a dieta mediterrânea também incluem outras fontes de compostos fenólicos através da diversidade alimentar[92].

3 JUSTIFICATIVA

Através do grande consumo de alimentos ultraprocessados, esses podem causar riscos à saúde entre os quais até mesmo mortalidade[93]. Faz-se necessário investigar a relação existente entre o consumo de ultraprocessados e o risco de mortalidade, desde a menor até a maior ingestão desses alimentos e qual seria a contribuição do consumo em tal risco através da realização de uma revisão sistemática. Além disso, a incidência das doenças crônicas não transmissíveis tende a aumentar, sendo considerado mais de 80% de todas as mortes prematuras do mundo sendo causadas por doenças cardiovasculares (DCV), doenças respiratórias, câncer e diabetes. Tendo em vista esse cenário e a pesquisa em alimentos, buscou-se então a proposta de alimentação como forma de proteção aos riscos à saúde, assim foi realizada uma *overview* buscando elucidar as propriedades antioxidantes e a utilização do azeite de oliva[12] como possível protetor na resposta metabólica e nos fatores de risco cardiovasculares.

4 OBJETIVO

4.1 Objetivo Geral

Relacionar dados sobre o consumo de alimentos ultraprocessados como fator de risco de mortalidade e também o consumo de azeite de oliva e sua composição como fator protetor de doenças cardiovasculares e seus fatores de risco.

4.2 Objetivos Específicos

- Realizar uma revisão sistemática relacionando o consumo de alimentos ultraprocessados e o risco de mortalidade.
- Realizar uma overview para analisar as revisões sistemáticas já publicadas nos efeitos cardioprotetores nos fatores de risco cardiovasculares do consumo de azeite de oliva.

5 REFERÊNCIAS

1 - GBD 2017 Diet Collaborators Efeitos sobre a saúde dos riscos alimentares em 195 países, 1990-2017: uma análise sistemática para o Global Burden of Disease Study 2017. Lancet 2019; 393 :1958-72. 10.1016/S0140-6736(19)30041

2 - WHO. Prevention and Control of Noncommunicable Diseases in the European Region: A Progress Report. World Health Organization. Regional Office for Europe; Geneva, Switzerland: 2014.

3 - Lean MEJ, Leslie WS, Barnes AC, Brosnahan N, Thom G, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet Diabetes Endocrinol. 2019 May;7(5):344-355. doi: 10.1016/S2213-8587(19)30068-3.

4 - Schnabel L, Kesse-Guyot E, Allès B, Touvier M, Srour B, Hercberg S, et al. Association Between Ultraprocessed Food Consumption and Risk of Mortality Among Middle-aged Adults in France. JAMA Intern Med. 2019 Feb 11. DOI: 10.1001/jamainternmed.2018.7289.

5 - Askari M, Heshmati J, Shahinfar H, Tripathi N, Daneshzad E. Ultra-processed food and the risk of overweight and obesity: a systematic review and meta-analysis of observational studies. Int J Obes (Lond). 2020 Oct;44(10):2080-2091. doi: 10.1038/s41366-020-00650-z.

6 - Mendonça RD, Lopes AC, Pimenta AM, Gea A, Martinez-Gonzalez MA, Bes-Rastrollo M. Ultra-Processed Food Consumption and the Incidence of Hypertension in a Mediterranean Cohort: The Seguimiento Universidad de Navarra Project. Am J Hypertens. 2017 Apr 1;30(4):358-366. doi: 10.1093/ajh/hpw137.

7 - Martínez Steele E, Juul F, Neri D, Rauber F, Monteiro CA. Dietary share of ultra-processed foods and metabolic syndrome in the US adult population. Prev Med. 2019 Aug;125:40-48. doi: 10.1016/j.ypmed.2019.05.004.

8 - Fiolet T, Srour B, Sellem L, Kesse-Guyot E, Allès B, Méjean C, et al. Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort. BMJ. 2018 Feb 14;360:k322. doi: 10.1136/bmj.k322.

9 – Monteiro CA, Levy RB, Claro RM, Castro IRR, Cannon G. A new classification of foods based on the extent and purpose of their processing. Cad Saude Publica. 2010; 26, 2039–2049.

10 – Brazil. Ministry of Health. Health Care Secretariat. Department of Primary Care. Food guide for the Brazilian population / Ministry of Health, Secretariat of Health Care, Department of Primary Care. - 2. ed., 1. reprint - Brasília: Ministry of Health, 2014.

11 - Juul F, Martinez-Steele E, Parekh N, Monteiro CA, Chang VW. Ultra-processed food consumption and excess weight among US adults. Br J Nutr. 2018 Jul;120(1):90-100. doi: 10.1017/S0007114518001046.

12 - Millman JF, Okamoto S, Teruya T, Uema T, Ikematsu S, Shimabukuro M, et al. Extra-virgin olive oil and the gut-brain axis: influence on gut microbiota, mucosal immunity, and cardiometabolic and cognitive health. Nutr Rev. 2021 Nov 10;79(12):1362-1374. doi: 10.1093/nutrit/nuaa148.

13 - Romani A, Ieri F, Urciuoli S, Noce A, Marrone G, Nediani C, et al. Health Effects of Phenolic Compounds Found in Extra-Virgin Olive Oil, By-Products, and Leaf of Olea europaea L. Nutrients. 2019 Aug 1;11(8):1776. doi: 10.3390/nu11081776.

14 - Pfeiler TM, Egloff B. Personality and eating habits revisited: Associations between the big five, food choices, and Body Mass Index in a representative Australian sample. Appetite. 2020 Jun 1;149:104607. doi: 10.1016/j.appet.2020.104607

15 - Escudero P. Alimentación. Buenos Aires: Hachette;1934.

16 - World Health Organization (WHO). Noncommunicable diseases progress monitor, 2015. Geneva: WHO; 2015

17 - World Health Organization (WHO). Global Strategy on Diet, Physical Activity and Health. Geneva: WHO; 2004. [Eighth plenary meeting, Committee A, third report].

18 - Raptou E, Papastefanou G. An empirical investigation of the impact of smoking on body weight using an endogenous treatment effects model approach: the role of food consumption patterns. Nutr J. 2018 Nov 5;17(1):101. doi: 10.1186/s12937-018-0408-0.

19 - Azadbakht L, Mirmiran P, Esmaillzadeh A, Azizi T, Azizi F. Beneficial effects of a Dietary Approaches to Stop Hypertension eating plan on features of the metabolic syndrome. Diabetes Care. 2005 Dec;28(12):2823-31. doi: 10.2337/diacare.28.12.2823.

20 - Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, et al. Major dietary patterns are related to plasma concentrations of markers of

inflammation and endothelial dysfunction. Am J Clin Nutr. 2004 Oct;80(4):1029-35. doi: 10.1093/ajcn/80.4.1029.

21 - Liu E, McKeown NM, Newby PK, Meigs JB, Vasan RS, Quatromoni PA, et al. Cross-sectional association of dietary patterns with insulin-resistant phenotypes among adults without diabetes in the Framingham Offspring Study. Br J Nutr. 2009 Aug;102(4):576-83. doi: 10.1017/S0007114509220836.

22 - Bouvard V, Loomis D, Guyton KZ, Grosse Y, Ghissassi FE, Benbrahim-Tallaa L, et al. International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of consumption of red and processed meat. Lancet Oncol. 2015 Dec;16(16):1599-600. doi: 10.1016/S1470-2045(15)00444-1.

23 - Castro, IRR. Challenges and perspectives for the promotion of adequate and healthy food in Brazil. Cadernos de Saúde Pública [online]. 2015, v. 31, n. 1. https://doi.org/10.1590/0102-311XPE010115

24 - Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Guia alimentar para a população brasileira / Ministério da Saúde, Secretaria de Atenção à Saúde, Departamento de Atenção Básica. – 2. ed., 1. reimpr. – Brasília : Ministério da Saúde, 2014.

25 - Kuppusamy S, Thavamani P, Megharaj M, Nirola R, Lee YB, Naidu R. Assessment of antioxidant activity, minerals, phenols and flavonoid contents of common plant/tree waste extracts. Industrial Crops and Products, 83, 630-634, 2016. DOI: 10.1016/j.indcrop.2015.12.060

26 - Monteiro CA, Levy RB, Claro RM, Castro IR, Cannon G. A new classification of foods based on the extent and purpose of their processing. Cad Saude Publica. 2010 Nov;26(11):2039-49. doi: 10.1590/s0102-311x2010001100005.

27 - Elizabeth L, Machado P, Zinöcker M, Baker P, Lawrence M. Ultra-Processed Foods and Health Outcomes: A Narrative Review. Nutrientes . 2020; 12 (7): 1955. https://doi.org/10.3390/nu12071955

28 - Monteiro CA, Cannon G. The role of the transnational ultra-processed food industry in the pandemic of obesity and its associated diseases: Problems and solutions. World Nutr. 2019, 10, 89–99.

29 - Chen X, Zhang Z, Yang H, Qiu P, Wang H, Wang F, et al. Consumption of ultra-processed foods and health outcomes: a systematic review of epidemiological studies. Nutr J. 2020 Aug 20;19(1):86. doi: 10.1186/s12937-020-00604-1.

30 - Fiolet T, Srour B, Sellem L, Kesse-Guyot E, Allès B, Méjean C, Deschasaux M, et al. Consumption of ultra-processed foods and cancer risk: Results from NutriNet-Santé prospective cohort. BMJ. 2018;360:k322. doi: 10.1136/bmj.k322.

31 - Suksatan W, Moradi S, Naeini F, Bagheri R, Mohammadi H, Talebi S, et al. Ultra-Processed Food Consumption and Adult Mortality Risk: A Systematic Review and Dose-Response Meta-Analysis of 207,291 Participants. Nutrients. 2021 Dec 30;14(1):174. doi: 10.3390/nu14010174

32 - Martínez Steele E, Baraldi LG, Louzada ML, Moubarac JC, Mozaffarian D, Monteiro CA. Ultra-processed foods and added sugars in the US diet: evidence from a nationally representative cross-sectional study. BMJ Open. 2016 Mar 9;6(3):e009892. doi: 10.1136/bmjopen-2015-009892.

33 - Suksatan W, Moradi S, Naeini F, Bagheri R, Mohammadi H, Talebi S, et al. Ultra-Processed Food Consumption and Adult Mortality Risk: A Systematic Review and Dose-Response Meta-Analysis of 207,291 Participants. Nutrients. 2021 Dec 30;14(1):174. doi: 10.3390/nu14010174.

34 - Rico-Campà A, Martínez-González MA, Alvarez-Alvarez I, Mendonça RD, de la Fuente-Arrillaga C, Gómez-Donoso C, et al. Association between consumption of ultra-processed foods and all cause mortality: SUN prospective cohort study. BMJ. 2019 May 29;365:l1949. doi: 10.1136/bmj.l1949..

35 - World Health Organization Noncommunicable diseases. http://www.who.int/mediacentre/factsheets/fs355/en/. Accessed September 24, 2022.

36 - Julia C, Martinez L, Allès B, Touvier M, Hercberg S, Méjean C, et al. Contribution of ultra-processed foods in the diet of adults from the French NutriNet-Santé study. Public Health Nutr. 2018 Jan;21(1):27-37. doi: 10.1017/S1368980017001367.

37 - Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 380: 2224-2260. doi: 10.1016 / S0140-6736 (12) 61766-8.

38 - Kelly B, Jacoby E. Public Health Nutrition special issue on ultra-processed foods. Public Health Nutr. Jan;21(1) (2018):1-4. doi: 10.1017/S1368980017002853

39 - Gökçebağ M., Dıraman H., Özdemir D. Classification of Turkish Monocultivar (Ayvalık and Memecik cv.) Virgin Olive Oils from north and south zones of Aegean

region based on their triacyglycerol profiles. J. Am. Oil Chem. Soc. 2013;90:1661–1671. doi: 10.1007/s11746-013-2308-y.
40 - Fernández AG, Adams MR, Fernández-Díez M. Table Olives: Production and Processing. Springer; Berlin, Germany: 1997.
41 - Gorzynik-Debicka M, Przychodzen P, Cappello F, Kuban-Jankowska A, Marino Gammazza A, Knap N, et al. Potential Health Benefits of Olive Oil and Plant Polyphenols. Int J Mol Sci. 2018 Feb 28;19(3):686. doi: 10.3390/ijms19030686.
42 - Kamm W, Dionisi F, Hischenhuber C, Engel KH. Authenticity assessment of fats and oils. Food Rev. Int. 2001;17:249–290. doi: 10.1081/FRI-100104702.
43 - Kalogeropoulos N., Tsimidou MZ Antioxidantes em azeites virgens gregos. Antioxidantes. 2014; 3:387-413. doi: 10.3390/antiox3020387
44 - Millman JF, Okamoto S, Teruya T, Uema T, Ikematsu S, et al. Extra-virgin olive oil and the gut-brain axis: influence on gut microbiota, mucosal immunity, and cardiometabolic and cognitive health. Nutr Rev. 2021 Nov 10;79(12):1362-1374. doi: 10.1093/nutrit/nuaa148.
45 – Piroddi M, Albini A, Fabiani R, Giovannelli L, Luceri C, Natella F, et al. Nutrigenomics of extra-virgin olive oil: A review. Biofactors. 2017 Jan 2;43(1):17-41. doi: 10.1002/biof.1318.
46 - Boskou D. Olive Oil: Minorconstituents and Health. CRC Press; Boca Raton, FL, USA: 2009. Other important minor constituents; pp. 45–54.
47 - Luchetti F. Importance and future of olive oil in the world market—An introduction to olive oil. Eur. J. Lipid Sci. Technol. 2002;104:559–563. doi: 10.1002/1438-9312(200210)104:9/10<559::AID-EJLT559>3.0.CO;2-Q.
48 - Ramirez-Tortosa MC, Granados S, Quiles JL. Chemical composition, types and characteristics of olive oil. Olive Oil Health. 2006:45–61. doi: 10.1079/9781845930684.0045.
49 - Bravo L. Polyphenols: Chemistry, dietary sources, metabolism, and nutritional significance. Nutr. Rev. 1998;56:317–333. doi: 10.1111/j.1753-4887.1998.tb01670.x.
50 - Del Rio D, Rodriguez-Mateos A, Spencer JP, Tognolini M, Borges G, Crozier A. Dietary (poly) phenolics in human health: Structures, bioavailability, and evidence of protective effects against chronic diseases. Antioxid. Redox Signal. 2013;18:1818–1892. doi: 10.1089/ars.2012.4581.

51 - Cicerale S, Conlan XA, Sinclair AJ, Keast RS. Chemistry and health of olive oil phenolics. Crit. Rev. Food Sci. Nutr. 2008;49:218–236. doi: 10.1080/10408390701856223.

52 - Cicerale S, Lucas L, Keast R. Biological activities of phenolic compounds present in virgin olive oil. Int. J. Mol. Sci. 2010;11:458–479. doi: 10.3390/ijms11020458

53 - Boss A, Bishop KS, Marlow G, Barnett MP, Ferguson LR. Evidence to support the Anti-Cancer effect of olive leaf extract and future Directions. Nutrients. 2016;8:513. doi: 10.3390/nu8080513.

54 - Ellis LZ, Liu W, Luo Y, Okamoto M, Qu D, Dunn JH, et al. Green tea polyphenol epigallocatechin-3-gallate suppresses melanoma growth by inhibiting inflammasome and IL-1β secretion. Biochem. Biophys. Res. Commun. 2011;414:551–556. doi: 10.1016/j.bbrc.2011.09.115.

55 - Panickar KS, Anderson RA. Effect of polyphenols on oxidative stress and mitochondrial dysfunction in neuronal death and brain edema in cerebral ischemia. Int. J. Mol. Sci. 2011;12:8181–8207. doi: 10.3390/ijms12118181.

56 - Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, et al. The diet and 15-year death rate in the seven countries study. Am J Epidemiol. 1986 Dec;124(6):903-15. doi: 10.1093/oxfordjournals.aje.a114480. PMID: 3776973.

57 - Mazzocchi A, Leone L, Agostoni C, Pali-Schöll I. The Secrets of the Mediterranean Diet. Does [Only] Olive Oil Matter?. Nutrients. 2019;11(12):2941. Published 2019 Dec 3. doi:10.3390/nu11122941

58 – Widmer RJ, Flammer AJ, Lerman LO, Lerman A. The Mediterranean diet, its components, and cardiovascular disease. Am J Med. 2015;128(3):229-238. doi:10.1016/j.amjmed.2014.10.014

59 - Davis C, Bryan J, Hodgson J, Murphy K. Definition of the Mediterranean Diet; a Literature Review. Nutrients. 2015 Nov 5;7(11):9139-53. doi: 10.3390/nu7115459.

60 - Hamdi HK, Tavis JH, Castellon R. Methods for Inhibiting Angiogenesis. WO/2002/094193. Patente. 28 de novembro de 2002

61 - Cumaoğlu A, Ari N, Kartal M, Karasu Ç. Polyphenolic extracts from Olea europea L. protect against cytokine-induced β-cell damage through maintenance of redox homeostasis. Rejuv. Res. 2011;14:325–334. doi: 10.1089/rej.2010.1111

62 - Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics-2013 update: A report from the American Heart Association. Circulation. 2013;127:e6–245

63 - Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004 Sep 11-17;364(9438):937-52. doi: 10.1016/S0140-6736(04)17018-9.64

64 – Organização Pan-Americana de Saúde. HEARTS nas Américas. https://www.paho.org/pt/hearts-nas-americas Acesso em dezembro de 2022.

