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RELAÇÃO ENTRE CAPACIDADE ANTIOXIDANTE DA DIETA, DEPRESSÃO E SONO EM GRADUADOS BRASILEIROS-*ESTUDO CUME*

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Tese de doutorado apresentada ao Programa de Pós-graduação em Saúde Coletiva, área de concentração: Processo, Saúde-Adoecimento e seus determinantes, da Faculdade de Medicina da Universidade Federal de Juiz de Fora como requisito parcial para a obtenção do título de Doutora em Saúde Coletiva.

Orientador: Profª. Drª. Aline Silva de Aguiar

Coorientadoras: Profª. Drª. Ana Paula Boroni Moreira

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Juiz de Fora

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“Porque se chamavam homens também se chamavam sonhos e sonhos não envelhecem”

Márcio Borges, Milton Nascimento, Lô Borges.

RESUMO

Introdução: A população brasileira vivencia uma grande transição demográfica e epidemiológica. Atrelada a essas mudanças, vem crescendo a incidência de transtornos mentais como a depressão. Dados da linha de base do estudo Coorte de Universidades Mineiras (Estudo CUME) mostram grande prevalência de depressão entre os seus participantes. Alterações no sono também são crescentes na população geral, sendo tanto consequência quanto fator de risco para a depressão. Visto que o estresse oxidativo pode contribuir para o agravamento das patologias supracitadas, uma maior Capacidade Antioxidante da Dieta (CATd) poderia atuar como um fator de proteção para essas comorbidades. **Objetivo Geral:** Avaliar a relação entre a CATd, depressão e sono em participantes do estudo CUME. **Metodologia:** O estudo CUME é uma coorte aberta com egressos de instituições federais de ensino superior do estado de Minas Gerais. A primeira coleta de dados da linha de base ocorreu, de forma online, no ano de 2016. O questionário da linha de base (Q_0) contou com questões relativas aos aspectos sociodemográficos, antropométricos, estilo de vida, saúde e um Questionário de Frequência do Consumo Alimentar (QFCA) validado para a população de estudo. Os questionários de seguimento se dão a cada dois anos (Q_2, Q_4 ...) e apresentam questões relativas às mudanças do estilo de vida, no consumo alimentar e, a alterações na saúde em relação à coleta basal. A cada onda de coleta novos potenciais participantes recebem o convite para responder o Q_0. Da mesma forma, novas universidades federais do estado de Minas Gerais são convidadas a participarem do estudo. Para a presente tese, foram realizados dois estudos: um com recorte transversal e outro com recorte longitudinal com participantes da coorte CUME. A CATd foi obtida pelo método Poder Antioxidante de Redução Férrica (FRAP), através dos dados do QFCA aplicado na linha de base. Para maior sensibilidade das análises os valores de Capacidade Antioxidante Total de Grupos Alimentares (CATga) também foram calculados. *Estudo transversal:* o estudo transversal foi realizado com dados da linha de base da coorte CUME. O tempo de sono foi classificado como sono muito curto/curto (≤ 6 horas por noite), sono normal (7-8 horas por noite) e sono longo (≥ 9 horas por noite). Para estimar o Odds Ratio e o Intervalo de Confiança de 95% (IC:95%) entre sono muito curto/curto e sono longo com quartis CATd e CATga, foram utilizados modelos de regressão logística multinomial, ajustados para variáveis sociodemográficas e de estilo de vida. *Estudo Longitudinal:* no estudo longitudinal a incidência de depressão foi estimada pelo diagnóstico médico autorreferido de depressão durante os anos de acompanhamento da coorte. Modelos de

regressão de Cox foram usados para relacionar quartis de CATd e a CATga com a incidência de depressão. **Resultados:** *Estudo transversal:* A amostra foi composta por 6.387 egressos, a idade média dos participantes foi de 35.32 ± 9.29 anos e 67.87% dos mesmos eram do sexo feminino (n= 4.335). Foi observada menor razão de chances de sono muito curto/curto apenas para o segundo quartil de CATd em relação ao primeiro. Associações inversas com sono muito curto/curto foram observadas para CATga de frutas, feijões e lentilhas, legumes e verduras e óleos e gorduras. Maiores chances de sono muito curto/curto foram observadas para a maior CATga de chás e cafés. Para o sono longo, associações inversas foram observadas para o maior quartil de CATga de oleaginosas e para o terceiro quartil de chás e cafés em relação ao primeiro quartil. *Estudo longitudinal:* A amostra do estudo longitudinal foi composta por 2.572 participantes, o tempo médio de acompanhamento foi de 2,96 ± 1,00 anos e foram observados 246 casos incidentes de depressão (32,3/1.000 pessoas-ano). Não foram observadas associações entre maior CATd e menor risco de desenvolver depressão após o ajuste para possíveis fatores de confusão. A incidência de depressão foi inversamente associada com CATga de feijão e lentilhas. Já a CATga de "Junk Food" associou-se positivamente com maior incidência de depressão após todos os ajustes. **Conclusões:** Nossos achados não suportam uma associação entre CATd e a incidência de depressão e tempo de sono em uma população brasileira com nível superior. Entretanto, importantes associações entre a CATga para alimentos como feijões e "Junk Food" foram observadas para a incidência de depressão. Da mesma forma, o tempo de sono apresentou associações com CATga para alimentos como feijões e lentilhas, frutas, hortaliças, chá e cafés, oleaginosas e óleos e gorduras. Os resultados aqui apresentados mostram a importância de se considerar a matriz alimentar em que os antioxidantes estão inseridos. Assim, antioxidantes inseridos dentro de um padrão alimentar saudável podem ser benéficos para o sono e saúde mental, sendo necessários mais estudos para confirmação desses achados.

Palavras chave: Capacidade Antioxidante da Dieta, Depressão, Sono, Estudo de Coorte, Consumo Alimentar.

ABSTRACT

Introduction: The Brazilian population is experiencing a major demographic and epidemiological transition, linked to these changes, the incidence of mental disorders such as depression has been increasing. In fact, baseline data from the Cohort of Universities of Minas Gerais (CUME Study) show a high prevalence of depression among its participants. Changes in sleep are also increasing in the general population, being both a consequence and a risk factor for depression. Since oxidative stress can contribute to the worsening of these conditions, a higher Dietary Antioxidant Capacity (dTAC) could act as a protective factor for these comorbidities. General **Objective:** To evaluate the relationship between dTAC, depression and sleep in participants of the CUME cohort. **Methodology:** The CUME study is an open cohort with graduates from federal institutions of higher education in the state of Minas Gerais. The first baseline data collection took place in the year 2016. The baseline questionnaire (Q_0) included questions related to sociodemographic, anthropometric, lifestyle, and health aspects, in addition to a food consumption frequency questionnaire (FFQ) validated for the study population. The follow-up questionnaires are given every two years (Q_2, Q_4...) and present questions related to changes in lifestyle, food consumption, and changes in health in relation to the baseline collection. At each collection follow-up new potential participants receive the invitation to answer Q_0. Likewise, new Federal Universities in the state of Minas Gerais are invited to participate in the study. Two studies were carried out, one with a cross-sectional approach and the other with a longitudinal approach, with participants from the CUME cohort. The dTAC was obtained by the Iron Reduction Antioxidant Power (FRAP) method, using the FFQ data applied at baseline. For greater sensitivity of the analysis, the values of Total Antioxidant Capacity of food groups (TACfg) were also calculated. The cross-sectional study was performed using baseline data from the CUME cohort. Sleep time was classified as very short/short sleep (≤ 6 hours per night), normal sleep (7-8 hours per night), and long sleep (≥ 9 hours per night). To estimate the Odds Ratio and 95% Confidence Interval between very short/short sleep and long sleep with TACd and TACfg quartiles, multinomial logistic regression models were used, adjusted for sociodemographic and lifestyle variables. In the longitudinal study, the incidence of depression was estimated by self-reported medical diagnosis of depression during the years of follow-up of the cohort. Cox regression models were used to associate the dTAC and TACfg quartiles with the incidence of depression. **Results:** In the cross-sectional study, the sample

consisted of 6,387 graduates, the average age of participants was 35.32 ± 9.29 years and 67.87% of them were female (n= 4,335). A lower odds ratio of very short/short sleep was observed only for the second quartile of dTAC compared to the first. Inverse associations with very short/short sleep were observed for TACfg of fruits, beans and lentils, legumes and vegetables, and oils and fats. Greater chances of very short/short sleep were observed for the highest TACfg for the teas and coffees group. For long sleep, inverse associations were observed for the highest TACfg quartile of oilseeds and for the third quartile of teas and coffees in relation to the first quartile. The longitudinal study sample consisted of 2,572 participants, the mean follow-up time was 2.96±1.00 years, and 246 cases of depression were observed (32.3/1,000 person-years). No associations were observed between higher dTAC and lower risk of developing depression after adjusting for potential confounders. The incidence of depression was inversely associated with TACfg of beans and lentils. The TACfg of the "Junk Food" group was positively associated with a higher incidence of depression after all adjustments. **Conclusions:** Our findings do not support an association between dTAC and the incidence of depression and sleep time in a highly educated Brazilian population. However, important associations between TACfg of beans and "Junk food" were observed for the incidence of depression. Likewise, sleep time was associated with TACfg for foods such as beans and lentils, fruits, vegetables, tea and coffee, oilseeds and oils and fats. The results presented here show the importance of considering the food matrix in which antioxidants are inserted. Thus, antioxidants included within a healthy eating pattern can be beneficial for sleep and mental health, and further studies are needed to confirm these findings.

Keywords: Dietary Antioxidant Capacity, Depression, Sleep, Cohort Study, Food Consumption.

LISTA DE FIGURAS

ARTIGO DE REVISÃO: Association of dietary total antioxidant capacity with depression, anxiety, and sleep disorders: A systematic review of observational studies

METODOLOGIA

ARTIGO ORIGINAL 2. Association between total dietary antioxidant capacity and food groups and incidence of depression in a cohort of Brazilian graduates (CUME Project)

LISTA DE TABELAS

ARTIGO DE REVISÃO: Association of dietary total antioxidant capacity with depression, anxiety, and sleep disorders: A systematic review of observational studies

ARTIGO ORIGINAL 1. Total dietary antioxidant capacity and food groups and their relationship with the sleep time of Brazilian graduates (CUME study).

ARTIGO ORIGINAL 2. Association between total dietary antioxidant capacity and food groups and incidence of depression in a cohort of Brazilian graduates (CUME Project)

SUMÁRIO

1. INTRODUÇÃO

O Brasil tem vivenciado uma grande transição demográfica, epidemiológica e nutricional. Ao longo da história, a transição nutricional tem sido caracterizada por modificações significativas na estrutura do padrão alimentar da população, com aumento do consumo de alimentos industrializados que apresentam alto teor de açúcares e gorduras em sua composição. Essas alterações relacionam-se diretamente com as mudanças sociodemográficas e de condições de saúde (ABLARD, 2021; MALTA et al., 2017). Desta forma, alterações no perfil alimentar e estilo de vida interferem na incidência e prevalência das Doenças Crônicas não Transmissíveis (DCNTs) e transtornos mentais comuns, como a depressão (LI et al., 2017; SANCHEZ-VILLEGAS et al., 2018).

Quando se trata de investigações epidemiológicas que tragam informações acerca de doenças crônicas em egressos brasileiros, destaca-se o estudo Coorte de Universidades Mineiras (CUME). Realizado com graduados brasileiros, o estudo CUME tem por objetivo principal avaliar o impacto do padrão alimentar brasileiro e da transição nutricional sobre as doenças e agravos não transmissíveis. Dados da linha de base deste estudo retratam alta prevalência de depressão em adultos jovens, mostrando que apesar do alto nível de instrução esse é um grupo vulnerável a essa patologia (DOMINGOS et al., 2018; SANTOS et al., 2021).

Em relação aos transtornos mentais comuns, a depressão é evidenciada pela sua alta prevalência. Estima-se que no ano de 2015 aproximadamente 4,4% da população mundial e 5,8% dos brasileiros apresentavam depressão. Destaca-se que o Brasil é o país com maior prevalência de depressão em toda América Latina, sendo que a prevalência de autorrelato de depressão em graduados brasileiros do estudo CUME foi de 12,8%, superior ao encontrado em nível nacional (DOMINGOS et al., 2018; WHO; WORLD HEALTH ORGANIZATION/WHO, 2017). Dados do Global Burden of Disease (GBD), com 195 países e regiões do mundo, mostram que os casos incidentes de depressão aumentaram de 17,2 milhões em 1990 para 25,8 milhões em 2017, representando um aumento de 49,86% (LIU et al., 2020).

O termo depressão pode ser utilizado de forma abrangente para designar vários tipos de transtornos depressivos. De acordo com o Manual Diagnóstico e Estatístico de Transtornos Mentais (DSM-V) os transtornos depressivos podem ter características e diagnósticos específicos. Entre as categorias de transtornos depressivos mais abrangentes destacam-se Transtorno Depressivo Maior (incluindo episódio depressivo maior) e o transtorno depressivo

persistente (Distimia) (AMERICAN PSYCHIATRIC ASSOCIATION, 2014). O Transtorno Depressivo Maior se manifesta com sintomas como baixa energia, perda de interesse, de prazer e humor deprimido, podendo ser classificado como leve, moderado ou grave. Já a Distimia apresenta sintomas parecidos aos do Transtorno Depressivo Maior, sendo que menos intensos e mais duradouros (WHO; WORLD HEALTH ORGANIZATION/WHO, 2017). Destaca-se que os transtornos depressivos podem afetar de forma substancial a vida cotidiana de um indivíduo, de modo que as formas mais graves destes transtornos podem levar ao suicídio (WHO; WORLD HEALTH ORGANIZATION/WHO, 2017). Ademais, a depressão está relacionada com doenças crônicas, menor capacidade de trabalho, pior qualidade de vida geral e, por consequência, aumento dos gastos em saúde (BOING et al., 2012; LINDER et al., 2020; MACQUEEN et al., 2017).

Um fator de risco importante a ser investigado com relação à depressão e às DCNTs são as alterações do sono (HUMER; PIEH; BRANDMAYR, 2020). O sono é um evento biológico de grande complexidade e está relacionado a restauração e promoção do funcionamento adequado do organismo, portanto é um importante processo psicofisiológico para a função cerebral e saúde mental (HUMER; PIEH; BRANDMAYR, 2020; MORAIS et al., 2017). Entretanto, alterações no estilo de vida decorrentes da transição epidemiológica, nutricional e comportamental dos últimos anos tem afetado os padrões normais de sono (QUADRA et al., 2022). Nesta perspectiva, estudos epidemiológicos destacam grandes prevalências de alterações e distúrbios no sono na população geral (BARROS et al., 2020; GAJARDO et al., 2021; HUMER; PIEH; BRANDMAYR, 2020). Dados de 60.202 participantes da Pesquisa Nacional de Saúde de 2013 mostraram que 28,9% dos participantes relataram algum problema no sono (dificuldade para adormecer, acordar frequentemente a noite ou dormir mais que o de costume) em pelo menos 50% dos dias nas últimas duas semanas (GAJARDO et al., 2021). Por sua vez, um estudo, realizado durante a pandemia do COVID-19, com 45.161 brasileiros mostrou que 43,5% dos mesmos passaram a observar problemas no sono (BARROS et al., 2020).