65 – Ros E, Martínez-González MA, Estruch R, Salas-Salvadó J, Fitó M, et al. Mediterranean diet and cardiovascular health: Teachings of the PREDIMED study. Adv Nutr. 2014 May 14;5(3):330S-6S. doi: 10.3945/an.113.005389.

66 - Tunstall-Pedoe H, Kuulasmaa K, Mahonen M, Tolonen H, Ruokokoski E, Amouyel P. Contribution of Trends in Survival and Coronary-Event Rates to Changes in Coronary Heart Disease Mortality: 10-Year Results from 37 WHO MONICA Project Populations. Monitoring Trends and Determinants in Cardiovascular Disease. Lancet. 1999;353:1547–1557. doi: 10.1016/S0140-6736(99)04021-0.

67 - McGovern PG, Pankow JS, Shahar E, Doliszny KM, Folsom AR, Blackburn H, et al. Recent Trends in Acute Coronary Heart Disease—Mortality, Morbidity, Medical Care, and Risk Factors. the Minnesota Heart Survey Investigators. N. Engl. J. Med. 1996;334:884–890. doi: 10.1056/NEJM199604043341403.

68 - Buckland G, Travier N, Cottet V, Gonzalez CA, Lujan-Barroso L, Agudo A, et al. Adherence to the Mediterranean Diet and Risk of Breast Cancer in the European Prospective Investigation into Cancer and Nutrition Cohort Study. Int. J. Cancer. 2013;132:2918–2927. doi: 10.1002/ijc.27958.

69 - Buckland G, Mayen AL, Agudo A, Travier N, Navarro C, Huerta JM, et al. Olive Oil Intake and Mortality within the Spanish Population (EPIC-Spain) Am. J. Clin. Nutr. 2012;96:142–149. doi: 10.3945/ajcn.111.024216.

70 - Psaltopoulou T, Kosti RI, Haidopoulos D, Dimopoulos M, Panagiotakos DB. Olive Oil Intake is Inversely Related to Cancer Prevalence: A Systematic Review and a Meta-Analysis of 13,800 Patients and 23,340 Controls in 19 Observational Studies. Lipids Health. Dis. 2011;10:127. doi: 10.1186/1476-511X-10-127.

71 - Bendinelli B, Masala G, Saieva C, Salvini S, Calonico C, Sacerdote C, et al. Fruit, Vegetables, and Olive Oil and Risk of Coronary Heart Disease in Italian Women: The EPICOR Study. Am. J. Clin. Nutr. 2011;93:275–283. doi: 10.3945/ajcn.110.000521

72 - Guasch-Ferre M, Hu FB, Martinez-Gonzalez MA, Fito M, Bullo M, Estruch R, et al. Olive Oil Intake and Risk of Cardiovascular Disease and Mortality in the PREDIMED Study. BMC Med. 2014;12:78. doi: 10.1186/1741-7015-12-78

73 - Schwingshackl L, Hoffmann G. Monounsaturated Fatty Acids, Olive Oil and Health Status: A Systematic Review and Meta-Analysis of Cohort Studies. Lipids Health. Dis. 2014;13:154. doi: 10.1186/1476-511X-13-154.

74 - George ES, Marshall S, Mayr HL, Trakman GL, Tatucu-Babet AO, Lassemillante AM, et al. The effect of high-polyphenol extra virgin olive oil on cardiovascular risk factors: A systematic review and meta-analysis. Crit Rev Food Sci Nutr. 2019;59(17):2772-2795. doi: 10.1080/10408398.2018.1470491.

75 - de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation. 1999 Feb 16;99(6):779-85. doi: 10.1161/01.cir.99.6.779.

76 - Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Ruiz-Gutiérrez V, Covas MI, et al. PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. Ann Intern Med. 2006 Jul 4;145(1):1-11. doi: 10.7326/0003-4819-145-1-200607040-00004.

77 - Itsiopoulos C, Brazionis L, Kaimakamis M, Cameron M, Best JD, O'Dea K, et al. Can the Mediterranean diet lower HbA1c in type 2 diabetes? Results from a randomized cross-over study. Nutr Metab Cardiovasc Dis. 2011 Sep;21(9):740-7. doi: 10.1016/j.numecd.2010.03.005.

78 – Farràs M, Castañer O, Martín-Peláez S, Hernáez Á, Schröder H, Subirana I, et al. Complementary phenol-enriched olive oil improves HDL characteristics in hypercholesterolemic subjects. A randomized, double-blind, crossover, controlled trial. The VOHF study. Mol Nutr Food Res. 2015 Sep;59(9):1758-70. doi: 10.1002/mnfr.201500030.

79 - Beauchamp GK, Keast RS, Morel D, Lin J, Pika J, Han Q, et al. Phytochemistry: ibuprofen-like activity in extra-virgin olive oil. Nature. 2005 Sep 1;437(7055):45-6. doi: 10.1038/437045a. PMID: 16136122.

80 - Perona JS, Cañizares J, Montero E, Sánchez-Domínguez JM, Catalá A, Ruiz-Gutiérrez V. Virgin olive oil reduces blood pressure in hypertensive elderly subjects. Clin Nutr. 2004 Oct;23(5):1113-21. doi: 10.1016/j.clnu.2004.02.004.

81 - Fito M, Cladellas M, de la Torre R, Marti J, Alcantara M, Pujadas-Bastardes M, et al. Antioxidant Effect of Virgin Olive Oil in Patients with Stable Coronary Heart Disease: A Randomized, Crossover, Controlled, Clinical Trial. Atherosclerosis. 2005;181:149–158. doi: 10.1016/j.atherosclerosis.2004.12.036.

82 - EFSA Panel on Dietetic Products Nutrition and Allergies (NDA) Scientific Opinion on the substantiation of health claims related to polyphenols in olive and protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865), maintenance of normal blood HDL-cholesterol concentrations (ID 1639), maintenance of normal blood pressure (ID 3781), “anti-inflammatory properties” (ID 1882), “contributes to the upper respiratory tract health” (ID 3468), “can help to maintain a normal function of gastrointestinal tract” (3779), and “contributes to body defences against external agents” (ID 3467) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal. 2011;9(4):p. 2033. doi: 10.2903/j.efsa.2011.2033.

83 - Cicero AF, Nascetti S, López-Sabater MC, Elosua R, Salonen JT, Nyyssönen K, et al. Changes in LDL fatty acid composition as a response to olive oil treatment are inversely related to lipid oxidative damage: The EUROLIVE study. J. Am. Coll. Nutr. 2008;27:314–320. doi: 10.1080/07315724.2008.10719705.

84 - Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N. Engl. J. Med. 2013;368:1279–1290. doi: 10.1056/NEJMoa1200303.

85 - Inaba Y, Chen JA, Bergmann SR. Prediction of future cardiovascular outcomes by flow-mediated vasodilatation of brachial artery: A meta-analysis. Int. J. Cardiovasc. Imaging 2010, 26, 631–640.

86 - Cook-Mills JM, Marchese ME, Abdala-Valencia H. Vascular cell adhesion molecule-1 expression and signaling during disease: Regulation by reactive oxygen species and antioxidants. Antioxid. Redox Signal. 2011, 15, 1607–1638.

87 – Inaba Y, Chen, JA, Bergmann SR. Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: a meta-analysis. Atherosclerosis. 2012 Jan;220(1):128-33. doi: 10.1016/j.atherosclerosis.2011.06.044.

88 - Tangney CC, Rasmussen HE. Polyphenols, inflammation, and cardiovascular disease. Curr. Atheroscler. Rep. 2013;15:324–340. doi: 10.1007/s11883-013-0324-x.

89 - Dell'Agli M., Fagnani R., Mitro N., Scurati S., Masciadri M., Mussoni L., Galli G.V., Bosisio E., Crestani M., De Fabiani E. Minor components of olive oil modulate proatherogenic adhesion molecules involved in endothelial activation. J. Agric. Food Chem. 2006;54:3259–3264. doi: 10.1021/jf0529161

90 - Venturi F, Sanmartin C, Taglieri I, Nari A, Andrich G, Terzuoli E, et al. Development of phenol-enriched olive oil with phenolic compounds extracted from wastewater produced by physical refining. Nutrients. 2017;9:916. doi: 10.3390/nu9080916.

91 - Casas R, Urpi-Sardà M, Sacanella E, Arranz S, Corella D, Castañer O, et al. Anti-Inflammatory Effects of the Mediterranean Diet in the Early and Late Stages of Atheroma Plaque Development. Med. Inflamm. 2017;2017:1–12. doi: 10.1155/2017/3674390.

92 - Souza PAL, Marcadenti A, Portal VL. Effects of Olive Oil Phenolic Compounds on Inflammation in the Prevention and Treatment of Coronary Artery Disease. Nutrients. 2017 Sep 30;9(10):1087. doi: 10.3390/nu9101087.

93 - Suksatan W, Moradi S, Naeini F, Bagheri R, Mohammadi H, Talebi S, et al. Ultra-Processed Food Consumption and Adult Mortality Risk: A Systematic Review and Dose-Response Meta-Analysis of 207,291 Participants. Nutrients. 2021 Dec 30;14(1):174. doi: 10.3390/nu14010174.

6 ARTIGOS

6.1 Artigo 1

Este artigo foi submetido para a revista Revista da Associação Brasileira de Nutrição (RASBRAN, ISSN 2357-7894, com Estrato Qualis C) na data de 28 de novembro de 2021, sendo aceito para publicação em julho de 2022, passando por edições para publicação.

Consumo de alimentos ultraprocessados e o risco de mortalidade: uma revisão sistemática

Ultra-processed food consumption and the risk of mortality: A Systematic Review

Kathleen Kruger Peres1, Rafaella Câmara Rocha Menezes2, Anna Caroline Cristofoli Bertoletti1, Isabella Rosa da Mata1, Simone Morelo Dal Bosco3

1 Graduate Program in Nutrition Sciences, Universidade Federal de Ciências da Saúde de Porto Alegre, Brazil.
2 Nutrition Department, Universidade Federal do Rio Grande do Sul, Brazil.
3 Nutrition Department, Universidade Federal de Ciências da Saúde de Porto Alegre, Brazil.

Kathleen Krüger Peres - ORCID: 0000-0001-7755-5758.
Contribution: Lead author, article writing, bias review.
No conflicts of interest.
Rafaella Câmara Rocha Menezes - ORCID: 0000-0003-3176-3716
Contribution: Initial review steps and article translation.
No conflicts of interest.
Anna Caroline Cristofoli Bertoletti - ORCID: 0000-0003-0702-4905
Contribution: Bias review.
No conflicts of interest.
Isabella Rosa da Mata - ORCID: 0000-0001-7884-9539
Contribution: Initial review steps.
No conflicts of interest.
Simone Morelo Dal Bosco - ORCID: 0000-0002-2388-0915

Contribution: Initial review steps, bias review and approved the final version submitted for publication.
No conflicts of interest.

ABSTRACT

Introduction and Objectives: Ultra-processed foods are determined by the level of processing. There has been a relationship between their consumption and several risk factors for diseases related to these foods, such as cardiovascular disease. These factors can corroborate the illness and increase the risk of mortality of the adult population. The objective of this systematic review was to verify the contribution of the consumption of ultra-processed foods to the risk of mortality. Methods: Through PubMed, Scopus and Web of Science, scientific databases, studies that examine the relationship between the consumption of ultra-processed foods and the risk of mortality up to February 2021 were systematically researched. Results and Conclusion: Evidence analysis was performed using robust tools to assess the risk of bias and methodological quality. A total of five studies were included. The consumption of ultra-processed foods was associated with a higher risk of mortality from all causes, proportional to their consumption (in the largest quartiles of consumption, greater risks were found).
Keywords: Ultra-Processed Foods, Food Consumption, Mortality, Systematic Reviews.

RESUMO

Introdução e objetivos: Alimentos ultraprocessados são determinados pelo nível de processamento. Existe uma relação entre seu consumo e diversos fatores de risco para doenças relacionadas a esses alimentos, como as cardiovasculares. Esses fatores podem corroborar o adoecimento e aumentar o risco de mortalidade da população adulta. O objetivo desta revisão sistemática foi verificar a contribuição do consumo de alimentos ultraprocessados e o risco de mortalidade. Métodos: Por meio do PubMed, Scopus e Web of Science, foram pesquisadas sistematicamente em tais bases de dados científicas, estudos que examinam a relação entre o consumo de alimentos ultraprocessados e o risco de mortalidade até fevereiro de 2021. Resultados e Conclusão: A análise de evidências foi realizada por meio de ferramentas robustas para avaliar o risco de viés e a qualidade metodológica. Um total de cinco estudos foram incluídos. O consumo de alimentos ultraprocessados foi associado a um maior risco de mortalidade por todas as causas, proporcional ao seu consumo (nos maiores quartis de consumo, foram encontrados maiores riscos).
Palavras-chave: Alimentos Ultraprocessados, Consumo de Alimentos, Mortalidade, Revisão Sistemática.

INTRODUCTION

Ultra-processed foods (UPFs) are determined through the level of processing, accordingly the NOVA classification, the UPFs contain predominantly industrial substances and little or no whole foods, being produced by large industries, in which the processing steps and techniques occur by the addition of various ingredients, such as: salt, sugar, oils, fats and in addition to substances whose use is only at the industrial level. This food category includes sweets, sweetened drinks with or without artificial sweeteners, soft drinks powders, sausages and other products derived from meat and animal fat, frozen products ready for heating, dehydrated products (such as cake mixes, powdered soups), Instant “noodles”and “seasoning” ready), and a plethora of new products that hit the market every year[1,2].

During the dissemination of these products in society, the relationship between their consumption and human health was perceived, in addition to the relationship with the quality of the diet, associating it to several risk factors for diseases related to food, whose contribution of food consumption is a determining factor for presence or not of these comorbidities, disorders or conditions[3,4]. The impact of ultra-processed foods on various lifestyle-related diseases has already been studied, including diabetes mellitus, metabolic syndrome, cardiovascular diseases (CVD), dyslipidemia, hypertension and cancer[5,6,7,8]. However, there are still gaps as to what the effective impact of the consumption of ultra-processed foods and their composition can have on human health, as well as the need to consider that its use is widely disseminated in the routine, due to its impression of practicality, being often allies in the lives of many who resort to these foods because they are often referred to as "ready to eat" or "ready to warm up" [9]. Preparations created by industrial formulations made from substances derived from food and additives, rich in added sugars, salt, energy density of the diet, together with trans and saturated fats, containing small amounts of fiber, protein, micronutrients, and phytochemicals may indeed be responsible due to several current comorbidities, which contribute to the population's illness and health problems[10].

This disease can generate an increased risk of mortality in the adult population. Cross-sectional studies showed a greater chance of obesity with greater consumption of ultra-processed foods[11-13], however it is known that cross-sectional studies do not have the potential to define the incidence of mortality in the population that consumes ultra-processed foods. Then, cohort studies were carried out to seek a possible association between the consumption of these foods and the risks of mortality, since their damage to human health is already known in the literature[14-18]. This systematic review aims to verify the consumption of ultra-processed foods in the risk of mortality.

METHODS

Protocol and registration

The systematic review protocol was reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P) protocol19. The protocol was registered at the international prospective register of systematic reviews (PROSPERO) database under the registration number CRD42020205382.

Search strategy and eligibility criteria

To identify potentially relevant studies to the present review, a systematic literature search of databases (PubMed, Scopus, and Web Of Science) was conducted through February 2021, following terms MeSH (1) "ultra-processed food", researched in combination with (2) “food consumption”, for more sensitive research that would encompass all the articles needed for the review. No restrictions or filters were applied.

Our research only included observational articles with human. Inclusion criteria were: (1) Studies that evaluate the consumption of ultra-processed products; (2) Mortality outcome; (3) the articles were published as full papers; (4) Studies in adults (<18 years) and previously healthy.

The exclusion criteria were as follows: (1) In vitro studies; (2) animal model; (3) Studies with children, adolescents, pregnant women or infants; (4) Case reports, meta-analyzes, editorials, narrative reviews.

Study selection

The articles were screening in two phases. Firstly, duplicate articles and triplicates articles were removed. In the first phase, two reviewers independently analyzed titles and abstracts in the electronic database and selected articles to identify potentially eligible articles. In the second phase, two reviewers independently analyzed and performed the full reading of the articles selected in the first phase, excluding all the articles that did not meet the eligibility criteria. At all stages, a third reviewer was consulted in the case of any concerns or disagreements between the other investigators, being, all disputes, resolved by consensus. At the end of the process, five studies were collectively included in the analysis.

Data extraction

Data extraction was completed independently by three authors. The extraction was performed required according to the PRISMA[19] statement for reporting systematic, was reconciled, and recorded on a purpose-designed Microsoft Excel® spreadsheet. The data from the articles were extracted: article title, study design, reference, sample size, aim study, population, exposure, control, year of publication, outcome, main findings, and limitation of the included studies. Constant meetings were held to maintain the standard of analysis.

Risk of bias assessment and quality of evidence

The Newcastle-Ottawa Scale (NOS)[20] tool is recommended for observational studies for observational studies[20]. The tool was used to assess the risk of bias and methodological quality of the cohort articles in this review, examining the following domains: selection, comparability and exposure.