São várias as variáveis utilizadas para avaliar a qualidade do sono, podendo ser citadas, tempo de cama, tempo de sono, latência do sono, eficiência do sono, estágios do sono com movimento oculares rápido (sono REM) e sem movimentos oculares rápidos (sono não REM), entre outros (SHRIVASTAVA et al., 2014). Entre os fatores relativos à qualidade do sono, a sua duração vem ganhando destaque e significância em estudos epidemiológicos (ANTZA et al., 2022). Durações do sono de 7 até 9 horas podem ser consideradas adequadas para adultos (HIRSHKOWITZ et al., 2015; WATSON et al., 2015). Assim, tanto as durações

do sono curtas quanto longas estão relacionadas com desfechos em saúde mental e metabólica. Um estudo com 4.417 idosos observou que durações do sono ≤ 6 horas e > 9 horas relacionaram-se com menor desempenho cognitivo, maior Índice de Massa Corporal (IMC) e sintomas depressivos (WINER et al., 2021). Por sua vez, uma recente revisão de estudos epidemiológicos mostrou que a curta duração do sono é um fator de risco independente para a obesidade e para o Diabetes Melito tipo 2 (ANTZA et al., 2022).

Devido às altas prevalências e aos seus impactos na qualidade de vida e saúde populacional, vê-se a importância de estudar os principais fatores de risco para depressão e alterações no sono (BAGLIONI et al., 2011; HUMER; PIEH; BRANDMAYR, 2020; JI; GRANDNER; LIU, 2017). Desta forma, é importante compreender a relação do sono e da depressão com o estresse oxidativo. Assim, o cérebro é um órgão extremamente vulnerável, devido a sua alta utilização de oxigênio, o que pode colaborar para o aumento da criação de Espécies Reativas de Oxigênio (EROs) (NG et al., 2008; CLARCK; VISSEL, 2014). Ao mesmo tempo, esse órgão possui uma constituição rica em lipídeos os quais são substratos para oxidação, levando a neuroinflamação, a qual relaciona-se a patologia da depressão e a alterações nos padrões de sono (BALMUS et al., 2016; BISWAS, 2016; CLARK; VISSEL, 2014; NG et al., 2008). O estresse oxidativo também pode relacionar-se a distúrbios do sono por meio de alterações no ciclo circadiano (WILKING et al., 2013).

Quando se trata de fatores de risco modificáveis, a alimentação deve ser investigada. Uma vez que há relação entre o aumento de estresse oxidativo com a depressão e alterações no sono, uma alimentação rica em antioxidantes poderia atuar como um fator preventivo (ABSHIRINI et al., 2019; DANESHZAD et al., 2020; FARHANGI; VAJDI; FATHOLLAHI, 2020; HERMSDORFF et al., 2011b). Desta forma, os antioxidantes da dieta são os principais contribuintes externos para melhora do potencial antioxidante humano. Assim, a utilização de métricas da Capacidade Antioxidante Total da Dieta (CATd) são importantes para observação do efeito sinérgico dos antioxidantes consumidos na alimentação (GÜLÇIN, 2012; NASCIMENTO-SOUZA et al., 2018; PAROHAN et al., 2019). Entretanto, até onde se tem conhecimento ainda são escassos os estudos que investigam a relação CATd, sono e depressão na população brasileira (DE OLIVEIRA et al., 2019; PEREIRA et al., 2021).

Devido à grande prevalência de depressão e alterações do sono e das complicações biológicas e sociodemográficas geradas, se torna importante entender a relação entre a CATd e essas comorbidades. Tais conhecimentos contribuirão para a programação de políticas públicas que fortaleçam medidas preventivas e de educação nutricional e, que visem um tratamento mais humanizado e multiprofissional para a depressão e as alterações no sono.

2. REFERENCIAL TEÓRICO

2.1. CAPÍTULO 1. SAÚDE COLETIVA, OBJETO DE ESTUDO E DETERMINANTES SOCIAIS

2.1.1. Objeto de estudo no campo da saúde coletiva e no planejamento em saúde

A Saúde Coletiva pode ser entendida como um campo onde são produzidos conhecimentos que visam explicar a relação saúde e seus determinantes sociais. Esse campo tem natureza interdisciplinar com suas ações direcionadas à prevenção e cuidado, priorizando o coletivo. Neste sentido, em Saúde Coletiva não há possibilidade de se analisar o biológico sem profunda compreensão do social (PAIM, 1982).

Assim, há o estabelecimento de práticas multiprofissionais, transdisciplinares, interinstitucionais e transsetoriais (RIBEIRO, 1991). Além da utilização das ciências sociais em suas construções de conhecimento, gerando uma articulação entre epidemiologia e política social. Desta forma, só é possível entender o fenômeno saúde/doença de uma população compreendendo seus determinantes sociais (PAIM, 1982). Ao entender as reais necessidades e condições de saúde de uma população, processos de trabalho, articulados com o social, poderão ser construídos, gerando maior efetividade na promoção da saúde (RIBEIRO, 1991).

No campo Saúde Coletiva, a saúde como um estado vital, campo de trabalho e saber, está intimamente ligada à estrutura social através dos setores econômico e ideais políticos, possuindo historicidade. A produção de conhecimento em saúde coletiva não se dá meramente pelo contato com a realidade e sim pela compreensão da sua organização e construção de instrumentos com capacidade de transformá-la (PAIM; FILHO, 1998).

De acordo com a explanação de Paim e Filho, 1998 “As ações de saúde (promoção, proteção, recuperação e reabilitação) constituem uma prática social e trazem consigo as influências do relacionamento dos grupos sociais." Neste sentido, conduzir práticas de pesquisa e ensino pautadas no social é de extrema importância para promoção eficaz de saúde e compreensão dos seus determinantes pelos grupos profissionais envolvidos (PAIM; FILHO, 1998).

Diante do exposto, o objeto deste estudo: “Avaliar a relação entre a Capacidade Antioxidante da Dieta com a depressão e o sono em participantes da Coorte de Universidades Mineiras-CUME” se enquadra no campo da Saúde Coletiva. Neste, busca-se entender a relação da qualidade da dieta, medida pela CATd, com o tempo de sono e a incidência de depressão, levando em consideração as características socioeconômicas e comportamentais da população estudada.

Para entender o papel da alimentação e sua relação com a Saúde Coletiva, é importante observar que os alimentos não são simples sistemas de transferências de nutrientes. O alimento é uma combinação complexa e seu benefício é a soma de seus nutrientes com componentes não nutrientes (LOUZADA., et al., 2019). Deve se ter em mente que as escolhas alimentares e as combinações entre os alimentos não ocorrem ao acaso, sendo os padrões alimentares resultantes de vários fatores como experiências evolutivas e culturais (LOUZADA., et al., 2019). Desta forma, o Novo Guia Alimentar para População Brasileira reconhece a importância do olhar abrangente para a alimentação nos seus aspectos sociais, culturais, econômicos, políticos e ambientais (BRASIL., 2014; LOUZADA., et al., 2019). O Guia Alimentar tem caráter intersetorial promovendo a intersecção entre o campo da saúde e a Segurança Alimentar e Nutricional (SAN) (BRASIL., 2014; LOUZADA., et al., 2019).