In the selection domain, the representativeness of the exposed cohort is evaluated, selection of the unexposed cohort, verification of the exposure and demonstration that the result of interest was not present at the beginning of the study. For this reason, we consider the cohort that had an adult population and studies with initial data, prior to the study, of comorbidities that could interfere with mortality, in addition to the use of validated tools to verify exposure.

In comparability the measurement would be a comparison of cohorts based on the project or analysis and the score was used when considering comorbidities to avoid potential bias and the consumption of ultra-processed by the sample.

In the exhibition, the tool uses the outcome evaluation, adequate time between the beginning of the cohort and the possible outcome and adequacy of the monitoring of the cohorts. With a higher score when the tools for assessing the frequency of food consumption were carried out by trained professionals, validated, and used other methods for analyzing the outcome (electronic medical records, biochemical assessments), the work should mention the cohort time and the number of participants lost while driving.

The application of the tool was carried out in duplicate by two independent evaluators and the discrepancies were resolved by a third evaluator, and other doubts were resolved in a scientific meeting of the research. All articles remained in this review because they did not demonstrate low quality or serious risk of bias in their conduct.

RESULTS

There were 1288 potentially relevant studies of the electronic research results identified in the first survey, (259 from PubMed, 950 from Scopus and 79 from Web of Science). After removing duplicates and triplicates, there were 1080 records for reading the title and sorting the abstracts. When updating the database with date filter 2020 until 2021, as the first survey had been carried out without filters in the year 2020, there were 350 potentially relevant studies of the electronic research results identified, (140 from PubMed, 167 from Scopus and

43 from Web of Science). After removing duplicates and triplicates, there were 203 records for reading the title and sorting the abstracts.

Of these, 7 articles were read in their entirety. After excluding 2 articles that did not meet the criteria for inclusion, 5 studies were included (14,15,16,17,18). A flow chart detailing the identification process, screening, eligibility and inclusion of studies is shown in Figure 1.

Study characteristics

As shown in Table 1, the main characteristics of the studies were summarized in the parameters established collectively by the authors: authors, place and year of publication, cohort follow-up time, exposure assessment, outcome, data measurement, objectives, and main findings. The studies are listed in Table 1 according to the year of publication, from the oldest to the most recent.

All articles selected for this review were observational cohort studies.

The samples of the five articles totaled 118,652 individuals, and a follow-up of 64 years. The sample size ranged from 12,94816 to 44,55115 participants, with a minimum age of 18 years or older[14-18]. The form used to measure food consumption of ultra-processed foods was Food Frequency Questionnaires[14,16,18] and 24-hour Food Recalls in sequential form[15] or the use of both[17]. The five included studies were published between 2019 and 2021, all in English. The studies were carried out in the following countries: Spain (Rico-Campà A et al and Blanco-Rojo et al), France (Schnabel L et al), United States (Kim et al) and Italy (Bonaccio M et al).

Bias risk assessment

Most of the studies included in this review had a low risk of bias, with few concerns for most items, as shown in Table 2. Two studies showed a low risk of bias[14,18] while the others scored between 7 and 6 stars[15-17] raised some concerns in the domains. Schnabel et al had a higher risk of potential biases regarding the selection domain, since their sample was obtained through volunteering by the population, in addition to the important data that would be about previous diseases and dietary records were self-reported, increasing the potential bias of underreporting[15]. Self-reported dietary data were considered potential biases and found in the work of Schnabel et al[15]. No study scored two stars in the comparability domain, due to the purpose of the domain, in which the reduction of biases that could result in mortality outcomes, such as the presence of diseases that are potential mortality risks were assessed only at the first moment of the study and not reassessed during the follow-up of the cohorts[14-18]. The works by Kim et al and Blanco-Rojo et al did not present data on the number of individuals lost during the follow-up of the cohort, and for this reason they scored only with two stars in the exposure domain[16,17] Table 2.

Consumption of Ultra-processed Products and Mortality for All Causes

The cohorts evaluated in this review, the risk of mortality from all causes included all the causes-deaths of the population, ascertained through reports from family members or from the register of the country of origin of the cohort. In general, causes of mortality were recorded, such as cardiovascular, cancer, cerebrovascular diseases, as well as unknown causes.

In the work of Rico-Campà et al 335 deaths occurred during the cohort of 19899 participants.

The consumption of ultra-processed foods was associated with the risk of mortality from all causes when in the highest quartile of these foods, obtaining a risk ratio (HR) of 1.62 (p = 0.05, 95% CI). An additional analysis of consumption for each additional portion the relative risk of mortality from all causes increased relatively 18% (adjusted HR of 1.18; p = 0.02). For the Cox model adjustments, the HR of the highest UPF consumption was 1.44 (p = 0.023). Adjustments for potential residual confounders, the association between UPF consumption and risk and mortality increased the risk ratio to 1.89[14].

During the follow-up of the Schnabel et al cohort, 602 deaths (1.4%) occurred, including 219 deaths from cancer and 34 from CVD. After adjusting for variables, the consumption of ultra-processed foods showed a risk ratio of 1.14 (95% CI, p = 0.008). When the cases of death in the first two years of study, mortality from cardiovascular diseases and cancer were excluded, the statistical power was reduced, and no significant statistic was found between the association of ultra-processed consumption and mortality[15].

Blanco-Rojo et al demonstrated that the increase in the intake of ultra-processed foods was associated with higher mortality after 7.7 years of follow-up of the cohort, in which 440 deaths of 11,898 individuals were incidents. Participants who were classified in the highest consumption quartile obtained a higher HR of mortality compared to the lowest quartiles, for the adjusted model 4 (the intake of ultra-processed foods contributed more than 33% of the total energy intake) to HR for mortality obtained a statistical value of 1.44 (95% CI, p = 0.03), whereas when analyzed in relation to the consumption of grams per day per kg of weight, the HR was 1.46 (95% CI, p = 0, 03). In view of the isocaloric substitution of these foods, when quartile 4 was analyzed, it only obtained a statistically significant result when 8.2% of the consumption of ultra-processed foods was replaced with minimally processed or fresh foods (p for non-linearity = 0.04)[16].

Kim et al contemplated a sample number of n = 18,779 and during the average follow-up of 19 years 2,451 deaths from all causes occurred, 648 deaths were due to cardiovascular diseases. The highest quartile of frequency of ingestion of ultra-processed foods generated a 31% higher risk of mortality from all causes, with Cox's adjustments for model 2 (HR 1.31; 95% CI; p = 0.001), however, the analysis of adjusted models was independent for the results of the highest quartile of UPF consumption, which demonstrated higher HR for mortality, all values being statistically significant when compared with the lowest quartiles. In addition, participants in the highest quartile had significantly higher intake of total energy, total fat, saturated fat, monounsaturated fat and added sugar, and lower protein intake (p <0.001 for all comparisons)[17].

Ultra-processed consumption and the stratified mortality analysis

Mortality when assessed in a stratified way was presented by two articles included in the present review.

The results by Kim et al did not demonstrate a statistically significant relationship regarding the risk of mortality from cardiovascular diseases when associated with the consumption of UPFs for the adjustment models and quartiles of consumption (p> 0.05)[17].

The Bonaccio et al cohort, on the other hand, assessed the risk of mortality during the mean follow-up of 8.2 years, with 1216 deaths from all causes, 439 from cardiovascular diseases, 255 from cerebrovascular diseases, 477 from cancer and 300 from other causes, in a sample of 22,475 individuals. Mortality from all causes (n = 1216) when adjusted to the Cox models showed higher HR in the highest consumption quartile (HR 1.28; 1.32; 1.26; respectively to the adjusted models), similar results were found when stratified analysis for mortality from: cardiovascular, cerebrovascular diseases and other causes. The consumption of ultra-processed products, when associated with cancer mortality, did not show significant results to the association, regardless of the adjusted models[18].

DISCUSSION

Bearing in mind that all the studies included[14-18] in this systematic review presented the classification of UPF by the NOVA category of foods, this categorization is determined through the composition of the foods, indicating levels of industrial processing of these: fresh or minimally processed foods; processed culinary ingredients; processed foods with salt, sugar or oil and the UPFs containing predominantly industrial substances and little or no complete food[1].

The nutritional composition of ultra-processed foods and the industrial processes to which they have been subjected, such as the use of contaminants and food additives, can potentially increase the consequences for human health[21-23].

The randomized study by Hall et al. reinforces that the intake of UPFs can cause factors harmful to human health, since it presented a higher intake of energy and carbohydrates in the group where the diet was predominantly of UPFs, in addition, there were changes in weight that were correlated with the intake of energy (p <0.0001), participants who gained weight (0.9 ± 0.3 kg; p = 0.009) were consuming the ultra-processed diet and losing weight during the unprocessed diet (0.9 ± 0.3 kg ; p = 0.007)[24].

Gibney et al brought an important counterpoint in his work when he mentions the NOVA classification and its wide range of interpretations, since it can be very imprecise and incomplete to form an adequate basis for making diet recommendations[25,26]. In addition, there are several attributes of these foods that make them more accessible and practical for consumption, being they the cost, the long useful life, they are relatively safe from the microbiological point of view and their high convenience, as they are often ready for eat or ready to warm up[27].

Consumption of Ultra-processed Products and Mortality

In the work by Rico-Campá et al, the risk of mortality from all causes was assessed according to the daily consumption of ultra-processed foods, the significant findings represented the consumption of> 4 servings of ultra-processed foods associated with the mortality risk of 62% higher than when consumed in fewer servings. In addition, with each additional portion of consumption, an 18% increase in mortality risk was found[14]. Bearing in mind that the consumption and feeding of these foods entails nutritional and health risks, the work of the GBD 2017 DIET COLABORATORS10 group showed that, in 2017, 11 million deaths (95% CI) were associated with diet and decreased quality of life. life, and 3 million deaths associated with cardiovascular diseases, it is worth mentioning that ultra-processed foods are rich in sodium.

During the follow-up of the Schnabel et al cohort, 602 deaths were recorded, among them 219 from cancer and 34 from cardiovascular diseases[15], considering these causes is related to data from the World Health Organization in the year 2021[25], in which 71% of causes of death worldwide were due to cardiovascular diseases, cancer and diabetes mellitus[28], in addition, the data show the increased risk of death associated with chronic non-communicable diseases and the diet. When the prevalent cardiovascular diseases and cancer cases were excluded in the research by Schnabel et al, the statistical power was reduced and no significant value was found[15], corroborating the idea that the chronic non-communicable diseases so prevalent are related to the quality of the diet, as well as in the nutritional profile of those who consume them[29].

In view of the quality of the diet, the study Kim et al analyzed that the consumption of ultra-processed foods when higher, presented a lower quality index for the diet using the NRF 9.3 and HEI-2000 tools, with statistically significant results of p <0.01 and p = 0.01, respectively. In their analysis, the consumption of ultra-processed products and the risk of mortality from all causes showed results like other studies, with significant measures for the Cox adjustments of model 2 when in the largest consumption quartile, the relative risk of 31%

(HR 1, 31; 95% CI; p = 0.001). In the evaluation of mortality from cardiovascular diseases, no result was statistically significant[17].

The research by Bonaccio et al also presented a stratified analysis of the risk of mortality, such as mortality from CVD, cancer, cerebrovascular diseases, and other causes. when the risk of mortality from CVD associated with the consumption of ultra-processed foods was evaluated, it presented HR from 1.5 to 1.58, adjusted to Cox's models, there was no presentation of p value[18], the values disagree with the study by Kim et al, as it was demonstrated lower HR values (1.04; 1.10; 1.13) and did not obtain statistical significance. In the analysis of mortality data when stratified, no study in the present review showed statistical significance.

Blanco-Rojo et al in their cohort study, demonstrated that participants whose consumption had the highest level of quartiles obtained a risk ratio of 44% (HR 1.44; 95% CI; p = 0.03), the highest rate of mortality from all causes than the others, which in fact reinforces the values found in the studies included in the review[16]. Mortality data may be associated with increased changes in eating habits, added to the increased incidence of chronic diseases at younger ages, as shown by the study by Lin et al[30], in addition, there is a prospect of increased consumption of these foods by the younger population[31], making the analysis of the risks of this consumption to human health essential. The meta-analysis study by Pagliai et al verified such associations, in addition to reaffirming that mortality from all causes is associated with the consumption of ultra-processed foods, which is statistically significant at a risk ratio of 1.25 (p <0.00001; I2% 2)[32].

Limitations

This systematic review has limitations inherent to the studies included. The included observational cohort studies should be analyzed as measurement potentials and biases, however, they have been minimized by the sensitivity analysis in some articles. Another bias is in relation to the instruments of investigation of food consumption, whether they are food frequency questionnaires or 24-hour reminders, which may be interfered with the interviewee's own memory. In addition, most of the cohorts in the present review obtained the answers to the questionnaires and other variables only at the baseline, making no new assessments during the follow-up, which are also potential limitations for data analysis.

The use of only two descriptors for the manual search of articles may be cause for doubts in relation to the methodology carried out in this review, however we reiterate that this proposal was determined through the construction of a database whose use will be for other systematic reviews, and, in addition furthermore, the use of two descriptors can minimize the risk of losses since the search becomes more sensitive and less specific, covering greater themes and content for later choice, which is also manual by researchers.

The same for of the PROSPERO record, which was recorded more broadly, but it was decided to make use of only one outcome so that such a systematic review is more focused and consequently highlights in detail only one outcome.

CONCLUSION

By investigating the contribution of the consumption of ultra-processed foods and the risk of mortality, it can be concluded that there is research in the literature that demonstrates a statistically positive association between consumption and the increased risk of mortality. The studies included in the present review reinforce this close relationship between the consumption of UPFs and mortality by presenting statistical measures of HR of at least 14%[15] more mortality to those who consume this food category in a greater frequency or quantity. It is even observed in one of the cohorts that, with each additional portion of UPF consumption, the risk of mortality increases approximately 18%[14], thus refuting the interaction between the consumption of foods with a high degree of industrialization and the risk of mortality.

CONFLICT OF INTERESTS

The authors have no conflicts of interest.

TRANSPARENCY DECLARATION

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with PRISMA guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained. The protocol was registered at the international prospective register of systematic reviews (PROSPERO) database under the registration number CRD42020205382.

REFERENCES

1 – Monteiro CA, Levy RB, Claro RM, et al (2010). A new classification of foods based on the extent and purpose of their processing. Cad Saude Publica. 2010; 26, 2039–2049.

2 – Brazil. Ministry of Health. Health Care Secretariat. Department of Primary Care. Food guide for the Brazilian population / Ministry of Health, Secretariat of Health Care, Department of Primary Care. - 2. ed., 1. reprint - Brasília: Ministry of Health, 2014.

3 – Monteiro CA, Cannon G (2019). The role of the transnational ultra-processed food industry in the pandemic of obesity and its associated diseases: Problems and solutions. World Nutr. 2019, 10, 89–99.

4 – Elizabeth L, Machado P, Zinöcker M, et al (2020). Ultra-Processed Foods and Health Outcomes: A Narrative Review. Nutrientes. 2020; 12 (7): 1955. https://doi.org/10.3390/nu12071955

5 - Askari M, Heshmati J, Shahinfar H, et al (2020). Ultra-processed food and the risk of overweight and obesity: a systematic review and meta-analysis of observational studies. Int J Obes (Lond). 2020 Oct;44(10):2080-2091. doi: 10.1038/s41366-020-00650-z. Epub 2020 Aug 14. PMID: 32796919.

6 - Mendonça RDD, Lopes ACS, Pimenta AM, et al (2017). Ultra-processed food consumption and the incidence of hypertension in a Mediterranean cohort: the Seguimiento Universidad de Navarra Project.Am J Hypertens.2017;30:358–66.

7 - Steele EM, Juul F, Neri D, et al (2019). Dietary share of ultra-processed foods and metabolic syndrome in the US adult population. Prev Med. 2019;125:40–8.

8 - Fiolet T, Srour B, Sellem L, et al (2018). Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort. BMJ. 2018;360: k322.

9 - Monteiro CA, Cannon G, Levy R, et al (2016). NOVA. The star shines bright. World Nutr. 2016;7:28–38.

10 - Afshin A, Sur PJ, Fay KA, et al (2017). Health effects of dietary risks in 195 countries, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019, 393, 1958–1972, doi:10.1016/s0140-6736(19)30041-8.

11 - Louzada ML da C, Baraldi LG, Steele EM, et al (2015). Consumption of ultra-processed foods and obesity in Brazilian adolescents and adults. Prev Med 81, 9–15. doi: 10.1016/j.ypmed.2015.07.018

12 - Canella DS, Levy RB, Martins APB, et al (2014). Ultra-processed food products and obesity in Brazilian households (2008–2009). PLoS One 9, e92752. doi: doi.org/10.1371/journal.pone.0092752

13 - Juul F, Martinez-Steele E, Parekh N, et al (2018). Ultra-processed food consumption and excess weight among US adults. Br J Nutr 120, 90–100. doi: 10.1017/S0007114518001046

14 - Rico-Campá A, Martínez-González MA, Alvarez-Alvarez I, et al (2019). Association between consumption of ultra-processed foods and all cause mortality: SUN prospective cohort study. BMJ. 2019 May 29;365:l1949. doi: 10.1136/bmj.l1949.