Para além da responsabilidade individual pelas escolhas alimentares, a adoção de uma alimentação que vise a promoção da saúde requer políticas e ações do estado para superação dos vários obstáculos envolvidos nas práticas alimentares (LOUZADA., et al., 2019). Sendo que a relação entre saúde, qualidade de vida e alimentação, expõe a necessidade da ampliação de ações que tragam melhorias nos diversos determinantes da saúde (BRASIL., 2014). Neste sentido, de acordo com a lei 8.080, alimentar-se de maneira adequada é um dos fatores determinantes para a promoção da saúde (BRASIL., 2013).

Em relação aos transtornos depressivos e demais transtornos mentais, a Política Nacional de Saúde Mental (PNSM) objetiva a organização da assistência a indivíduos com a necessidade de cuidados específicos em saúde mental. De acordo com as diretrizes do Sistema Único de Saúde (SUS) a PNSM propõe uma rede de atenção com diferentes graus de complexidade e que seja integral na sua assistência. A construção desta rede é um processo que deve ser humanizado e contínuo (BRASIL., 2005).

Quando se trata da inserção do nutricionista no tratamento de transtornos de ordem mental é importante ter em mente o papel da Reforma Psiquiátrica, que teve, entre seus objetivos, o olhar para o indivíduo como um ser complexo o qual precisa de cuidado, acolhimento e humanização (FERNANDES., et al, 2022). Nesta perspectiva, o sujeito deve ser visto de forma integral, seu tratamento deve sempre buscar sua reinserção social e qualidade de vida de forma multidisciplinar, rompendo com o modelo meramente medicamentoso e hospitalocêntrico (VASCONCELLOS; AZEVEDO, 2012; FERNANDES., et al, 2022). Assim, o nutricionista, a partir de uma visão holística, utilizando de diferentes tecnologias e com a base da neuronutrição está entre os profissionais que podem contribuir para as demandas sociais relativas a saúde mental (FERNANDES., et al, 2022).

O Relatório Mundial de Saúde de 2001 (WHO, 2001) salienta a importância da saúde mental e seus impactos para a qualidade de vida. Destaca também ampla prevalência e incidência de transtornos mentais, atingindo indivíduos das mais diversas idades, culturas e níveis sociais. Tal relatório mostra, entre outros aspectos, a importância da adequada formação dos profissionais que irão atuar na saúde mental, apoio às pesquisas relativas aos aspectos biológicos e psicossociais das doenças mentais, além de articulação com outros setores como a educação, o trabalho e a cultura (WHO, 2001; DAL POZ; LIMA; PERAZZI, 2012).

Visto a importância da formação de profissionais nutricionistas capacitados para promoção e cuidado da saúde mental e da necessidade de políticas públicas que apoiem equipes multidisciplinares no tratamento dos transtornos mentais, o estudo epidemiológico aqui exposto, poderá gerar resultados para o planejamento estratégico situacional no SUS (TANCREDI; BARRIOS; FERREIRA, 1998). Além disso, pode contribuir, juntamente com outros estudos, para o estabelecimento de prioridades, alocação de recursos, orientação programática e resolubilidade na linha de saúde mental. Assim, o presente objeto de estudo está incluído no momento explicativo, onde se busca observar como a dieta pode atuar como um fator protetivo para depressão e qualidade do sono em graduados brasileiros (GIOVANELLA, 1991), podendo trazer informações confiáveis, visto ser uma população com alto grau de instrução o que tem gerado alta taxa de retenção (SOUZA E SOUZA et al., 2020). Essas informações também poderão servir para análise situacional e contribuir para evidenciar a necessidade da nutrição e de profissionais nutricionistas no cuidado integral da saúde.

2.1.2. Fatores socioeconômicos, consumo alimentar e capacidade antioxidante da dieta

Ao estudar os determinantes que influenciam em hábitos saudáveis e na saúde, entender o conceito de classe social e posição socioeconômica é de fundamental importância (CANUTO; FANTON; LIRA, 2019). Para a compreensão de classe social é importante observar como a sociedade se organiza de modo social, econômico e jurídico. Por sua vez, para entender posição socioeconômica é importante considerar diversas variáveis como gênero, orientação sexual, privação social e material, raça, etnia, situação conjugal, posição de trabalho, vizinhança, entre outros (GALOBARDES; LYNCH; SMITH, 2007; KRIEGER; WILLIAMS; MOSS, 1997). Deste modo, a posição socioeconômica poderá determinar o

acesso a bens e serviços como, por exemplo, a alimentação (CANUTO; FANTON; LIRA, 2019).

Como destacado por Krieger e colaboradores (1997) nenhum fator único explica as ligações entre posição socioeconômica e saúde, o que existe é uma interconexão de várias vias (KRIEGER; WILLIAMS; MOSS, 1997). Quando falamos de alimentação e fatores socioeconômicos é possível observar que esta relação já está bem estabelecida em países de alta renda (CANUTO; FANTON; LIRA, 2019; GISKES et al., 2009). Assim, grupos socioeconômicos mais desfavorecidos consomem menos fibras, frutas e vegetais (GISKES et al., 2009). Já em países de baixa e média renda esses fatores ainda são controversos (CANUTO; FANTON; LIRA, 2019; DINSA et al., 2012).

Em relação à posição socioeconômica e o consumo de alimentos na população brasileira, a revisão sistemática de Canuto e colaboradores (2019) traz resultados bem interessantes. Ao observarem os principais inquéritos dietéticos brasileiros, mostraram que indivíduos de maior renda e escolaridade possuíam perfil alimentar contraditório. Esses indivíduos apresentavam alimentação rica em nutrientes e alimentos *in natura* e por outro lado alto consumo de alimentos ultraprocessados. Mostraram também que o maior consumo de frutas e verduras esteve predominantemente presente entre grupos como os brancos, as mulheres e os casados (CANUTO; FANTON; LIRA, 2019).

Neste mesmo sentido, um estudo com 400 residentes de uma cidade no sul do Brasil observou que o padrão alimentar mais saudável esteve relacionado ao sexo feminino e ao fato de residir em locais de maior condição socioeconômica. Por sua vez, o consumo de um padrão alimentar rico em açúcares e carboidratos foi associado à população mais jovem, de cor da pele preta, com menor escolaridade e renda. O consumo de alimentos tipo *fast foods* foi associado a indivíduos mais jovens, brancos e de maior renda (CUNHA et al., 2022). Dados de 930 residentes da cidade de Ribeirão Preto mostraram que o consumo de frutas e verduras esteve positivamente associado à escolaridade e renda somente para mulheres. Além disso, homens que viviam com suas companheiras apresentaram maior consumo de frutas e verduras que os demais (MONDINI et al., 2010). Outra pesquisa, com 4.202 jovens adultos participantes da Coorte de Nascido em Pelotas, observou que padrões alimentares ricos em alimentos processados eram mais comuns em homens e indivíduos com posição social média e alta. Já padrões ricos em vegetais e frutas não tiveram nenhuma associação com fatores socioeconômicos após ajuste para variáveis de confusão (OLINTO et al., 2011). Da mesma forma, um estudo com 28.901 indivíduos participantes dos Inquéritos Nacionais de Alimentação, observou que o padrão alimentar “Ocidental” caracterizado por refrigerantes,

pizzas, salgados, farinhas, massas e doces teve maior adesão entre indivíduos do sexo masculino, com maior renda e escolaridade. Observaram que em nenhum dos padrões encontrados houve participação importante de frutas, legumes e verduras (ANTUNES et al., 2021). Por fim, dados de 88.531 adultos, participantes da Pesquisa Nacional de Saúde (PNS), mostraram que entre mulheres houve maior presença dos marcadores de alimentação saudável como as frutas e os vegetais em relação aos homens (SANTIN et al., 2022). Entre negros e pardos e indivíduos de menor renda houve menor prevalência de adequação de frutas e verduras e maior adequação para o grupo feijões. Com relação a idade, indivíduos mais velhos tiveram maior adequação no consumo de marcadores de alimentação saudável (SANTIN et al., 2022).