15 - Schnabel L, Kesse-Guyot E, Allès B, et al (2019). Association Between Ultraprocessed Food Consumption and Risk of Mortality Among Middle-aged Adults in France. JAMA Intern Med. 2019 Apr 1;179(4):490-498. doi: 10.1001/jamainternmed.2018.7289.

16 - Blanco-Rojo R, Sandoval-Insausti H, López-Garcia E, et al (2019). Consumption of Ultra-Processed Foods and Mortality: A National Prospective Cohort in Spain. Mayo Clin Proc. 2019 Nov;94(11):2178-2188. doi: 10.1016/j.mayocp.2019.03.035.

17 - Kim H, Hu EA, Rebholz CM (2019). Ultra-processed food intake and mortality in the USA: results from the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994). Public Health Nutr. Jul;22(10):1777-1785. doi: 10.1017/S1368980018003890. Epub 2019 Feb.

18 - Bonaccio M, Di Castelnuovo A, Costanzo S, et al (2021). Ultra-processed food consumption is associated with increased risk of all-cause and cardiovascular mortality in the Moli-sani Study. Am J Clin Nutr. Feb ;113(2):446-455. doi: 10.1093/ajcn/nqaa299.

19 - Page MJ, McKenzie JE, Bossuyt PM, et al (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 372:n71. doi: 10.1136/bmj.n71

20 - Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa: Ottawa Hospital Research Institute. [cited 2021 April]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

21 - EFSA Panel on Contaminants in the Food Chain Scientific Opinion on acrylamide in Food. (2015) EFSA J. 13(6):4104. doi:10.2903/j.efsa.2015.4104

22 - Bettini S, Boutet-Robinet E, Cartier C et al (2017). Food-grade TiO2 impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions and promotes aberrant crypt development in the rat colon. Sci Rep. 40373. doi:10.1038/srep40373

23 - Chassaing B, Koren O, Goodrich JK et al (2015). Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome. Nature. 519(7541):92-96. doi:10.1038/nature14232

24 - Hall KD, Ayuketah A, Brychta R, et al (2019). Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake. Cell Metab. Jul 2;30(1):67-77.e3. doi: 10.1016/j.cmet.2019.05.008.

25 - Gibney MJ, Forde CG, Mullally D, et al (2017). Ultra-processed foods in human health: a critical appraisal. The American Journal of Clinical Nutrition, Volume 106, Issue 3, September, Pages 717-724, https: //doi.org/10.3945/ajcn.117.160440

26 - Gibney MJ (2019). Ultra-Processed Foods: Definitions and Policy Issues. Current developments in nutrition. Sep 14;3(2):nzy077. doi: 10.1093/cdn/nzy077

27 - Weaver CM, Dwyer J, Fulgoni VL, et al (2014). Processed foods: contributions to nutrition. Am J Clin Nutr 99, 1525–1542. doi: 10.3945/ajcn.114.089284

28 - World Health Organization Noncommunicable diseases. http://www.who.int/mediacentre/factsheets/fs355/en/. Accessed April 13, 2021.

29 - Julia C, Martinez L, Allès B et al (2018). Contribution of ultraprocessed foods in the diet of adults from the French NutriNet-Santé study. Public Health Nutr. 21(1):27-37. doi: 10.1017/S1368980017001367

30 - Lim SS, Vos T, Flaxman AD et al (2012). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 380: 2224-2260. doi: 10.1016 / S0140-6736 (12) 61766-8.

31 - Kelly B, Jacoby E (2018). Public Health Nutrition special issue on ultra-processed foods. Public Health Nutr. Jan;21(1):1-4. doi: 10.1017/S1368980017002853.

32 - Pagliai G, Dinu M, Madarena M, et al (2021). Consumption of ultra-processed foods and health status: A systematic review and meta-analysis. British Journal of Nutrition, 125(3), 308-318. doi:10.1017/S0007114520002688

ACKNOWLEDGMENTS

There was no funding for the administration of the research. The authors would like to thank the NUGAGE research group at the Federal University of Health Sciences of Porto Alegre for participating in the project.

Table 1. Data from the cohort studies included in the systematic review

Authors, Country and Year	Cohort "follow up"	Exposure Assessment	Outcome	Measurement	Objective	Main Findings
Rico-Campà A, Martínez-González MA, Alvarez-Alvarez I, Mendonça RD, de la Fuente-Arrillaga C, Gómez-Donoso C, Bes-Rastrollo M. Spain. (2019)	1999 - 2014	Semiquantitative Food Frequency Questionnaire (136 items, previously validated)	Mortality from all causes	Cox proportional risk ratios (95% confidence intervals)	To evaluate the association between the consumption of ultra-processed foods and all causes of mortality.	The consumption of ultra-processed foods was associated with mortality risk from all causes. Through the participants in the highest quartile of food consumption, they obtained an HR of 1.62 (p = 0.05, 95% CI) compared to the lowest quartile. For each additional portion of consumption, the relative risk of mortality from all causes increased relatively by 18% (adjusted HR of 1.18; p = 0.02). When using the Cox model with repeated measures (all follow-up data), the HR of the highest UPF consumption was 1.44 (p = 0.023). in propensity scores for adjustments of potential residual confounders, the association between UPF consumption and risk and mortality increased the risk ratio to 1.89. The mean age

						of the study was 37.6 years (SD 2.3). During the average follow-up of 10.4 years, 335 deaths occurred. Analyzes by type of mortality or by characteristics of the sample (subgroup analyzes) had no statistical significance.
Schnabel L, Kesse-Guyot E, Allès B, Touvier M, Srour B, Hercberg S, Buscail C, Julia C. France. (2019)	2009 - 2017	24-hour dietary records, 3 of which are non-consecutive (the records were randomly assigned over a period of 2 weeks) every 6 months and complete all 5 questionnaires each year.	Mortality from all causes	Cox proportional risk ratios (95% confidence intervals)	To analyze the association between the consumption of ultra-processed foods and risk of all-cause mortality.	The highest consumption of ultra-processed foods was associated with younger age, with an average of 45%, SD 0.04% p <0.01. There were 602 deaths (1.4%), after adjusting for the variables, the consumption of ultra-processed foods showed a risk ratio of 1.14 (95% CI, p = 0.008). The relative risk was assessed by a 10% increase in ultra-processed ingested. The associations were statistically significant for the adjustment of the variables, however, when excluding the cases of death in the first two years of study, prevalent cardiovascular diseases,

						and cases of cancer, the statistical power was reduced, thus generating no significant statistics between the association. consumption of ultra-processed products and mortality.
Blanco-Rojo R, Sandoval-Insausti H, López-Garcia E, Graciani A, Ordovás JM, Banegas JR, Rodríguez-Artalejo F, Guallar-Castillón P. Spain. (2019)	2008 - 2016	Food Frequency Questionnaire -DH-ENRICA- of the study itself was completed by a trained professional on home visits to the study participants.	Mortality from all causes	Cox proportional risk ratios (95% confidence intervals)	To elucidate the association between consumption of ultra-processed foods and all causes of mortality. Also, examine the effect of the theoretical substitution of isocaloric unprocessed foods in this relationship.	The average consumption of ultra-processed foods was 385g / day (24.4% kcal of the daily total). The 7.7-year follow-up resulted in 440 deaths. Participants who were classified in the highest consumption quartile obtained a higher HR of mortality in relation to the lower quartiles, for the model adjusted 4 to HR for mortality obtained a statistical value of 1.44 (95% CI, p = 0.03), when analyzed in relation to the consumption of grams per day per kg of weight, the HR was 1.46 (95% CI, p = 0.03). All associations between consumption and risk of mortality were statistically significant. The analysis of quartile 4 with

						isocaloric substitution only obtained a statistically significant result when 8.2% of the consumption of ultra-processed foods was substituted for minimally processed or fresh foods (p for non-linearity = 0.04).
Kim H, Hu EA, Rebholz CM. United States. (2019)	1988 - 2011	Food Frequency Questionnaire and 24-hour recalls, applied by the survey interviewers.	Mortality from all Causes and Cardiovascular	Cox proportional risk ratios (95% confidence intervals)	To investigate the association between the consumption of ultra-processed foods and mortality from all causes and mortality from cardiovascular diseases.	The 19-year follow-up resulted in 2451 deaths from all causes and 648 deaths from cardiovascular disease. When analyzing the quality of the diet using tools such as NRF9.3 and HEI-2000, the participants in the highest quartile had low quality of the diet, with statistically significant results with p <0.001 and p = 0.001, respectively. Cox adjustments for model 2, the highest consumption quartile, obtained an HR of 31% (HR 1.31; 95% CI; p = 0.001) for all-cause mortality when related to the other quartiles. Regardless of the adjusted models, the highest quartile of UPF consumption

						showed higher HR for mortality, with statistically significant values when compared to the lowest quartiles. The risk of mortality from cardiovascular diseases associated with the consumption of UPF did not show significant results for the adjustment models and quartiles of consumption (p> 0.05).
Bonaccio M, Di Castelnuovo A, Costanzo S, De Curtis A, Persichillo M, Sofi F, Cerletti C, Donati MB, de Gaetano G, Iacoviello L. Italy. (2021)	2005 - 2015	Semiquantitative Food Frequency Questionnaire validated and adapted for the Italian population, administered by the interviewer.	Mortality from all Causes, Cardiovascular and from Cancer	Cox proportional risk ratios (95% confidence intervals)	To estimate the association between the consumption of ultra-processed products and mortality risk.	During an average follow-up of 8.2 years, 1216 deaths from all causes occurred, 439 from cardiovascular disease, 255 from cerebrovascular disease, 477 from cancer, and 300 from other causes. The relative risks were analyzed according to the causes of mortality in a stratified way and the quartiles of consumption. All-cause mortality (1216) when adjusted to the models showed higher HR in the highest consumption quartile (HR 1.28; 1.32; 1.26; respectively to the

						adjusted models), similar results were found when stratified analysis for mortality from cardiovascular, cerebrovascular diseases, and other causes. When the consumption of ultra-processed products was associated with cancer mortality, they did not obtain significant results for the association, regardless of the adjusted models. The p values have not been demonstrated, only HR.

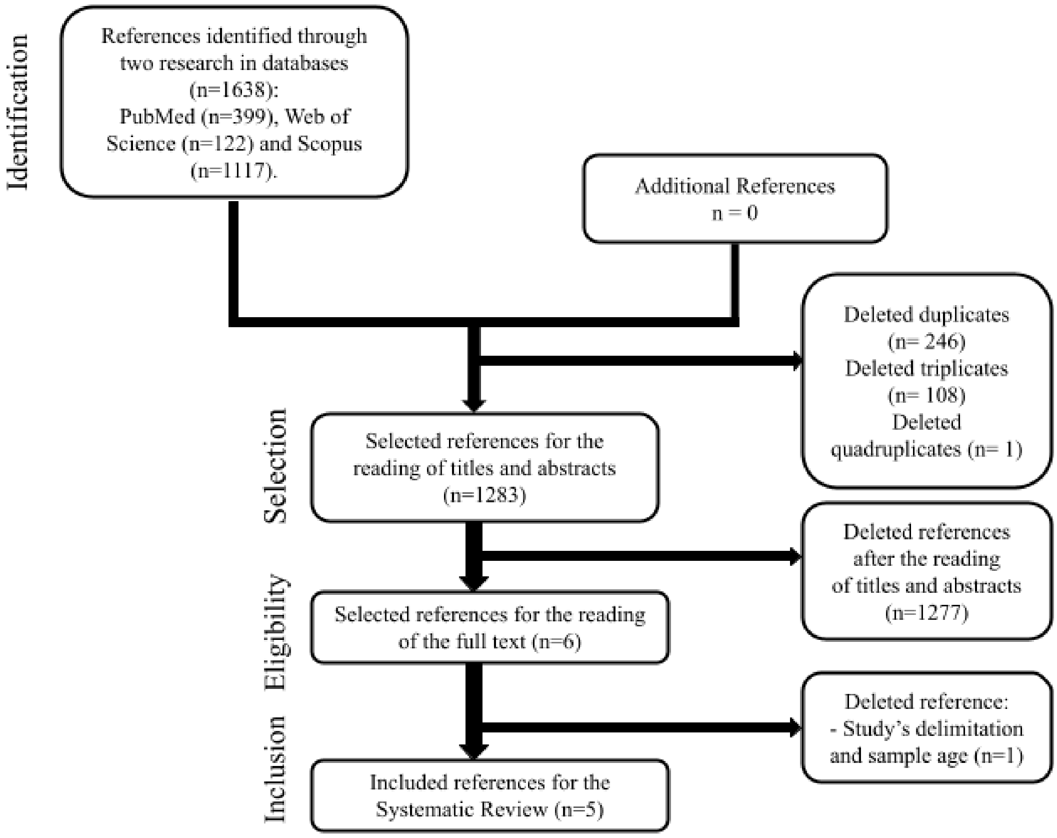
HR - Risk Ratio
UPF - ultra-processed foods
SD - Standard Deviation
NRF9.3 - New category-specific nutrient rich food score
HEI-2000 - Healthy Eating Index

Table 2. Methodological quality assessment of observational studies included in the systematic review using the Newcastle–Ottawa Scale (NOS)

First author, year	Study design	Selection	Comparability	Exposure/ Outcome	Total scores
Rico-Campà A *et al* (2019)	Cohort	★★★★	★	★★★	8
Schnabel L *et al* (2019)	Cohort	★★★	★	★★	6
Blanco-Rojo R *et al* (2019)	Cohort	★★★★	★	★★	7
Kim H *et al* (2019)	Cohort	★★★★	★	★★	7
Bonaccio M *et al* (2021)	Cohort	★★★★	★	★★★	8

NOS - Newcastle–Ottawa Scale tool
Selection - NOS tool selection domain
Comparability - comparability domain between the observed groups of the NOS tool
Exposure/Outcome - exposure domain and outcome
★ - point assigned to the article according to the questions in each domain of the NOS tool
The selection section has four questions and can score up to four points. Comparability has only one question that can score up to two points. In the outcome section are thee questions which can score thee points. The score depends on the methodological quality of the observational articles and possible risks of bias, where the higher the score, the better the quality and the lower the risk of bias.

Figure 1 - Results of studies selection



6.2 Artigo 2

Este artigo foi submetido para a revista *Food Reviews International*, ISSN 1525-6103, com Estrato Qualis unificado A2.

Olive oil consumption and cardiovascular risk factors: a review of systematic reviews

Olive oil and cardiovascular risk factors

Kathleen Kruger Peres[1], Isabella Rosa da Mata[1], Rafaella Câmara Rocha Menezes[2], Simone Morelo Dal Bosco[3]

1 Graduate Program in Nutrition Sciences, Universidade Federal de Ciências da Saúde de Porto Alegre, Brazil.

2 Nutrition Department, Universidade Federal do Rio Grande do Sul, Brazil.

3 Nutrition Department, Universidade Federal de Ciências da Saúde de Porto Alegre, Brazil.

List of Abbreviations

Cardiovascular Diseases CDV

C-Reactive Protein - CRP

Interleukin 6 - IL6

Interleukin 1 - IL1

Tumor Necrosis Factor Alpha - TNF-α

Monocyte chemotactic protein-1 - MCP-1

Circulating Vascular Cell Adhesion Molecule-1 - sVCAM-1

Vascular Cell Adhesion Molecule 1 -VCAM-1

Intercellular adhesion molecule-1 - ICAM-1

Malondialdehyde and thiobarbituric acid reactive substances - TBARS

Paraoxonase-3 protein - PON-3

Apo lipoprotein A1 - ApoA1

Apo lipoprotein B - ApoB

Monocyte chemoattractant protein-1 - MCP-1

Flow-mediated dilatation - FMD

Systolic blood pressure - SBP

Diastolic blood pressure - DBP

Triglycerides - TG

Total Cholesterol - CT

Low-Density Lipoproteins - LDL

High Density Lipoproteins - HDL

Olive Oil - OO

Refined Olive Oil - ROO

Extra virgin olive oil - EVOO

High phenolic olive oil - HPOO or HP(E)VOO

Low phenolic olive oil - LPOO or LP(E)VOO

Mixed OO = ROO + virgin OO - MOO

Polyunsaturated fatty acids - PUFAs

Monounsaturated Fatty Acids - MUFAs

\

ABSTRACT

Olive oil has been the basis of primary studies and systematic reviews in recent. This overview aims to investigate the effect of olive oil consumption on risk factors for cardiovascular diseases and their possible predictors. Through PubMed, Web of Science, and the Cochrane Library, systematic reviews that analyzed the relationship between olive oil consumption and cardiovascular disease were systematically searched. Was performed tools to assess the risk of bias (ROBIS), methodological quality (AMSTAR-2), and qualification of evidence (GRADE). The reviews included in this overview showed a more significant cardioprotective effect in the consumption of olive oil when higher phenolic content.

Keywords: Heart Disease Risk Factors; Cardiovascular Risks; Olive Oils; *genus Olea*

1. INTRODUCTION

Olive oil can be classified through its production processes, such as Virgin olive oil (VOO), extra virgin olive oil (EVOO), refined olive oil (ROO), olive oil, olive pomace oils, and lampante oil (EEC Regulation 1513). /2001; EU Regulation No. 29/2012 and EU Regulation 1348/2013). Extra virgin olive oil (EVOO), obtained by the mechanical extraction of the fruit of the olive, without the use of heat or solvents, is well known for its nutritional properties, in addition to its benefits in several health markers, such as chronic and cardiometabolic diseases. EVOO's health properties are largely attributed to its high concentration of monounsaturated fatty acids, as well as the presence of a variety of polyphenols[1-3].

The term “Mediterranean diet” refers to the dietary pattern typical in the 1960s in olive-growing countries around the Mediterranean Sea. Such a dietary pattern showed curiosity, the Seven Countries Study showed in its research that mortality from coronary heart disease in the Mediterranean area was 2 to 3 times lower than in northern Europe and the United States[4,5].

The Mediterranean dietary pattern consists of the consumption of fish, monounsaturated fats, olive oil, fruits, vegetables, whole grains, legumes/nuts, and moderate alcohol consumption[6]. With this, we know that the Mediterranean diet is rich in several micronutrients and olive oil, in its predominance of olive oils rich in polyphenols[7], these may be the possible actors in the regulation of diseases such as cardiovascular diseases.

Given the cardioprotective effect of eating habits, the study by George et al (2019) presents several epidemiological studies and clinical trials that demonstrate the Mediterranean diet has a cardioprotective function[8-10], as well as clinical trials and animal studies, demonstrate that EVOO can improve CVD outcomes, including blood pressure, inflammatory markers, and lipid profile[11-13].

Cardiovascular diseases (CVD) are the most important threat to population health in the 21st century[14]. Healthy lifestyles and diets at younger and middle ages are key factors for a chronic disease-free life at older ages. It is concluded that the prevention of CVD through diet and lifestyle is a public health priority, CVD can be generated through certain dysfunctions of blood pressure and lipid profile, increase in inflammatory markers, among other factors that can generate the body the potential cardiovascular risk[15].

Inflammatory markers related to cardiovascular disease are potential predictors of endothelial disease[16]. Chronic diseases have a high potential in the production and synthesis of pro-inflammatory cytokines such as IL-1, TNF-α and both act on endothelial health, increasing the mechanism of platelet and lipid aggregation in arterial walls, increasing the potential for atherogenesis, thus causing future cardiovascular events[17,18].

Due to the number of studies on the subject and the increase in systematic research on the consumption of olive oil and its cardiovascular effects, the objective of this overview is to investigate the effect of olive oil consumption on risk factors for cardiovascular and cardiovascular diseases. its possible predictors, to elucidate in the literature the dose/response update of olive oil consumption and the metabolic response.

2 METHODS

2.1 Overview of reviews

This overview of reviews follows the guidelines outlined by Chapter V: Overviews of Reviews of the Cochrane Handbook, using the PRISMA protocol[19] for writing and is registered in the PROSPERO database (registration number CRD42022322569).

2.1.1 Research Strategy

In three electronic databases (PubMed, Web of Science, and Cochrane Library) systematic reviews and meta-analyses published up to November 2021 were searched, following the MeSH terms using the strategy: “Olive Oil” OR “Oil, Olive” OR “ Oils, Olive” OR “Olive Oils” AND “Cardiovascular Diseases” OR “Cardiovascular Disease” OR “Disease, Cardiovascular” OR “Diseases, Cardiovascular” AND "systematic review" OR "meta-analysis" OR "systematic literature review" OR " systematic review" OR review. No filters or language restrictions were used. Reference lists of the resulting reviews and articles were also selected to identify additional articles.

2.1.2 Selection, inclusion, and exclusion of studies

The articles that were included in the overview when contemplating the structure of the PICO question: (1) studies that included adults and/or elderly (< 18 years); (2) consumption of olive oil (3) studies whose control was the non-consumption of olive oil, or the use of placebo or other oils (4) with an outcome evaluating the effectiveness of olive oil consumption on risk factors for diseases cardiovascular disease (5) systematic reviews or meta-analyses that included only intervention studies (clinical trials). Studies that mention only the Mediterranean diet without emphasis on the use of olive oil, reviews with animal or in vitro studies, primary studies (clinical trials, observational studies) and narrative or scoping review studies were exclusion criteria.

The articles were selected in two phases. First, duplicate articles and triplicate articles were removed. In the first phase, two reviewers (KKP and IRM) independently analyzed titles and abstracts in the electronic database and selected articles to identify potentially eligible studies, disagreements were resolved by a third reviewer (RCRM).

In the second phase, two reviewers (KKP and IRM) independently analyzed and fully read the articles selected in the first phase, excluding all articles that did not meet the eligibility criteria. At this stage, a third reviewer (RCRM) was consulted in case of doubts or disagreements among the other researchers, and all disputes were resolved by consensus. At the end of the process, six studies were collectively included in the analysis.

2.1.3 Data extraction and synthesis

Data extraction was independently completed by three authors (KKP, RCRM, and IRM). Data from articles were extracted: article title, study design, reference, sample size, study objective, population, intervention and its description (intervention duration, type of olive oil used, polyphenol content), control (specifying which type of control was used), year of publication, outcome, main findings and limitations of the included studies. Constant meetings were held to maintain the standard of analysis and the data were organized and recorded in a Microsoft Excel® spreadsheet specially designed for the work.

2.1.4 Quality assessment

The quality of the included reviews was evaluated using the tool A measurement tool to assess the methodological quality of systematic reviews - AMSTAR-2 -, registered through the website itself with its evaluation criteria for classifying the methodological quality of systematic reviews, with its criteria: Protocol registered before the start of the review; Adequacy of bibliographic research; Justification for exclusion of individual studies; Risk of bias for individual studies included in the review; Adequacy of meta-analytic methods; Consideration of risk of bias when interpreting review results; Assessment of the presence and likely impact of publication bias. The judgment of each methodological quality can be between High, Moderate, Low, and Critically low[20]. The judgment of the tool for each review present in this overview was contemplated later in the results session (Table 1).

To assess the risk of bias for each review included in this overview, the Cochrane Collaboration's ROBIS risk of bias for systematic review studies tool was used[21]. Its domains include Domain 1 - Study eligibility criteria; Domain 2 - Identification and selection of studies; Domain 3 - Data collection and study appraisal; Domain 4 - Synthesis and findings. The application of the tool was performed by two independent reviewers (KKP and IRM) and discrepancies were discussed until consensus. The determination of the risk of bias judgment was performed according to the summary of the answers of each domain as recommended by the tool and its results will be shown in Table 3.

2.1.5 GRADE Assessment of Meta-Analysis: Certainty of evidence

The GRADE (Grading of Recommendations Assessment, Development, and Evaluation) was applied to assess the quality of evidence from the meta-analyses in this overview. The evidence was classified into four levels: high, moderate, low, or very low. The quality of the evidence was considered 'high' due to the design of the included studies - clinical trials - by default of the tool and later updated to 'moderate or 'low' or downgraded to 'very low depending on the following criteria: risk of bias within the studies, inconsistency across heterogeneity, imprecision of effect estimates, indirect evidence and risk of publication bias, effect magnitude, and residual confounders. We rated the certainty of the evidence considering the information available in each meta-analysis. Therefore, we did not assess the primary studies included in each systematic review to verify data and/or assess the potential risk of bias. We choose to downgrade the certainty of the evidence if 1. Authors do not mention the risk of evaluating publication bias; 2. The authors obtained imprecision assessed by confidence intervals; 3. The authors did not assess or describe the results of risk of bias in the primary studies; 4. The authors did not present I2 statistics.

3 RESULTS

3.1 Selection of Studies

The search in the three databases resulted in 687 articles (519 after removing duplicates and triplicates), 71 articles generated disagreement between the two researchers after reading the title and abstract, of which, after the third researcher had broken the tie, 23 articles remained for reading. in full. In this phase, 11 articles remained selected according to the Kappa coefficient of agreement. Of these 11 reviews, 4 did not meet the eligibility criteria in our overview and 6 that met those criteria were included (Figure 1).

From these reviews, the evaluation performed by each study was to present the effect of olive oil consumption and cardiovascular risk factors, with 1 the evaluation of the polyphenols that make up extra virgin olive oil and the effects on cardiovascular risk factors (stress oxidative stress, inflammation, blood pressure, lipid profile and other outcomes), 1 evaluated the impact of different types of olive oil on cardiovascular risk factors, 1 evaluated the lipid profile comparing the use of olive oil and oils from other plants, 1 the effects of olive oil on inflammatory markers and endothelial function, 1 the effects of olive oil on blood pressure, and 1 evaluated the effects of olive oil and its phenolic compounds (oleic acid and hydroxytyrosol) on the metabolic syndrome (which includes factors of cardiovascular risk in its classification).

3.2 Data from the Systematic Reviews included

Table 1 details the methodological characteristics of the systematic reviews included in the current overview of systematic reviews. Two systematic reviews were carried out in Spain [22, 23], two in Germany[24,25], one in Australia[26], and one in Iran[27].

All of the included reviews used at least three indexed databases to carry out the bibliographic search and used clinical trials as the primary study to compose the systematic review, whether randomized or non-randomized[22-27], only one review did not provide data on the search strategy[25] and another left only generic data as the search strategy described[24].

Five of the systematic reviews included used the risk of bias tool suggested by the Cochrane Library[22,23,24,25,27] and only one used the Jaad to check for possible risk of bias in the primary articles included[26].

Only one study used the GRADE system to assess the quality of evidence of the primary studies included in their systematic review[25], the others did not report the use of assessment tools.

3.3 Bias Risk Assessment and Methodological Quality

According to Table 1, the results of the application of the AMSTAR-2 tool assessing the methodological quality of the articles, two systematic reviews were classified as Critically low-quality reviews (33.3%)[26,27], and two others classified as Low-quality review (33.3%)[22,23], one review classified as Moderate quality review (16.67%)[26] and the last High-quality review (16.67%)[25].

Most of the classification occurred due to the lack of information about the primary studies and also about the methodology used, either by publishing study protocols before execution, not investigating the risk of publication bias, or not adequately exposing it throughout the systematic review. the research question or acronym PICO.

The ROBIS risk of bias of systematic reviews tool[21] presented in Table 3 resulted in two reviews (33.3%) with a low risk of bias[24,25] for not having concerns in the domains of the tool. The other reviews (n=4 66.6%) were classified as High risk of bias[22,23,26,27] due to concerns in the domains, this being predominantly domain 4 of the tool (Synthesis and findings), which is related to the synthesis of the results present in the primary studies included in each systematic review.

3.4 Certainty of the evidence according to the GRADE

According to Tables 4, 5, 6, and 7, the GRADE system was applied to assess the certainty of the evidence of systematic reviews according to each outcome present in each review included in this overview. Studies were downgraded due to their high heterogeneity, lack of assessment of confounding factors, lack of publication bias, and data imprecision when data were summarized in the meta-analysis.

3.4.1 Olive oil consumption and Blood Pressure

Four of the six reviews presented the blood pressure outcome. The application of the tool resulted in only one study with a high quality of evidence[23], the others had a moderate quality of evidence[22,25,26].

3.4.2 Olive oil consumption and inflammatory markers

Two of the studies that presented the outcome of the evaluation of inflammatory markers, according to the GRADE system, presented high-quality evidence, with only one point being lowered, one study due to the non-presentation of publication bias[26] and the other one lowered one point due to the inconsistency in the results[24].

3.4.3 Olive oil consumption and lipid profile

Of the six systematic review studies presented in this overview, four presented the analysis of the outcome of the lipid profile and the consumption of olive oil. Among such studies, two presented high-quality evidence[26,27], one presented moderate quality evidence by identifying inconsistency and not ascertaining heterogeneity between the sample[25], and only one presented low-quality of evidence due to the downgrade of 3 points, being the presence of inconsistency of the analysis, non-presentation of publication bias and presence of sample heterogeneity[22].

3.4.4 Olive oil consumption and metabolic syndrome

Only the meta-analysis by Pastor et al evaluated the outcome of the metabolic syndrome, and according to the application of the GRADE system, it presented a low quality of evidence due to the downgrade of 3 points, the same being presented in its outcome for lipid profile[22]

.

3.5 Results of the Systematic Reviews Included

Table 2 summarizes the results of all systematic reviews present in this overview. Systematic reviews included 15 to 76 primary articles.

The sample number was at least 611 participants in the sum of primary studies included. The sample of each systematic review varied according to the outcome, being presented as a healthy sample or already presenting some comorbidity or risk factor.

3.5.1 Blood Pressure

The study by Zamora-Zamora et al included 15 primary studies, with n= 6651, their results were represented by the consumption of olive oil as an intervention - capsules (1-6g/day) or EVOO (extra virgin olive oil) of 10 to 50ml/day -. Liquid EVOO consumption demonstrated a significant reduction in BPD with a fixed effects model of -0.73 mm Hg, (95% CI (-1.07, -0.40); $p < 0.001$). The use of olive oil capsules as a supplement did not show a significant influence on DBP. No significant effect was observed for both capsules and liquid on SBP. Olive oil showed no reduction in SBP more than other fats, MDs = -0.11, 95% CI (-0.68, 0.46), I2 = 85.1%; heterogeneity <0.001[23].

Schwingshackl et al (2019) included 16 studies totaling n=611 participants, who used olive oil in capsules or oral intake, used for at least 3 to 12 weeks, with consumption ranging from 20ml/d to 75ml/d. The systematic review showed no differences in secondary analyzes comparing ROO, MOO, VOO, and EVOO, and comparing different daily doses of phenolic compounds OO intake (<1 ml/d, 1 to <5 ml/d, and 5 ml/d) were observed for BPD. However, VOO can improve SBP compared to ROO (MD: 3.28 mmHg, 95% CI: 5.53, 1.03), and a 5 ml/d dose of phenolic OO compounds can reduce SBP compared to a daily dose of <1 ml/d[25].
Pastor et al investigated supplementation with oleic acid, hydroxytyrosol, or olive oil, from 2 weeks to 6 months of intervention in a sample population of 10,966 participants. Olive oil consumption showed a significant reduction in mean difference only in body composition data and when blood pressure was evaluated, the mean difference was null[22].
Of the 26 articles included in the systematic review by George et al, 5 studies carried out with normotensive individuals showed improvement in SBP when extra virgin olive oil rich in HPOO polyphenols was consumed, unlike other types of olive oil[26].

3.5.2 Inflammatory markers

Schwingshackl et al (2015) in their systematic review included 30 primary studies, with n= 3106. The average consumption of olive oil was 50ml/day or 1-10g/day of capsules. The total polyphenol content was from 35mg/100g of olive oil to 328g/kg. Olive oil interventions resulted in a reduction in CRP (MD: -0.64 mg/L, p<0.0001) compared to the respective controls. Likewise, there were reductions in IL-6 levels in the olive oil intervention groups compared to controls (MD: -0.29, p < 0.04). In 8 studies included, FMD when compared between the intervention group (consumption of olive oil) and controls showed an increase in a mean difference of 0.76% (p<0.002. CI 95%) generating an increase in flow due to the increase of the average dilation[24].

George et al included 26 articles in their systematic review, 3 of which evaluated CRP, IL6, TNF alpha, fecal calprotectin, and resistin, two showed a reduction in CRP when HPOO was consumed and 1 also showed a reduction in IL6 when HPOO was consumed. A primary study demonstrated improvement in resistin and MCP-1 when LPOO was consumed[26].

Pastor et al presented results for antioxidant capacity demonstrating improvement when the diet was supplemented with olive oil, hydroxytyrosol and oleic acid, showing a mean difference of SMD = 0.31 (95% CI: [-0.34, 0.95], I 2 = 81%)]; p = 0.35)[22].

3.5.3 Lipid Profile

Ghobadi et al included 27 primary articles in their systematic review, with n=1089 participants. In two studies, the effect of olive oil compared to corn oil and evening primrose showed a significant increase in HDL-c in the intervention group, as well as a significant reduction in total cholesterol, triglycerides, and LDL-c. Compared with palm and sunflower oil, there was a significant reduction in LDL-c and TC (total cholesterol) markers in the intervention group. ApoA1 was reduced in the group that consumed olive oil compared to evening primrose and sunflower oil. However, there were no statistically significant effects on ApoA1 and ApoB. When analyzed in subgroups, there was a reduction in TC in groups that consumed olive oil, but a smaller reduction than when compared to oils rich in omega-3. In individuals younger than 50 years, the reduction in TC was lower when using olive oil and with consumption less than or equal to 30 days. Refined olive oil showed less TC reduction when compared to virgin olive oil. The results of this study showed that, compared to other vegetable oils, the high-density lipoprotein level increased significantly more for OO (1.37 mg/dl: 95% CI: 0.4, 2.36). Olive oil consumption also reduced total cholesterol (TC) (6.27 mg/dl, 95% CI: 2.8, 10.6), low-density lipoprotein (LDL-c) (4.2 mg/dl). dl, 95% CI: 1.4, 7.01) and triglycerides (TG) (4.31 mg/dl, 95% CI: 0.5, 8.12) significantly lower than other vegetable oils. There were no significant effects on Apo lipoprotein A1 and Apo lipoprotein B[27].

Schwingshackl et al (2019) compared the use of ROO, with all other types of OO (MOO, LP(E)VOO, and HP(E)VOO, such comparison showed no difference in LDL-C reduction, but HP(E))VOO slightly lowers LDL-C compared to LP(E)VOO (MD:0.14 mmol/L, 95% CI:0.28.0.01; high certainty of evidence). In addition, HP(E)VOO can reduce xLDL-C compared to ROO (SMD: 0.68, 95% CI: 1.31.0.04, low certainty of evidence; MD: 4.18, 95% CI: 7 .06, 1.31 U/L). Regarding the reduction of oxLDL-C, EVOO was more effective compared to ROO (SMD: 1.25, 95% CI: 2.32, 0.19) and a dose of 5 ml/d of OO phenolic compounds can improve xLDL-C compared to ROO (SMD: 0.60, 95% CI: 1.18, 0.03) and (MD: 4.21 U/L, 95% CI: 7.08, 1.33). In further analyses, EVOO was rated as the best treatment for lowering LDL-C (0.70) and oxLDL-C (0.96)[25].