Informações sobre fatores socioeconômicos que afetam diretamente a CATd são escassas. Entretanto é possível observar que café, chás, frutas, verduras e grãos integrais são alimentos que contribuem em muito para a CATd em estudos nacionais (FREITAS LIMA et al., 2020; SABIÃO et al., 2021; STEDILE et al., 2016). Assim, é possível pressupor, de acordo com os estudos anteriormente citados, que uma dieta com maior CATd pode estar associada a fatores como renda, escolaridade, situação conjugal, sexo, idade, entre outros.

2.1.3. Fatores socioeconômicos, depressão e qualidade do sono

Quando se trata de fatores relacionados à depressão, o sexo tem sido um fator intimamente observado. Dois estudos, um utilizando dados de 501.945 participantes da Pesquisa Nacional por Amostras de Domicílios (PNAD) de 1998, 2003 e 2008 e outro 60.202 participantes da Pesquisa Nacional de Saúde (PNS) de 2013 observaram maior prevalência de depressão entre indivíduos do sexo feminino (MUNHOZ et al., 2016; SANTOS; KAWAMURA; KASSOUF, 2012). Foi observado também, para mulheres, diferentemente dos homens, que ser chefe de família representou um maior risco para a depressão (SANTOS; KAWAMURA; KASSOUF, 2012). Estudo com 936 adultos brasileiros, durante a pandemia de COVID-19, também observou que mulheres apresentaram maior probabilidade de sintomas depressivos em relação aos homens (RIBEIRO et al., 2021). De forma contrária, um estudo com 70.806 participantes da PNS de 2019 observou uma maior prevalência de subdiagnóstico de depressão para indivíduos do sexo masculino (FAISAL-CURY et al., 2022). Destaca-se que fatores sociais, psicológicos e biológicos como mudanças hormonais podem estar ligados a maior prevalência de depressão entre as mulheres na maioria dos estudos (DE OLIVEIRA et al., 2019; MUNHOZ et al., 2016).

Ao analisar a idade e situação conjugal o estudo com dados da PNAD (1998, 2003 e 2008) observou para homens um risco máximo de depressão por volta dos 48 anos e para mulheres por volta dos 43,8 anos. Para ambos os sexos, morar com o cônjuge foi um fator relacionado ao menor risco de depressão (SANTOS; KAWAMURA; KASSOUF, 2012). Já no estudo com dados da PNS de 2013 foram observadas maiores razões de prevalência de depressão para grupos populacionais com idade entre 40 e 49 anos e maiores de 80 anos quando comparados ao grupo de referência (18-29 anos) (MUNHOZ et al., 2016). Por sua vez, os dados do PNS de 2019 observaram prevalência de subdiagnóstico de depressão mais frequente na população idosa quando comparada às demais faixas etárias (FAISAL-CURY et al., 2022).

Com relação à área de moradia, o estudo com dados da PNS de 2013 mostrou que indivíduos residentes nas áreas urbanas apresentaram maiores prevalências de depressão (MUNHOZ et al., 2016). Tal fato pode ser explicado pela maior exposição a aglomerações, ruídos, crimes, medo e desigualdades sociais (MUNHOZ et al., 2016). Ao se considerar o nível educacional, os dados do PNS de 2013 e PNAD mostraram maiores prevalências de depressão em indivíduos com menor escolaridade (MUNHOZ et al., 2016; SANTOS; KAWAMURA; KASSOUF, 2012). Da mesma forma, uma maior renda foi inversamente associada com a depressão (FAISAL-CURY et al., 2022; SANTOS; KAWAMURA; KASSOUF, 2012).

Embora a escolaridade tenha se mostrado inversa a prevalência depressão (MUNHOZ et al., 2016; SANTOS; KAWAMURA; KASSOUF, 2012), estar inserido em um programa de pós-graduação pode ser um fator de risco para tanto para depressão quanto para distúrbios do sono. Neste sentido, um estudo com 2.900 pós-graduandos brasileiros mostrou que 39% dos entrevistados relataram alta frequência de episódios de deitar e não conseguir dormir e sentimento de culpa ao ir dormir, além disso, 30% relataram acordar várias vezes durante a noite. Do total de estudantes, 25% relataram a presença de depressão (COSTA; NEBEL, 2018).

Com relação à cor da pele, uma revisão sistemática, com 14 estudos transversais, mostrou que a maioria dos estudos com análises multivariadas revelaram maior prevalência de transtornos mentais em raças não brancas. Como não existe base biológica para relação raça e saúde mental, outros pontos devem ser considerados. Assim, destaca-se o fator descriminalização relacionada à raça, que pode relacionar-se ao aumento do estresse psicológico (SMOLEN; ARAÚJO, 2017).

Em se tratando de transtornos no sono, um estudo com 743 adultos brasileiros investigou os fatores que poderiam estar associados. Observaram maiores prevalências desses transtornos em mulheres, pessoas com menor escolaridade e, indivíduos com idade igual ou superior a 60 anos (ZANUTO et al., 2015). Por sua vez, um estudo transversal, com 158 idosos, observou maior frequência de insônia entre mulheres e em participantes com menor escolaridade (OLIVEIRA et al., 2010). Um estudo de base populacional com 1.421 residentes na área rural do sul do Brasil também observou maior prevalência de distúrbios do sono em indivíduos do sexo feminino, com idade maior ou igual a 40 anos e com menor escolaridade (MACHADO; WENDT; WEHRMEISTER, 2018).

No mesmo sentido, Lima e colaboradores (2021) ao analisarem dados 45.160 brasileiros observaram maior incidência de distúrbios do sono em mulheres, indivíduos jovens, solteiros, e para aqueles com mais de cinco moradores no domicílio (LIMA et al., 2021). Um estudo transversal, com 1.998 participantes do Inquérito de Saúde de Campinas, observou que a prevalência de autoavaliação de sono ruim esteve significativamente mais elevada entre mulheres, indivíduos desempregados, com idade entre 40 e 50 anos, fisicamente inativos e com a presença de transtornos mentais comuns (BARROS et al., 2019).

A partir dos estudos epidemiológicos acima citados é possível observar que fatores sociodemográficos como sexo, cor da pele, idade, renda, escolaridade, situação conjugal e profissional relacionam-se frequentemente com a depressão e qualidade do sono na população brasileira. Esses são fatores sociodemográficos importantes de serem analisados em estudos que investigam como desfecho o sono e a depressão.