George et al performed their meta-analysis of the primary studies (26 articles were included) and showed a reduction in oxidized LDL when comparing the intake of HPOO and LPOO. 12 primary studies that evaluated (LDL, HDL, TG, ApoB, ApoA1, ApoA2, flow capacity, and cholesteryl esters) showed that consumption of HPOO improved total cholesterol content and added to it an increase in serum HDL content[26].

Pastor et al demonstrated that oleic acid supplementation had a brief effect on the lipid profile, however, the results were not statistically significant in summarizing meta-analysis data[22].

3.5.4 Metabolic syndrome

The systematic review by Pastor et al presented results through risk factors present in metabolic syndrome and demonstrated effects according to supplementation. The use of hydroxytyrosol demonstrated an overall effect on 22 MetS factors, a brief result in favor of the intervention (diet supplemented with hydroxytyrosol), however, such results were not statistically significant (p=0.920). The meta-analysis studies showed low accuracy, however, when evaluating the diet supplemented with oleic acid, the global effects on 117 MetS factors showed a small effect in favor of the intervention[22].

4 DISCUSSION

Inflammatory markers in cardiovascular diseases and olive oil consumption

The review by Schwingshackl et al (2015) evaluated the consumption of the Mediterranean diet supplemented with olive oil on inflammatory markers and endothelial function, this study showed significant results with the consumption of olive oil in the reduction of CRP with a value of p<0 .0001), as well as in IL6 (p<0.04)[24]. The clinical trial by Foshati et al (2021)[28] allocated groups of participants with depression and consumption of EVOO and sunflower oil (n=31 per group), with intervention lasting 52 days with consumption of 25 ml/day of sunflower oil or EVOO. In the trial, the consumption of EVOO reduced the mean CRP, but without statistically significant results and its authors assumed that the lack of effect was due to benign, if any, inflammatory and oxidative conditions in our participants, in addition to small sample size. Another review of this overview, by George et al (2019) also evaluated inflammatory markers such as CRP, IL6, sVCAM-1, MCP-1, TNF alpha, resistin, fecal calprotectin and showed statistically significant results only in the reduction of IL6 (p< 0.002) regarding HPOO supplementation and also reduction of CRP (p<0.01)[26].

The FMD showed a significant difference in the intervention group of olive oil plus omega-3, as for the other oils (p<0.003) in the review by Schwingshackl et al (2015)[24]. When evaluated in a trial, as in Davis et al[29] (2017) using the Mediterranean diet for 6 months in a group of 80 people, the effect of the diet on FMD was also significant (p<0.001), with the mean FMD in the 2.5% Mediterranean diet group and 1.3% for the other diets, bias in the analysis may be possible because it did not only investigate the effect of olive oil or its polyphenols on FMD (Davis et al 2015)[7].

As for oxidative stress, the review by Schwingshackl et al (2015), the levels of sE-selectin and sP-selectin also showed significant effects on the consumption of olive oil ($p<0.00001$ and $p<0.002$ respectively)[24]. The study by Carnevale et al (2014) used 10g of EVOO for 30 days and such intervention corroborated the review by Schwingshackl et al (2015), given a significant value of $p<0.001$, a significant reduction in oxidative stress marked by sE - selectin[30].

As in the work by George et al (2019), oxidative stress by demonstrating the enzyme malondialdehyde had a significant effect when dietary HPOO supplementation ($p<0.004$), encouraging the idea that the higher the polyphenol content of olive oils, the greater the serum antioxidant capacity[26].

Blood pressure and olive oil consumption

In the review by Zamora et al (2018), the assessment of the consumption of olive oil in capsules and liquid form was analyzed in terms of blood pressure outcome. The reduction in SBP was not significant in any consumption model, since when DBP was evaluated for the consumption of olive oil, a statistically significant reduction ($p<0.001$) was demonstrated, only in the consumption of liquid olive oil[23].

The study by Rozati et al (2015)[31] showed a significant reduction in systolic blood pressure when compared to other oils (soy, corn, butter) when consuming 39g/day of EVOO, which is a contrary result to the review by Zamora et al (2018)[23].

Two other systematic reviews of this overview brought the effects of olive oil consumption on blood pressure. Another review by Schwingshackl et al (2019)[25] presented the comparison between different types of olive oil and their impact on blood pressure. LP(EVOO) olive oil in PAS when compared to ROO (refined olive oil) brought a total average reduction of -2.87mmHg, and when HP(EVOO) with ROO a reduction of -2.99mmHg, but also did not demonstrate statistically significant results. A dose greater than or equal to 5mL/d of phenolic compounds in olive oil demonstrated a reduction in SBP. In contrast, and contrary to the review by Zamora et al (2019), the consumption of olive oil did not show a significant difference in the reduction of DBP[25].

In the review by George et al (2019), 5 studies included the consumption of HPOO had no effect on SBP when compared to LPOO, as well as did not significantly reduce DBP in the HPOO group (p=0.08). Such studies show discrepant results in values and are mainly due to the high heterogeneity of the articles included in each meta-analysis of our overview[26].

Lipid Profile and Olive Oil

Ghobadi et al (2019) in their systematic review compared the consumption of various oils to the lipid profile and aimed to evaluate this effect on the reduction of serum markers. Two of the studies included in the review found a significant increase in HDL in the group that consumed olive oil compared to the groups that consumed corn oil and evening primrose[27]. A review that evaluated the potential of oleic acid in canola oil obtained a discrepant result, where it evaluated serum fatty acids and canola oil with a high content of polyphenols - in this case, oleic acid - when compared to canola oil, such a review did not demonstrate a significant result in HDL levels (Bowen et al 2019)[32].

Also in the review by Ghobadi et al (2019) total cholesterol, free triglycerides, and LDL were reduced more in the groups that consumed vegetable oil than olive oil, in the review[27] by Huth et al (2015) compared soybean oil rich in oleic acid with other oils, including olive oil. Such comparison did not show a statistically significant increase in serum HDL levels, corroborating the studies discussed above, however, there was an improvement in the reduction of LDL, total cholesterol, and triglycerides, for this reason, we can argue that oils-rich in oleic acid or rich in n -6 PUFAs have favorable effects on the lipid profile[33], so knowing that olive oil has a lower content of n-6 and PUFAs such a reduction was not statistically significant in the review by Ghobadi et al (2019)[27].

Regarding olive oils and their variations, the review by Schwingshackl et al (2019) showed a reduction in LDL when related to the use of HP(EVOO) compared to LP (EVOO), in addition to daily doses of polyphenols when compared there were no differences significant in TG, Total Cholesterol or LDL markers[25].

Corroborating the overview studies, the review by George et al (2019) showed a reduction in total cholesterol with the consumption of HPOO ($p<0.0001$), however, when compared to LPOO, HPOO, and the increase in serum HDL, the result was not demonstrated to be statistically significant ($p=0.02$), as well as in LDL reduction ($p=0.06$)[26].

Metabolic Syndrome and Olive Oil

The 67 articles included in the review by Pastor et al (2021) were subdivided between hydroxytyrosol, oleic acid, and olive oil supplementation, due to the high heterogeneity of the studies, no result was statistically significant, only this review of our overview mentioned the metabolic syndrome as a possible risk factor for cardiovascular diseases evaluating the consumption of olive oil as protective factors[22].

The trial by Galvão et al (2017) brought some factors considered as part of the metabolic syndrome, such as excess weight and high blood pressure. This study supplemented 25ml/day of soybean oil (control) and 25ml/day of EVOO (intervention) during the subjects' breakfast, the supplementation of the intervention group demonstrated a reduction in body fat weight ($p=0.037$), in addition to SBP reduction ($p=0.011$), which demonstrates a positive effect of the consumption of polyphenol-rich virgin olive oil[34].

LIMITATIONS

The findings of this review are limited by the small number of articles included, with only 6 classified according to the eligibility criteria. The potential biases analyzed in systematic reviews according to the tools may also be potential limitations to this overview, such as the lack of information on primary studies and also on the methodology used. Among other limiting factors, one can also observe the performance of the GRADE system analysis, the proposal to assess the certainty of the evidence according to the outcomes of the systematic reviews, and the non-performance of such a system by the included systematic reviews. The lack of publication of the protocol of the review studies present in this overview can be considered a limitation, in addition to the lack of analysis of the risk of publication bias in all six articles included. In addition, studies that included olive oil as a supplement to the Mediterranean diet may also lead to an overestimated analysis of the effect of olive oil, as the Mediterranean diet has a higher phenolic content in its composition.

CONCLUSION

To elucidate and synthesize the evidence present in the literature on the dose and response of olive oil consumption and cardiovascular risk factors, we can conclude that the systematic reviews found, the protective association of olive oil in the factors as active in the improvement in blood pressure, reducing the average rate of BPD, reduction of lipid profile markers, improvement in cellular inflammatory markers and determinants of metabolic syndrome. The reviews included in this overview evaluated the consumption of olive oil in different forms (liquid or capsules), supplemented with the diet, and also compared with other oils, in addition to performing a comparative analysis between the types of olive oil (ROO, VOO, EVOO, LPOO, HPOO), with such comparisons, it is concluded that the higher the phenolic content, the more potent is the protective metabolic response to cardiovascular risk factors.

REFERENCES

1 - Millman, J. F.; Okamoto, S.; Teruya, T.; Uema, T.; Ikematsu, S.; Shimabukuro, M.; Masuzaki, H. Extra-virgin olive oil and the gut-brain axis: influence on gut microbiota, mucosal immunity, and cardiometabolic and cognitive health. Nutr Rev. **2021** Nov 10;79(12):1362-1374. doi: 10.1093/nutrit/nuaa148.

2 - Romani, A.; Ieri, F.; Urciuoli, S.; Noce, A.; Marrone, G.; Nediani, C.; Bernini, R. Health Effects of Phenolic Compounds Found in Extra-Virgin Olive Oil, By-Products, and Leaf of Olea europaea L. Nutrients. **2019** Aug 1;11(8):1776. doi: 10.3390/nu11081776.

3 - Piroddi, M.; Albini, A.; Fabiani, R.; Giovannelli, L.; Luceri, C.; Natella, F.; Rosignoli, P.; Rossi, T.; Taticchi, A.; Servili, M.; Galli, F. Nutrigenomics of extra-virgin olive oil: A review. Biofactors. **2017** Jan 2;43(1):17-41. doi: 10.1002/biof.1318.

4 - Keys, A.; Menotti, A.; Karvonen, M. J.; Aravanis, C.; Blackburn, H.; Buzina, R.; Djordjevic, B. S.; Dontas, A. S.; Fidanza, F.; Keys, M. H.; et al. The diet and 15-year death rate in the seven countries study. Am J Epidemiol. **1986** Dec;124(6):903-15. doi: 10.1093/oxfordjournals.aje.a114480. PMID: 3776973.

5 - Mazzocchi, A.; Leone, L.; Agostoni, C.; Pali-Schöll, I. The Secrets of the Mediterranean Diet. Does [Only] Olive Oil Matter?. Nutrients. **2019**;11(12):2941. Published 2019 Dec 3. doi:10.3390/nu11122941

6 - Widmer, R. J.; Flammer, A. J.; Lerman, L. O.; Lerman, A. The Mediterranean diet, its components, and cardiovascular disease. Am J Med. **2015**;128(3):229-238. doi:10.1016/j.amjmed.2014.10.014

7 - Davis, C.; Bryan, J.; Hodgson, J.; Murphy, K. Definition of the Mediterranean Diet; a Literature Review. Nutrients. **2015** Nov 5;7(11):9139-53. doi: 10.3390/nu7115459.

8 - de Lorgeril, M.; Salen, P.; Martin, J. L.; Monjaud, I.; Delaye, J.; Mamelle, N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after

myocardial infarction: final report of the Lyon Diet Heart Study. Circulation. **1999** Feb 16;99(6):779-85. doi: 10.1161/01.cir.99.6.779.

9 - Estruch, R.; Martínez-González, M. A.; Corella, D.; Salas-Salvadó, J.; Ruiz-Gutiérrez, V.; Covas, M. I., Fiol, M.; Gómez-Gracia, E.; López-Sabater, M. C.; Vinyoles, E.; Arós, F.; Conde, M.; Lahoz, C.; Lapetra, J.; Sáez, G.; Ros, E. PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. Ann Intern Med. **2006** Jul 4;145(1):1-11. doi: 10.7326/0003-4819-145-1-200607040-00004.

10 - Itsiopoulos, C.; Brazionis, L.; Kaimakamis, M.; Cameron, M.; Best, J. D.; O'Dea, K.; Rowley, K. Can the Mediterranean diet lower HbA1c in type 2 diabetes? Results from a randomized cross-over study. Nutr Metab Cardiovasc Dis. **2011** Sep;21(9):740-7. doi: 10.1016/j.numecd.2010.03.005..

11 - Farràs, M.; Castañer, O.; Martín-Peláez, S.; Hernáez, Á.; Schröder, H.; Subirana, I.; Muñoz-Aguayo, D.; Gaixas, S.; Torre Rde, L.; Farré, M.; Rubió, L.; Díaz, Ó.; Fernández-Castillejo, S.; Solà, R.; Motilva, M. J.; Fitó, M. Complementary phenol-enriched olive oil improves HDL characteristics in hypercholesterolemic subjects. A randomized, double-blind, crossover, controlled trial. The VOHF study. Mol Nutr Food Res. **2015** Sep;59(9):1758-70. doi: 10.1002/mnfr.201500030.

12 - Beauchamp, G. K.; Keast, R. S.; Morel, D.; Lin, J.; Pika, J.; Han, Q.; Lee, C. H.; Smith, A. B.; Breslin, P. A. Phytochemistry: ibuprofen-like activity in extra-virgin olive oil. Nature. **2005** Sep 1;437(7055):45-6. doi: 10.1038/437045a. PMID: 16136122.

13 - Perona, J. S.; Cañizares, J.; Montero, E.; Sánchez-Domínguez, J. M.; Catalá, A.; Ruiz-Gutiérrez, V. Virgin olive oil reduces blood pressure in hypertensive elderly subjects. Clin Nutr. **2004** Oct;23(5):1113-21. doi: 10.1016/j.clnu.2004.02.004.

14 - Go, A. S.; Mozaffarian, D.; Roger, V. L.; Benjamin, E. J.; Berry, J. D.; Borden, W. B.; Bravata, D. M.; Dai, S.; Ford, E. S.; Fox, C. S.; et al. Heart disease and stroke statistics-2013 update: A report from the American Heart Association. Circulation. **2013**;127:e6–245

15 - Ros, E.; Martínez-González, M. A.; Estruch, R.; Salas-Salvadó, J.; Fitó, M.; Martínez, J. A.; Corella, D. Mediterranean diet and cardiovascular health: Teachings of the PREDIMED study. Adv Nutr. **2014** May 14;5(3):330S-6S. doi: 10.3945/an.113.005389.

16 - Inaba, Y.; Chen, J. A.; Bergmann, S. R. Prediction of future cardiovascular outcomes by flow-mediated vasodilatation of brachial artery: A meta-analysis. Int. J. Cardiovasc. Imaging **2010**, 26, 631–640.

17 - Cook-Mills, J.M.; Marchese, M.E.; Abdala-Valencia, H. Vascular cell adhesion molecule-1 expression and signaling during disease: Regulation by reactive oxygen species and antioxidants. Antioxid. Redox Signal. **2011**, 15, 1607–1638.

18 - Inaba, Y.; Chen, J. A.; Bergmann S. R. Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: a meta-analysis. Atherosclerosis. **2012** Jan;220(1):128-33. doi: 10.1016/j.atherosclerosis.2011.06.044.

19 - Page, M.J., J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ **2021**;372:n71. doi: 10.1136/bmj.n71

20 - Shea, B. J.; Reeves, B. C.; Wells, G.; Thuku, M.; Hamel, C.; Moran, J.; Moher, D.; Tugwell, P.; Welch, V.; Kristjansson, E.; Henry, D. A. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomized or non-randomized studies of healthcare interventions, or both BMJ **2017**; 358 :j4008 doi:10.1136/bmj.j4008

21 - Whiting, P.; Savović, J.; Higgins, J. P.; Caldwell, D. M.; Reeves, B. C.; Shea, B.; Davies, P.; Kleijnen, J.; Churchill, R. ROBIS group. ROBIS: A new tool to assess risk of bias in

systematic reviews was developed. J Clin Epidemiol. **2016** Jan;69:225-34. doi: 10.1016/j.jclinepi.2015.06.005.

22 - Pastor, R.; Bouzas, C.; Tur, J. A. Beneficial effects of dietary supplementation with olive oil, oleic acid, or hydroxytyrosol in metabolic syndrome: Systematic review and meta-analysis. Free Radic Biol Med. **2021** Aug 20;172:372-385. doi: 10.1016/j.freeradbiomed.2021.06.017.