2.2. CAPÍTULO 2. ESTRESSE OXIDATIVO E CAPACIDADE ANTIOXIDANTE DA DIETA

2.2.1. Estresse oxidativo e saúde

Geração de Radicais Livres

Radiais livres em que o elétron desemparelhado se encontra em átomos de oxigênio são chamados de Espécies Reativas de Oxigênio (EROs), quando ocorre em átomos de nitrogênio são denominados Espécies Reativas de Nitrogênio (ERNs) (BARREIROS; DAVID; DAVID, 2006). Tantos as EROs quando as ERNs são liberadas no organismo por serem subprodutos de processos metabólicos. Assim, os mecanismos biológicos de geração de radicais livres podem ocorrer nas mitocôndrias, retículo endoplasmático, peroxissomos,

citosol, membrana plasmática e espaço extracelular (KRUK et al., 2019). A geração de EROs e ERNs são favorecidas pela presença dos íons de ferro e cobre (BARBOSA et al., 2010).

Com relação às EROs, a redução do oxigênio pode contribuir para formação de radicais superóxido (O2-), hidroxila (OH-) e peróxido de hidrogênio (H2O2). Apesar do H2O2 não apresentar elétrons desemparelhados, possui alto poder reativo e capacidade de atravessar membranas celulares. Por sua vez, as ERNs como peroxinitrito (ONOO) podem ser geradas a partir da reação do O2- com o radical óxido nítrico (NO-) (BARBOSA et al., 2010).

Além da sua produção devido ao funcionamento normal do corpo, fatores exógenos também podem induzir a produção de EROs e ERNs. Dentre esses fatores é possível citar, luz ultravioleta solar, raios X e radiações, exposição à poluição, patógenos, tabagismo, uso de álcool, sobrecarga de ferro, traumas, drogas, metais pesados entre outros fatores (BARBOSA et al., 2010; KRUK et al., 2019; MOLDOGAZIEVA et al., 2019).

Estresse oxidativo e seu processo patogênico

Tanto EROs quanto ERNs quando formadas em baixas concentrações podem desempenhar papel regulador em vias de sinalização celular, na expressão gênica, na regulação da resposta imune e na homeostase celular (KRUK et al., 2019; MOLDOGAZIEVA et al., 2019). Em condições normais, através de um sistema antioxidante, as células conseguem a manutenção das baixas concentrações dos radicais livres. Entretanto o desbalanço desse mecanismo gera o estresse oxidativo (MOLDOGAZIEVA et al., 2019). Neste sentido, é importante destacar que o estresse oxidativo é um processo patogênico que pode gerar lesão e morte celular (GOTTLIEB; MORASSUTTI; CRUZ, 2011; KRUK et al., 2019). Os seus danos ao longo da vida estão relacionados à patogênese de doenças neurodegenerativas, cardiovasculares, cânceres, doenças pulmonares, digestivas, entre outras (KRUK et al., 2019).

Mecanismos enzimáticos de defesa antioxidante

O sistema enzimático do organismo humano inclui as enzimas antioxidantes, Superóxido Dismutase (SOD), Catalase (CAT) e Glutationa Peroxidase (GPx) (BARBOSA et al., 2010; GOTTLIEB; MORASSUTTI; CRUZ, 2011; KRUK et al., 2019). Também destacam enzimas que representam um segundo estado de prevenção antioxidante como a Glutationa Redutase (GR), Tiorexidina (TR) e a Glicose-6-fosfato Desidrogenase (GbPD) (KRUK et al., 2019). É importante observar que a atividade de muitas dessas enzimas

depende de cofatores enzimáticos dietéticos como: cobre, zinco, manganês e selênio (BARBOSA et al., 2010).

Mecanismos não enzimáticos de defesa antioxidante.

O sistema antioxidante não enzimático também ajuda na proteção celular contra geração excessiva de EROs e ERNs. Como componentes principais destacam-se os compostos de origem dietética: vitaminas, minerais e compostos fenólicos (BARBOSA et al., 2010; KRUK et al., 2019). Deste modo, a vitamina C atua inibindo EROs e cooperando com a atuação da vitamina E e do selênio. Já as vitaminas E e A destacam-se por funções na proteção à peroxidação lipídica. Por sua vez, minerais como cobre, zinco, manganês e selênio são importantes cofatores para enzimas antioxidantes. Componentes como carotenoides sem atividade de vitamina A (licopeno, luteína e zeaxantina), fitoquímicos como resveratrol, catequinas, quercetina, entre outros, também se destacam pela função antioxidante (BARBOSA et al., 2010; RODRIGO; GUICHARD; CHARLES, 2007).

2.2.2. Capacidade antioxidante total da dieta

A proteção contra espécies reativas de oxigênio a partir da cooperação dos diferentes antioxidantes dietéticos é muito mais eficaz do que quando se considera qualquer componente dietético isolado (SERAFINI; DEL RIO, 2004). Assim, a utilização de métricas que resultem na Capacidade Antioxidante da Dieta (CATd) são úteis para captar o efeito antioxidante de uma ampla gama de nutrientes, inclusive aqueles que não são bem caracterizados ou medidos. Um bom exemplo são os carotenoides, sendo que mais de 600 tipos já foram identificados e, destes, cerca de 50 podem ocorrer na dieta humana (GÜLÇIN, 2012). Outro ponto vantajoso é a eliminação de problemas de múltiplas comparações, quando se considera os vários antioxidantes dietéticos separadamente (DEVORE et al., 2013).

Sabendo que os antioxidantes da dieta exercem um papel crucial no potencial antioxidante do corpo, sendo os principais contribuintes externos para o estado redox plasmático, o estudo da Capacidade Antioxidante da Dieta (CATd) se mostra importante para observar a interação entre antioxidantes advindos da alimentação e desfechos de saúde (NASCIMENTO-SOUZA et al., 2018; PAROHAN et al., 2019; SERAFINI; DEL RIO, 2004). Desta forma, a CATd considera todos os antioxidantes provindos da alimentação e a ação sinérgica entre os mesmos (PELLEGRINI et al., 2003).

Saber sobre as defesas antioxidantes presentes em amostras biológicas é de extrema importância, entretanto quantificar separadamente cada componente antioxidante exige técnicas complexas, caras, trabalhosas, além de demoradas. Devido aos métodos de quantificação isolada desfavoráveis e do fato do efeito dos antioxidantes ser sinérgico, a utilização da medida da CATd se torna interessante (EREL, 2004). Assim, os ensaios para determinar a capacidade antioxidante total de um alimento envolvem a mensuração do poder antioxidante de uma amostra como um todo, sendo uma forma simples, de baixo custo e rápida (RUBIO et al., 2016).

Os ensaios de CAT são divididos em dois grupos principais: Os que medem capacidade de transferência de átomos de hidrogênio como os métodos Capacidade de Absorção do Radical Oxigênio (Oxygen Radical Absorbance Capacit-ORAC) e Capacidade Antioxidante Total (Total Radical-Trapping Antioxidant Parameter-TRAP) (GÜLÇIN, 2012; RUBIO et al., 2016). Outros métodos, são os baseados em transferência de elétrons, ou seja, medem a capacidade que um antioxidante tem de transferir elétrons para reduzir algum composto específico. Dentre os métodos baseados em transferência de elétrons podem ser citados os métodos Poder Antioxidante Redutor do Ferro (Ferric Reducing Antioxidante Power-FRAP) e Capacidade Antioxidante Equivalente ao Trolox (Trolox Equivalent Antioxidant Capacit-TEAC) (GÜLÇIN, 2012; RUBIO et al., 2016). Assim, os ensaios TEAC medem a capacidade das moléculas antioxidantes de um alimento extinguirem o composto ABTS em comparação com a capacidade de um análogo de vitamina E. O FRAP é medido baseado na capacidade de redução do complexo Fe^{3+} (ion férrico) para Fe^{2+} (ion ferroso). Já o TRAP mede a proteção fornecida por antioxidantes em uma reação de peroxidação controlada. Por fim, o ORAC é medido através da inibição antioxidante de oxidações induzidas por radicais peroxil (GÜLÇIN, 2012; PAROHAN et al., 2019; PELLEGRINI et al., 2003).

Como descrito, esses métodos se diferenciam nas suas técnicas de medição e componentes químicos utilizados. É importante considerar, a partir das diferentes técnicas, que nenhum dos métodos de avaliação da CATd determina totalmente a capacidade antioxidante de um alimento (PAROHAN et al., 2019). Sendo possível afirmar que não existe um “padrão ouro” para a avaliação da CATd (DEVORE et al., 2013)

2.2.3. Capacidade Antioxidante total da dieta e associações com a capacidade antioxidante total do plasma, Doenças Crônicas não Transmissíveis e qualidade da dieta

Quando se trata da ingestão de alimentos antioxidantes e o aumento da Capacidade Antioxidante Plasmática (CAT plasmática) Pellegrini e colaboradores mostram em sua revisão que os resultados ainda são conflitantes (PELLEGRINI et al., 2020). Destacam que há limitações entre a comparação da CATd com a CAT plasmática. A medição da CAT plasmática é influenciada por diferentes abordagens analíticas, por outros compostos antioxidantes além dos de origem alimentar presentes nos fluidos biológicos, também, por fatores biológicos individuais como capacidade de absorção intestinal, fatores genéticos e comportamentais (PELLEGRINI et al., 2020).

Outro ponto a ser considerado é que a CAT plasmática pode não ser refletida em dietas de longo prazo sendo mais uma limitação para a comparação com a CATd (NASCIMENTO-SOUZA et al., 2018; PELLEGRINI et al., 2007). Entretanto, como destacado por Nascimento *et al.*, (2018), a CAT plasmática pode estar aumentada logo após o consumo de alimentos ricos em antioxidantes. Assim, Pinzani e colaboradores (2010) demonstraram uma elevação significativa na CAT plasmática após a ingestão de vinho branco ou tinto (PINZANI et al., 2010). Esses resultados também foram observados para o consumo de chá verde (KOUTELIDAKIS et al., 2014). Desde modo, a CAT plasmática pode ser uma forma ineficaz de medir a ingestão de antioxidantes dietéticos em longo prazo. Sendo que a influência de diversos fatores, como os acima citados, pode contribuir para as correlações conflitantes (NASCIMENTO-SOUZA et al., 2018).

Entretanto, ao considerar estudos epidemiológicos, a CATd tem se mostrado uma ferramenta muito útil para a avaliação da relação entre alimentação e desfechos de saúde (NASCIMENTO-SOUZA et al., 2018; PELLEGRINI et al., 2020). Assim, uma meta-análise com dados de 226.297 indivíduos entre 30 e 80 anos observou diminuição do risco de morte por todas as causas, câncer e doenças cardiovasculares em indivíduos com alta CATd (PAROHAN et al., 2019).

Além disso, a CATd pode ser considerada uma medida útil para a caracterização do padrão alimentar (PELLEGRINI et al., 2020). Puchau *et al.,* (2009) associaram a CATd à indicadores validados da qualidade geral da dieta em adultos jovens. Observaram que maiores valores de CATd foram associados a maiores escores de qualidade da dieta, entre eles, o Índice de Alimentação Saudável e o Índice de Qualidade da Dieta Mediterrânea (PUCHAU et al., 2009). A CATd também tem sido associada ao maior consumo de alimentos ricos em antioxidantes como, vegetais, frutas e oleaginosas, mostrando sua importância e aplicabilidade (DANESHZAD et al., 2020; HERMSDORFF et al., 2011b; MILAJERDI et al., 2019; PUCHAU et al., 2009).

2.3. CAPÍTULO 3. CAPACIDADE ANTIOXIDANTE DA DIETA SONO E DEPRESSÃO

Para investigar, na literatura epidemiológica disponível, a relação entre a CATd com Transtornos Mentais Comuns (Depressão e Ansiedade) e o sono, foi redigido o manuscrito intitulado "Association of dietary total antioxidant capacity with depression, anxiety, and sleep disorders: A systematic review of observational studies", que foi submetido e publicado na revista Journal of Clinical and Translational Research, número do doi: http://dx.doi.org/10.18053/jctres.07.202105.005 (**ANEXO I**). A formatação aqui apresentada está de acordo com as normas que constam nas instruções aos autores da revista à qual foi publicado.

2.3.1. Associação da capacidade antioxidante total da dieta com depressão, ansiedade e distúrbios do sono: uma revisão sistemática de estudos observacionais

Association of dietary total antioxidant capacity with depression, anxiety, and sleep disorders: A systematic review of observational studies.

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Abstract

Background and aim: We aimed to systematically review observational studies that evaluated the potential association of the dietary total antioxidant capacity (dTAC) with common mental disorders (depression and anxiety) and sleep disorders.

Methods: Studies with an observational design that evaluated the association between the dTAC and common mental disorders and sleep disorders were identified using the PubMed and Scopus databases. The meta-analysis guideline of observational studies in epidemiology and the preferred reporting items for systematic reviews and meta-analysis were used to conduct and report the data of this systematic review.

Results: Of the 439 records, seven studies were included in this review. There was a sample variation of 41-3297 participants. We highlight that five of the studies analyzed were conducted in the Iranian population. Four studies analyzed only women, and three studies were conducted with postmenopausal or climacteric women. Four cross-sectional studies showed inverse associations between the dTAC and depression, anxiety, and sleep disorders in Iranians.

Conclusion: The consumption of a diet rich in antioxidants, characterized by high dTAC scores, seems to be inversely associated with depression, anxiety, and sleep disorders. However, further studies with different populations and designs are necessary for a better understand this relationship.

Relevance to patients: This review assesses the association of the dTAC with common mental disorders (depression and anxiety) with sleep disorders. This will help guide further studies on the relationship between diet and mental disorders and sleep disorders. Knowledge about these relationships is essential for the creation of non-pharmacological practices for the prevention of these disorders.

Keywords: antioxidants; common mental disorders; dietary total antioxidant capacity; mental health; nutrition.

1. Introduction

Depression and anxiety are common mental disorders due to their high prevalence in the contemporary society [1]. Depression has been diagnosed in more than 322 million individuals worldwide, and is one of the major contributors to the global burden of disease [1,2]. Anxiety disorders have affected approximately 264 million people worldwide. Although anxiety is an important and necessary feeling in certain situations, it may be indicative of mental disorders when observed to be in an uncontrolled degree [1]. This condition can be classified into generalized anxiety disorders, panic syndrome, and obsessive-compulsive disorder among others [1,3].

Sleep disorders can be characterized as manifestations that cause impairment in the sleep quality, among which changes in the circadian rhythm and insomnia stand out [4,5]. Such disorders are risk factors for the development of anxiety and depression; additionally, such sleep disorders may arise as a consequence of common mental disorders [4,5]. Notably, insomnia affects approximately 6 to 10% of the general population. Nowadays, both sleep disorders and depressive and anxiety disorders have been evidenced as indirect effects of the COVID-19 pandemic [6–8].