23 - Zamora-Zamora, F.; Martínez-Galiano, J. M.; Gaforio, J. J.; Delgado-Rodríguez, M. Effects of olive oil on blood pressure: A systematic review and meta-analysis. grasasaceites. **2018**. Dec.30;69(4):e272.

24 - Schwingshackl, L.; Christoph, M.; Hoffmann, G. Effects of Olive Oil on Markers of Inflammation and Endothelial Function-A Systematic Review and Meta-Analysis. Nutrients. **2015** Sep 11;7(9):7651-75. doi: 10.3390/nu7095356.

25 - Schwingshackl, L.; Krause, M.; Schmucker, C.; Hoffmann, G.; Rücker, G.; Meerpohl, J. J. Impact of different types of olive oil on cardiovascular risk factors: A systematic review and network meta-analysis. Nutr Metab Cardiovasc Dis. **2019** Oct;29(10):1030-1039. doi: 10.1016/j.numecd.2019.07.001.

26 - George, E. S.; Marshall, S.; Mayr, H. L.; Trakman, G. L.; Tatucu-Babet, O. A.; Lassemillante, A. M.; Bramley, A.; Reddy, A. J.; Forsyth, A.; Tierney, A, C.; Thomas, C. J.; Itsiopoulos, C.; Marx, W. The effect of high-polyphenol extra virgin olive oil on cardiovascular risk factors: A systematic review and meta-analysis. Crit Rev Food Sci Nutr. **2019**;59(17):2772-2795. doi: 10.1080/10408398.2018.1470491.

27 - Ghobadi, S.; Hassanzadeh-Rostami, Z.; Mohammadian, F.; Nikfetrat, A.; Ghasemifard, N.; Raeisi Dehkordi, H.; Faghih, S. Comparison of blood lipid-lowering effects of olive oil and other plant oils: A systematic review and meta-analysis of 27 randomized placebo-

controlled clinical trials. Crit Rev Food Sci Nutr. **2019**;59(13):2110-2124. doi: 10.1080/10408398.2018.1438349.

28 - Foshati, S.; Ghanizadeh, A.; Akhlaghi, M. The effect of extra virgin olive oil on anthropometric indices, lipid profile, and markers of oxidative stress and inflammation in patients with depression, a double-blind randomised controlled trial. Int J Clin Pract. **2021** Jul;75(7):e14254. doi: 10.1111/ijcp.14254.

29 - Davis, C. R.; Hodgson, J. M.; Woodman, R.; Bryan, J.; Wilson, C.; Murphy, K. J. A Mediterranean diet lowers blood pressure and improves endothelial function: results from the MedLey randomized intervention trial. Am J Clin Nutr. **2017** Jun;105(6):1305-1313. doi: 10.3945/ajcn.116.146803.

30 - Carnevale, R.; Pignatelli, P.; Nocella, C.; Loffredo, L.; Pastori, D.; Vicario, T.; Petruccioli, A.; Bartimoccia, S.; Violi, F. Extra virgin olive oil blunt post-prandial oxidative stress via NOX2 down-regulation. Atherosclerosis. **2014** Aug;235(2):649-58. doi: 10.1016/j.atherosclerosis.2014.05.954.

31 - Rozati, M.; Barnett, J.; Wu, D.; Handelman, G.; Saltzman, E.; Wilson, T.; Li, L.; Wang, J.; Marcos, A.; Ordovás, J. M.; Lee, Y. C.; Meydani, M.; Meydani, S. N. Cardio-metabolic and immunological impacts of extra virgin olive oil consumption in overweight and obese older adults: a randomized controlled trial. Nutr Metab (Lond). 2015 Aug 7;12:28. doi: 10.1186/s12986-015-0022-5.

32 - Bowen, K. J.; Kris-Etherton, P. M.; West, S. G.; Fleming, J. A.; Connelly, P. W.; Lamarche, B.; Couture, P.; Jenkins, D. J. A.; Taylor, C. G.; Zahradka, P.; et al. Diets Enriched with Conventional or High-Oleic Acid Canola Oils Lower Atherogenic Lipids and Lipoproteins Compared to a Diet with a Western Fatty Acid Profile in Adults with Central Adiposity. J Nutr. **2019** Mar 1;149(3):471-478. doi: 10.1093/jn/nxy307.

33 - Huth, P. J.; Fulgoni, V. L.; Larson, B. T. A systematic review of high-oleic vegetable oil substitutions for other fats and oils on cardiovascular disease risk factors: implications for novel high-oleic soybean oils. Adv Nutr. **2015** Nov 13;6(6):674-93. doi: 10.3945/an.115.008979.

34 - Galvão, F. C.; Xavier, F. V.; da Silva, L. E.; Gonçalves, O. L. C.; Gouveia, P. M. D. C.; Gonçalves, A. R. C. Consumption of extra virgin olive oil improves body composition and blood pressure in women with excess body fat: a randomized, double-blinded, placebo-controlled clinical trial. Eur J Nutr. **2018** Oct;57(7):2445-2455. doi: 10.1007/s00394-017-1517-9. Epub 2017

Table 1. Synthesis of Data from Systematic Reviews and Methodological Quality Analysis - AMSTAR 2

Authors, Country and Year	Aim	Databases	Descriptors	Studies Included	Bias Risk Analysis	Methodological quality of primary studies	AMSTAR 2
George ES, Marshall S, Mayr HL, Trakman GL, Tatucu-Babet OA, Lassemillante AM, Bramley A, Reddy AJ, Forsyth A, Tierney AC, Thomas CJ, Itsiopoulos C, Marx W. Australia 2019	to evaluate the effect of high versus low polyphenol olive oil on risk factors for cardiovascular disease (CVD) in clinical trials.	CINAHL, PubMed, Embase, and Cochrane	Search terms related to polyphenols (eg, polyphenol, phenol, phytochemical) and olive oil.	Randomized controlled trials that investigated CVD risk markers	Jadad scale	Not applied/Not informed	Critcially low-quality review
Ghobadi S, Hassanzadeh-Rostami Z, Mohammadian F, Nikfetrat A, Ghasemifard N, Dehkordi HR, Faghih S Iran 2019	evaluate the effects of olive oil consumption compared to other vegetable oils on blood lipids.	PubMed, web of science, Scopus, ProQuest, and Embase	(“Olive oil”) AND ("lipid" OR "lipidemia" OR "hyperlipidemia" OR "dyslipidemia" OR "cholesterol" OR "hypercoasterolemia" OR "lipoprotein" OR "LDL" OR "low density lipoprotein" OR "HDL " OR "high density lipoprotein" OR "triglyceride" OR "hypertriglyceridemia" OR “Apolipoprotein A-I” OR “Apolipoprotein B” OR ”Apo A1” OR “Apo B”) AND ("Controlled Clinical Trial" OR	Randomized controlled trials (RCTs)	Evaluation using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions	Not applied/Not informed	Critically low-quality review

			"Randomized Controlled Trial" OR "intervention" OR "controlled trial" OR randomized" OR "random" OR "randomly" OR "placebo" OR "assignment" OR "trial" OR “RCT” OR “Cross-over” OR “Parallel”				
Pastor R, Bouzas C, Tur JA Spain 2021	to evaluate whether the antioxidant effects in the metabolic syndrome are related to the levels of hydroxytyrosol or oleic acid, or their combination in olive oil	MEDLINE, Pubmed, Web of Science core collection (WOS) and Virtual Health Library (VHL) via LILACS and IBECS (Spain)	MeSH terms: "obesity", "body weight", "body mass index", "adipose tissue", "lipid metabolism", "LDL", "HDL", "VLDL", "insulin resistance", "glucose", "insulin", "hypertension", "arterial pressure", "olive oil", "oleic acid", and other (non-MeSH) terms: "total antioxidant capacity", "total antioxidant status", "hydroxytyrosol"	Clinical Trial, Controlled Clinical Trial or Randomized Controlled Trial	Evaluation using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions	Not applied/Not informed	Low-Quality Review
Schwingshackl L, Christoph M, Hoffmann G. Germany 2015	to synthesize data from randomized controlled trials investigating the effects of olive oil on markers of inflammation or endothelial function.	Cochrane Trial Register, EMBASE and MEDLINE	(“olive oil”) AND (“endothelial” OR “inflammation” OR “CRP” OR “C-reactive protein” OR “FMD” OR “flow-mediated dilatation”) AND (“randomized controlled trial” OR “randomized” OR “clinical trials as topic” OR “placebo” OR “randomly” OR “trial”) NO (“animals”)	intervention with pure olive oil or as a supplement (capsules); (2) randomized controlled trials (RCT) with parallel or crossover design	Evaluation using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions	Not applied/Not informed	High-quality review

Schwingshackl L, Krause M, Schmucker C, Hoffmann G, Rücker G, Meerpohl JJ. Germany 2019	to compare the effects of different types of olive oil (OO) on cardiovascular risk factors.	Medline, Web of Science and Cochrane Central	Not informed	Randomized controlled trials (RCTs; with a parallel or crossover design).	Evaluation using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions	GRADE	Moderate-quality review
Zamora-Zamora F, Martinez-Galiano JM, Gaforio JJ, Delgado-Rodriguez M Spain 2019	assessing olive oil consumption reduces blood pressure in adults without previous cardiovascular events	PubMed, Embase, Cochrane plus, Web of Science, Ovid, Scopus, BVS, TDR.	olive oil. Arterial Pressure. Hypertension. Blood Pressure. Diastolic Pressure. Systolic Pressure. (Randomized Controlled Trial OR systematic review OR Meta-Analysis) AND humans VHL - olive oil. hypertension. Humans.	The designs used by the studies were: double-blind parallel RCTs, double-blind, randomized crossover study, and unblinded RCTs	Evaluation using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions	Not applied/Not informed	Low-Quality Review

Table 2. Synthesis of the Results of the Articles of the Systematic Reviews

Firts Author, year (REF)	Aim	Number of Articles	Total sample	Interventions and Time	Outcomes	Main findings
George ES *et al*. (2019)	effect of high versus low polyphenol olive oil on risk factors for cardiovascular disease (CVD)	26 articles were included. 15 with an outcome evaluated in the European population and oxidative stress (EUROLIVE).	10 to 49 participants, except EUROLIVE, which included 200 participants	The use of olive oil was from 3 weeks to 3 months, there were studies with two weeks of washout. The use of olive oil was 25ml/d (n=16) and the others 25-75ml/d. The studies had HPOO (extra virgin olive oil with 150mg-800mg of polyphenols per kg of oil) and LPOO (0-132mg per kg). In 22 studies out of 26 requested a diet low in polyphenols, antioxidants, and foods rich in vitamin E.	Oxidative Stress: TBARS, LDL, HDL, lipid oxidation, glutathione peroxidase, total antioxidant capacity and antioxidant status, isoprostane excretion, protein carbonyl, 8-hydroxy-2'-deoxyguanosine, superoxide dismutase, catalase, ferric reducing ability of plasma, measures of oxidative DNA damage, paraoxonase-3 (PON-3) protein, lactonase activity, paraoxonase activity, hydroxy fatty acids, and conjugated dienes. Inflammation: CRP, IL-6, sICAM-1, sVCAM-1, MCP-1, TNF-α, fecal calprotectin, and resistin.	*Oxidative stress* *malondialdehyde* (MD: -0.07μmol/L; p=0.004) oxLDL (SMD: -0.44; p=0.01) total antioxidant capacity (SMD: 0.30; p=0.29) glutathione peroxidase (SMD: -0.04; p=0.91) *Inflammation* CRP (p=0.024) and (p<0.001) IL-6 was reduced in one study (p<0.002). Resistin was improved in the LPOO group only MCP-1 also improved in one study (p=0.022) *Blood pressure* SBP (MD: -2.03mmHg; p=0.38). DBP (MD: -2.70mmHg;

					Blood Pressure: BPD, SBP. Lipid Profile: LDL, HDL, TG, ApoB, A1 (ApoA1), and A2 (ApoA2); LDL and HDL particle size; HDL cholesterol efflux capacity; HDL fluidity, and cholesterol esters. Other outcomes: BMI, endothelial function, and blood glucose.	p=0.08) *Lipid profile* TC redução de 4.47mg/dL (p<0.0001) HDL cholesterol by 2.37mg/d (p=0.02) Lower HDL cholesterol compared to LPOO (by 3.95mg/dL; p=0.01) LDL cholesterol following intervention with HPOO (MD: 1.12mg/dL; p=0.37). HPOO had no effect on TG compared to LPOO in a mixed sample of healthy and hypercholesterolemia adults (MD 0.34mg/dL; p=0.85).

Ghobadi S *et al*. (2019)	evaluate the effects of olive oil consumption compared to other vegetable oils on blood lipids.	27 articles	1089 participants	Olive oil was compared with vegetable oils, and 11 studies used virgin olive oil. 8 studies compared olive oil with rapeseed oil, 6 with flower oil, 4 with corn oil, 3 with palm oil, 3 with soybean oil, 2 with Flaxseed oil and only 1 study used several (Soybean, primrose, camellia , peanut, and rice).	TC, LDL-c, HDL-c, TG, ApoA1, ApoB	*Olive oil and other plant oils* Serum CT (WMD= 6.27 mg/dl; p=0.001), in the subgroup of participants aged ≤ 50 years (WMD= 8.1 mg/dl) and consumption ≤ 30 days subgroup of intervention duration (WMD = 8 .23 mg/dl). LDL-c (WMD = 4.2 mg/dl; p = 0.003) Serum LDL-c (WMD=6.43 mg/dl; p=0.005), in the subgroup of participants ≤ 50 years of age (WMD=7 mg/dl) and olive oil treatment for ≤ 30 days, decreased LDL-c (WMD = 7 mg/dl), normolipemic subgroup (WMD = 5.9 mg/dl), all significantly lower results compared to oils from other plants. HDL-c (WMD=1.37 mg/dl; p=0.007). Serum HDL-c was significantly higher in olive oil compared to W3-rich oils (WMD=1.9 mg/dl; p=0.008) and miscellaneous oils (WMD=4.11 mg/dl; p=0.01), Subgroup analyzes indicated that at > 30 days of intervention

						duration (WMD = 1.77 mg/dl; p=0.02), participants aged ≤ 50 years (WMD= 1.55 mg/dl; p=0, 01) and the normolipidemic group (WMD= 1.53 mg/dl; p=0.03). TG (WMD=4.31 mg/dl; p=0.03). Pooled effects demonstrated that olive oil decreased serum TG less than W3-rich (WMD=8.32 mg/dl; p=0.004). *Types of Olive Oil* ROO decreased serum CT minus (WMD=5.21 mg/dl; p=0.023). Unrefined virgin olive oil decreased serum TG less (WMD=7.75 mg/dl; p=0.002)

Pastor R *et al*. (2021)	to evaluate whether the antioxidant effects in the metabolic syndrome are related to the levels of hydroxytyrosol or oleic acid, or their combination in olive oil	76 articles 4 - hydroxytyrosol 23 - oleic acid 49 - olive oil	10,966 participants	Supplementation with oleic acid, hydroxytyrosol or olive oil. From 2 weeks to 6 months of intervention.	Subgroups based on the MetS Body composition; Lipid profile; Glycid Profile; Blood pressure	*Diet supplemented with Hydroxytyrosol* 22 MetS factors (p=0.920) *Diet supplemented with Oleic Acid* 117 MetS factors (p = 0.150) Body composition (SMD − 0.06; p = 0.300) Lipid profile (SMD 0.06; p = 0.050) Glycemic profile (SMD = 0.04; p = 0.59) Blood pressure (SMD = 0.02; p = 0.800) *Olive Oil Supplemented Diet* 246 MetS factors (SMD - 0.01; p = 0.550) Body composition (SMD = − 0.02; p = 0.560) Lipid profile (SMD = 0.01; p = 0.81) Glycemic Profile (SMD = -

						0.00; p = 0.95) Blood Pressure (SMD = − 0.00; p = 1.00) *Diet supplemented with Olive Oil, Hydroxytyrosol and Oleic Acid* Antioxidant Capacity (SMD = 0.31; p = 0.35).
Schwingshackl L *et al*. (2015)	effects of olive oil on markers of inflammation or endothelial function.	30 studies included	3106 participants	The comparison was made between the Mediterranean diet rich in olive oil and extra virgin through capsules and control with other oils. The average consumption of olive oil was 50ml/day or 1-10g/day of capsules. The total polyphenol content was from 35mg/100g of olive oil to 328g/kg. Total duration of 208 weeks.	PCR, IL-6, TNF-alfa, Adiponectina, ICAM-1, VCAM-1, FMD (%).	Olive oil resulted in a significant reduction in CRP (MD: -0.64 mg/L; p <0.0001). Reduction in IL-6 levels (MD: -0.29; p <0.04). FMD showed a significant increase (MD: 0.76; p < 0.002). With respect to subgroups comparing olive oil to oil with W3, changes in FMD were significantly greater (MD: 0.63; p < 0.003). sE-Selectin (SMD: 3.16ng/mL; p=0.00001) sP-Selectin (SMD: 10.78ng/mL; p=0.002)

						sICAM-1 (SMD: -0.02 ng/L; p=0.02)
Schwingshackl L *et al*. (2019)	to compare the effects of different types of olive oil (OO) on cardiovascular risk factors.	16 studies in the systematic review and only 14 used in the meta-analysis	611 participants	Olive oil was used in capsules or taken orally, used for at least 3 to 12 weeks. Olive oil consumption ranged from 20ml/d to 75ml/d. The consumption of total polyphenols averaged from 0mg/d to 21.6mg/d.	LDL-c, oxLDL-c, HDL-c, TC, TG, SBP, DBP	HP(E)VOO slightly reduced LDL-C compared to LP(E)VOO (MD: -0.14 mmol/L; p= not shown), compared to ROO, all other types of OO (MOO, LP (E)VOO and HP(E)VOO did not show a significant reduction in LDL-C. HP(E)VOO can reduce xLDL-C compared to ROO (SMD: 0.68; p= not shown). oxLDL-C EVOO was more effective compared to ROO (SMD: 1.25) and a 5 ml/d dose of OO phenolic compounds can improve oxLDL-C compared to ROO (SMD: 0.60).

						HP(E)VOO compared to ROO (MD: 2.99 mmHg; p=not shown) can generate a reduction in SBP. VOO may improve SBP compared to ROO (MD: 3.28 mmHg; p=not shown), and a dose of 5 ml/d of phenolic OO compounds may reduce SBP compared to a daily dose of <1 ml/d. d.
Zamora-Zamora F *et al.* (2018)	consumption of olive oil reduces blood pressure in adults without previous cardiovascular events	15 studies	6651 participants	The use of olive oil as an intervention was capsules (1-6g/day) or EVOO (extra virgin olive oil) from 10 to 50ml/day. Only 1 article recommended associating 30min of physical activity (walking) 3x a week.	SBP and DBP	DBP (SMD: -0.73 mm Hg, p < 0.001). EVOO showed a reduction in BPD (SMD: -1.44 mm Hg; p < 0.001). Capsules showed no significant reduction in BPD (SMD: 0.14 mm Hg, p = 0.5). Olive oil showed no more SBP reduction than other fats (MDs = -0.11). no significant effect was obtained for either capsules or liquid olive oil on SBP.

Subtitle: See list of abbreviations

Table 3. Results of the ROBIS tool - Risk of bias from Systematic Reviews

Firts Author, year (REF)	Domain 1: Study eligibility criteria	Domain 2: Identification and selection of studies	Domain 3: Data collection and study appraisal	Domain 4: Synthesis and findings	Judging risk of bias
George ES *et al.* (2019)	Low concern	Low concern	Low concern	High concern	High risk of bias
Ghobadi S *et al*. (2019)	Low concern	Low concern	Unclear concern	High concern	High risk of bias
Pastor R *et al.* (2021)	Low concern	Low concern	Low concern	High concern	High risk of bias
Schwingshackl L *et al.* (2015)	Low concern	Low concern	Low concern	Low concern	Low risk of bias
Schwingshackl L *et al.* (2019)	Low concern	Low concern	Low concern	Low concern	Low risk of bias
Zamora-Zamora F *et al.* (2018)	Low concern	Low concern	Low concern	High concern	High risk of bias

Table 4. GRADE Assessment of Meta-Analysis: Certainty of evidence for the association between olive oil consumption and outcomes

Firts Author, year (REF)	Risk of bias	Inconsistency	Imprecision	Indirectness	Publication bias	Large effect	Confounders	Evidence Grading
Outcome: olive oil consumption and blood pressure								
George ES *et al.* (2019)	Present	Present SBP I2: 79% DBP I2: 78%	NI SBP (95%CI -6.57-2.50) DBP (95%CI -5.71, -0.31)	NI	Absent	Reported SBP (MD: -2.03mmHg) DBP (MD: -2.70mmHg)	NR	Moderate ⊕⊕◯◯
Zamora-Zamora F *et al.* (2018)	Present	Present SBP I2= 85,1% DBP I2= 84,5%	Identified SBP (95%CI: -2,34, 1,23) DBP (95%CI: -1,24, 0,82)	NI	Present	NS SBP (SMD = -0,55) DBP (SMD = -0,21)	NR	High ⊕⊕⊕◯
Schwingshackl L *et al* (2019)	Present	NR	Identified Compared types of OO (95%CI: 5,39, 0,35)	NI	Present	NS (MD: 2,87 mmHg) and (MD: 2,99 mmHg)	NR	Moderate ⊕⊕◯◯

			and (95%CI: 6,12, 0,15)					
Pastor R *et al* (2021)	Present	Present I2 = 37%	Identified (95%CI: -0.06, 0.05)	NI	Absent	NS SMD = − 0.00	Considered, but not detailed.	Moderate ⊕⊕◯◯
Outcome: olive oil consumption and inflammatory markers								
George ES *et al.* (2019)	Present	Present Malondialdehyde I2: 88%	NI Malondialdehyde (95%CI -0,12, -0,02)	NI	Absent	Reported Malondialdehyde (SMD -0,07)	NR	High ⊕⊕⊕◯
Schwingshackl L *et al* (2015)	Present	Present CRP I2: 66% Adiponectin I2: 56% IL-6 I2: 62% TNFα I2: 95% sE-Selectin I2: 0 sP-Selectin I2: 41	Identified CRP (95%CI -0,96, -0,31) Adiponectin (95%CI -0,20, 1,09) IL-6 (95%CI -0,57,-0,02) TNFα (95%CI -0,02,0,07)	NI	Present	Reported CRP (SMD - 0,24) IL-6 (SMD - 0,29) FMD (SMD 0,76)	NR	High ⊕⊕⊕◯

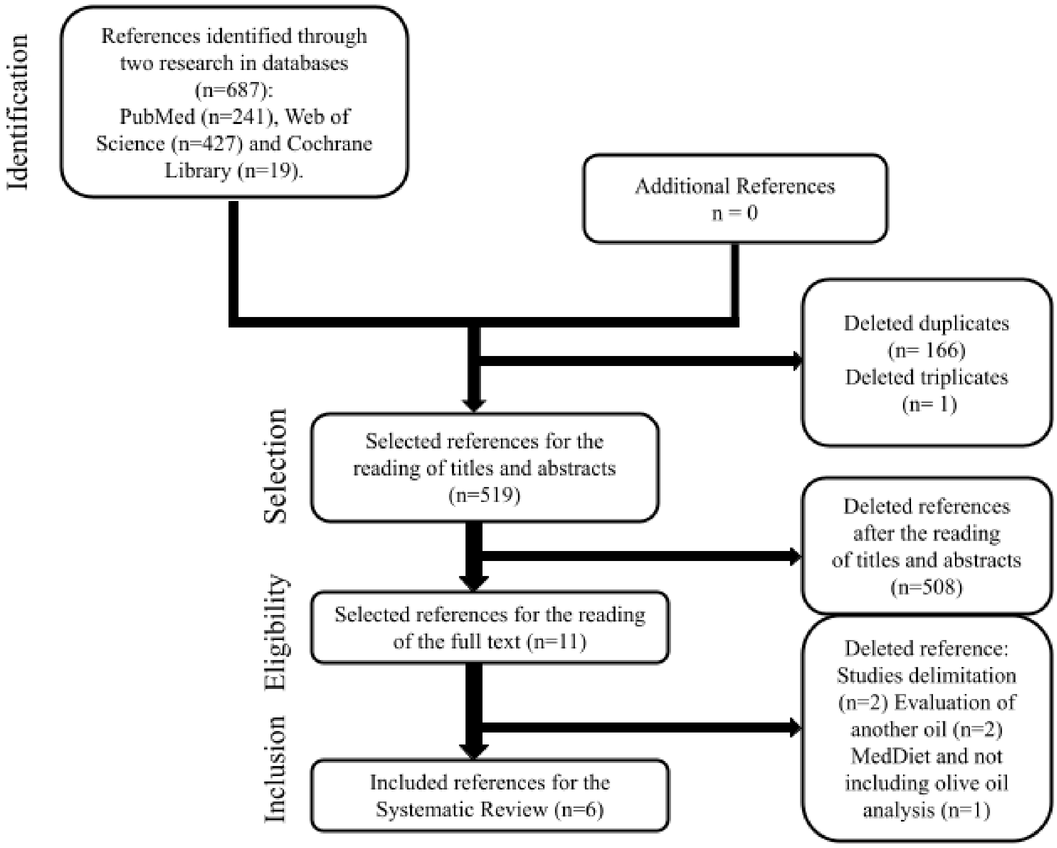
		sICAM-1 I2: 84 sVCAM-1 I2: 37% FMD I2: 26%	sE-Selectin (95%CI -4,07, -2,25) sP-Selectin (95%CI 4,01, 17,54) sICAM-1 (95%CI -0,04, 0,00) sVCAM-1 (95%CI -0,05, 0,01) FMD (95%CI 0,27, 1,24)					
Outcome: olive oil consumption and lipid profile								
George ES *et al.* (2019)	Present	Present TC I2: 0% LDL I2: 83,5% oxLDL I2: 49% HDL-c I2: 66,2%	NI TC (95%CI: -6,54, -2,39) LDL (95%CI: - 7,27, 0,19) oxLDL (95%CI: -0,78, -0,10) HDL-c (95%CI: 0,41, 5,04)	NI	Absent	Reported TC (SMD: - 4,47) LDL (SMD: -3,54) oxLDL (SMD: -0,44) HDL-c (SMD: 2,73)	NR	High ⊕⊕⊕◯
Ghobadi S *et al* (2019)	Present	Present TC I2: 38,2%	NI TC (95%CI: 4,23,	NI	Present	Reported TC (SMD 7,48)	Considered, but not	High ⊕⊕⊕◯

		LDL I2: 22,9% HDL-c I2: 0% TG I2: 0%	10,72) LDL (95%CI: 1,39, 7,01) HDL-c (95%CI 0,38, 2,36) TG (95% 0,5, 8,12)			LDL (SMD 4,2) HDL-c (SMD 1,37) TG (SMD 4,31)	detailed	
Schwingshackl L *et al* (2019)	Present	NR	Identified Compared types of OO LDL-C (95% CI: 0.28, 0.01) oxLDL-C (95% CI: 1.31, 0.04)	NI	Present	Reported LDL-C (MD: 0.14 mmol/L) oxLDL-C (SMD: 0.68)	NR	Moderate ⊕⊕◯◯
Pastor R *et al* (2021)	Present	Present I2 = 32%	Identified (95%CI: -0.06, 0.05)	NI	Absent	NS SMD = − 0.01	Considered, but not detailed.	Low ⊕◯◯◯
Outcome: olive oil consumption and metabolic syndrome								
Pastor R *et al* (2021)	Present	Present I2 = 55%	Identified (95%CI -0.05, 0.03)	NI	Absent	NS SMD − 0.01	Considered, but not detailed	Low ⊕◯◯◯

SMD - combined standardized mean differences;
I2 - Heterogeneity statistics;
CI - confidence interval;
NI = not identified;

NR = not reported;
NS = not significant
GRADE Working Group Degrees of Evidence: High Quality: More research is very unlikely to change our confidence in the effect estimate. Moderate quality: Additional research is likely to have a major impact on our confidence in the effect estimate and may change the estimate. Low quality: More research is very likely to have a major impact on our confidence in the effect estimate and will likely change the estimate. Very low quality: we are very uncertain about the estimate.

Figure 1 - Results of studies selection



7 CONSIDERAÇÕES FINAIS

Buscando construir uma relação entre os alimentos e a saúde humana, esse trabalho visou caracterizar científicamente os alimentos como possíveis fontes de proteção e também potenciais fatores de risco para doenças, de acordo com a análise de consumo e composição. Como proposta inicial, foi determinada a relação entre a contribuição do consumo de alimentos ultraprocessados e o risco de mortalidade, através da realização de uma revisão sistemática pode-se concluir que é existente na literatura pesquisas que demonstram uma associação positiva entre o consumo e o aumento do risco de mortalidade.

Os trabalhos incluídos na presente revisão reforçaram essa íntima relação entre o consumo de ultraprocessados e mortalidade ao apresentarem medidas estatísticas de razão de risco maiores de mortalidade em quem consome essa categoria alimentar em uma maior frequência ou quantidade.

Em relação aos efeitos protetores dos alimentos, nossa revisão de revisões sistemáticas buscou elucidar e sintetizar as evidências presentes na literatura sobre o consumo de azeite de oliva e os fatores de risco cardiovascular. Podemos concluir que nas revisões sistemáticas encontradas é evidente a associação protetora do azeite de oliva nos fatores como atuante na melhora da pressão arterial, reduzindo a taxa média da pressão arterial diastólica, redução de marcadores de perfil lipidico, melhora nos marcadores inflamatórios celulares e em fatores determinantes de síndrome metabólica.

As revisões incluídas avaliaram o consumo de azeite de oliva de diversas formas (líquido ou cápsulas), suplementado à dieta e também comparado com outros óleos, além de realizar uma análise comparativa entre os tipos de azeite de oliva (ROO, VOO, EVOO, LPOO, HPOO), com tais comparações conclui-se que quanto maior o teor fenólico, mais potente é a resposta metabólica protetora aos fatores de risco cardiovasculares.

Dados os resultados sugestivos e favoráveis alcançados pelo consumo de azeite de oliva como alimento para auxiliar na redução dos fatores de risco cardiovascular tem sido cada vez mais importantes e devem ser incentivados como forma de fator de proteção. A educação nutricional adequada é importante para que o consumo de alimentos ultraprocessados seja realizado de maneira consciente e moderada, para menor impacto prejudicial à saúde.

Por fim, espera-se que os resultados encontrados nesta dissertação contribuam para o reconhecimento dos alimentos como uma terapia complementar para a prevenção de doenças e para a promoção de saúde.

8 ANEXOS

Anexo I – Primeira página do Cadastro PROSPERO (Artigo 1)

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

The effect of olive oil consumption on cardiovascular disease in the adult population: an overview of systematic reviews and meta-analyses

To enable PROSPERO to focus on COVID-19 submissions, this registration record has undergone basic automated checks for eligibility and is published exactly as submitted. PROSPERO has never provided peer review, and usual checking by the PROSPERO team does not endorse content. Therefore, automatically published records should be treated as any other PROSPERO registration. Further detail is provided here.

Citation

Kathleen Kruger Peres, Rafaella Câmara Rocha Menezes, Isabella Rosa da Mata, Simone Morelo Dal Bosco. The effect of olive oil consumption on cardiovascular disease in the adult population: an overview of systematic reviews and meta-analyses. PROSPERO 2022 CRD42022322569 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022322569

Review question

What is the effect of olive oil consumption in cardiovascular diseases?

Searches

Databases: Cochrane Library, Web of Science e PubMed

Inclusion criteria: Studies that evaluate the consumption of olive oil orally. Human studies. Adults with the previously cardiovascular disease aged above 18. Review articles and meta-analysis of Clinical trials and randomized clinical trials.

Exclusion criteria: experimental studies in vitro, experimental studies with animals, cross-sectional, case-control, cohort studies, Clinical trials and randomized clinical trials. Review articles and meta-analysis of cross-sectional, case-control, cohort studies. Pregnant Women and Infants. Studies with children or adolescents.

- Keywords: "Olive Oil" OR "Oil, Olive" OR "Oils, Olive" OR "Olive Oils"

AND

"Cardiovascular Diseases" OR "Cardiovascular Disease" OR "Disease, Cardiovascular" OR "Diseases, Cardiovascular"

AND

"systematic review" OR "meta-analysis" OR "systematic literature review" OR "systematic review" OR review

No date / language restrictions.

Filter: no filters

Search strategy

https://www.crd.york.ac.uk/PROSPEROFILES/322569_STRATEGY_20220401.pdf

Types of study to be included

Anexo II – Primeira página do Cadastro PROSPERO (Artigo 2)

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

Consumption of Ultra-Processed Foods and the Impact Human Health: A Systematic Review

To enable PROSPERO to focus on COVID-19 submissions, this registration record has undergone basic automated checks for eligibility and is published exactly as submitted. This protocol has been amended since registration with changes to the PICOS criteria, data extraction, quality assessment, or data synthesis methods. Previous versions of the registration may be viewed for comparison. PROSPERO has never provided peer review, and usual checking by the PROSPERO team does not endorse content. Therefore, automatically published records should be treated as any other PROSPERO registration. Further detail is provided here.

Citation

Kathleen Kruger Peres, Simone Morelo Dal Bosco, Rafaella Câmara Rocha Menezes, Isabella Rosa da Mata, Anna Caroline Bertoletti. Consumption of Ultra-Processed Foods and the Impact Human Health: A Systematic Review. PROSPERO 2020 CRD42020205382 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020205382

Review question

How does ultra-processed foods consumption impact in the health human?

Is there a association between the consumption of ultra-processed foods and the risk of comorbidities?

Searches

-Databases: Scopus, Web of Science e PubMed

- Keywords: "Ultra-processed food"

No date / language restrictions. Filter: no filters

-Inclusion criteria: Studies that evaluate the consumption of ultra-processed products. Health outcomes in general. Human studies. Previously healthy adults (18-60 years) without comorbidities. No comorbidities.

-Exclusion criteria: Pregnant Women and Infants. Studies with children or adolescents. Studies with the Elderly. Adults with comorbidities. Review studies, meta-analyzes. Animal studies. In vitro studies.

Search strategy

https://www.crd.york.ac.uk/PROSPEROFILES/205382_STRATEGY_20200821.pdf

Types of study to be included

Inclusion criteria: cross-sectional, case-control, cohort studies.

Exclusion criteria: experimental studies in vitro, experimental studies with animals, review articles and metaanalyzes.

Condition or domain being studied