The occurrence of common mental disorders and sleep disorders may have multiple etiologies, including behavioral, biological, social, and psychological factors [1,9,10]. Oxidative stress is generated by an imbalance between the reactive oxygen species (ROS) and enzymatic and non-enzymatic antioxidant defense systems [11,12]. Since oxidative stress can impair the neuronal and neurotransmitter function and lead to a dysregulation of circadian rhythms, it has also been linked to the pathophysiology of mental disorders and sleep disorders [11–14]. Thus, oxidative stress reduction may mediate protection against common mental disorders [15].

Antioxidant dietary factors are the main external contributors to the non-enzymatic antioxidant defense [16]. Studies have shown associations between antioxidant compounds, such as vitamin C, vitamin A, polyphenols, beta-carotene, and mental health [17–19]. Moreover, the interaction between the different antioxidants in the diet appears to be more effective than the action of an isolated nutrient [20–22].

The dietary total antioxidant capacity (dTAC) is the sum of all or most antioxidants consumed, which estimates the cumulative effect of the antioxidants in the overall diet [23]. Studies have shown an inverse relationship between higher dTAC values and the risk of developing chronic diseases [24], central obesity, and oxidative stress markers [20]. The relationship between the dTAC and depression and anxiety scores [25–30] and sleep

disorders [26,31] have currently been investigated; however, the results are controversial. Thus, we systematically reviewed observational studies that evaluated the potential association between the dTAC and common mental disorders (depression and anxiety) and sleep disorders.

2. Materials and methods

2.1 Protocol and registration

To conduct and report the data of this systematic review, the meta-analysis guidelines of observational studies in epidemiology (MOOSE) [32] and Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) were used [33]. This review was registered in PROSPERO (www.crd.york.ac.uk/prospero/) under the number CRD42020212014.

2.2 Eligibility criteria

In this review, the inclusion criteria were original observational articles in humans that related the dTAC with depression, depressive symptoms, anxiety, or sleep disorders. In addition, studies that reported the association of data as β-values or odds ratios followed by the 95% confidence interval were included, as well as studies that reported the data as measures of central tendency and dispersion. The studies that reported dTAC data in averages, tertiles, quartiles, and quintiles were also included. The criteria for non-inclusion in the systematic review were review articles, letters, book chapters, articles with animals, articles that did not analyze the dTAC, and the outcomes of interest. The review did not include language or date restrictions.

2.3 Search strategies

Two researchers (GAP and AS) independently conducted the search for original observational studies that evaluated the association between dTAC and depression or depressive symptoms, anxiety or anxiety related symptoms, and sleep disorders. To identify articles according to the inclusion criteria, we searched the online databases PubMed/Medline (https://pubmed.ncbi.nlm.nih.gov/advanced/) and Scopus (https://www.scopus.com/home.uri) between October 2020 and July 2021. An exhaustive literature review was conducted with the following search terms: “Total dietary antioxidant capacity”; “Dietary total antioxidant

capacity"; and "Non enzymatic antioxidant capacity." The search terms were selected from previous readings of published manuscript that related dTAC and health outcomes.

2.4 Selection of studies and data extraction

The selection of studies was based on the analysis of titles, abstracts, and full texts by two independent authors (GAP and AS). Duplicate articles were manually identified. Consensus between the authors resolved divergent decisions. In the absence of the full article or sufficient information to interpret the articles, we contacted the corresponding author to request such information. From the eligible studies, the two authors (GAP and AS) independently extracted the following information: (i) name of the first author, year, and country where the study was conducted; (ii) sample characteristics; (iii) methodology to quantify dTAC and to evaluate the outcomes; (iv) adjustment variables used in the analyses; and (v) main results.

2.5 Evaluation of the quality of studies

The National Heart, Lung, and Blood Institute study quality assessment tools were used [34]. The tool for evaluating cohort and cross-sectional studies was composed of 14 criteria, and questions 6, 7, 10, and 13 were applicable only to the cohort studies. In turn, the tool for assessing the quality of case-control studies was composed of 12 criteria. In both tools, for each question, the score 1 was considered in case of a positive answer "yes." A zero score has been assigned for "no" answers, which can be "not applicable," "not reported," or "not possible to determine" questions. These evaluations were not a decision criterion for the inclusion of the studies, but rather to contribute to the evaluation of the quality of the evidence pointed out by each one.

We classified the studies as good, fair, or poor according to the evaluation of the quality of the studies applied by two authors (GAP and AS). Consensus resolved divergences regarding the studies score and quality classification. The main criteria considered for classifying the studies were the use of validated measures for results and exposure, a clearly defined study population, the use of possible confounding variables, and the evaluation of the participation rate in the study.

3. Results

3.1 Search

Of the 439 articles from the two databases, 197 articles were duplicates. Of the remaining 242 articles, 235 articles were excluded after reading the titles and abstracts. Subsequently, a total of seven articles were selected for full reading. After reading, one article was excluded because it did not present any outcome of interest (depression, anxiety, or sleep disorders). From the list of references of the six remaining articles, a reverse search was performed, and one additional article was included. Thus, seven articles were selected for this review (**Figure 1**).

3.2 Characteristics of included studies

Of the seven studies included in this systematic review, five studies presented a cross-sectional design [25,26,28,29,31], one study was a case-control study [30], and one study was a prospective cohort study with 3 years follow-up [27]. The sample size ranged from 41 [29] to 3,297 participants [28]. Regarding the studied population, four studies investigated associations only in women, three studies in postmenopausal or climacteric women [25,29,31], and one in adult or elderly women with type 2 diabetes [26]. Two studies analyzed both men and women, one with young, adult, and elderly workers [27], and the other with apparently healthy adults [28]. Finally, one study analyzed only young men [30].

Regarding the origin of the studies, five studies were conducted with Iranian participants [25,26,28,30,31], one study with Brazilian participants [29], and one study with Japanese participants [27].

To determine the dTAC, two studies used the oxygen radical absorbance capacity (ORAC) and ferric reducing antioxidant power (FRAP) assays [26,27]; one study used the Trolox equivalent antioxidant capacity (TEAC) and FRAP assays [30]; two studies used only ORAC [25,31]; one study used the vitamin C equivalent antioxidant capacity (VCAC) method [29]; and one study analyzed only the FRAP [28].

Regarding the tools used to measure the outcomes, Daneshzad et al. (2020) analyzed the sleep quality using the Pittsburgh Sleep Quality Index (PSQI) and symptoms of depression and anxiety using the Depression, Anxiety, and Stress Scale (DASS-21) [26]. Abshirini et al. (2018) observed the presence of depressive mood, anxiety symptoms, and sleep problems using the Menopause Rating Scale (MRS) [31]. Abshirini et al. (2019) used the Depression Anxiety Stress Scale (DASS-42) [25]. The Hospital Anxiety and Depression Scale questionnaire [28], Center for Epidemiological Studies Depression Scale (CES-D) [27]

and Beck Depression Inventory-II (BDI-II) [30] were also used. Additionally, Oliveira et al. (2019) used the self-report of medical diagnosis of depression and for measuring the depressive symptoms used Beck Depression Inventory (BDI) [29].

3.3 Results of individual studies

Of the seven studies included in this systematic review, four studies observed an inverse association between the dTAC and the outcomes of interest [25,26,28,31] **(Table 1).**

3.3.1 Cross-sectional studies

Type 2 diabetic women, who were classified in the highest tertiles of FRAP and ORAC exhibited a 94% and 87% lower chance of sleeping poorly, respectively. They also had lower chances of depression compared to the first tertile. The highest FRAP tertile was associated with a lower chance of anxiety than the first tertile. These results were independent of age, BMI, energy consumption, physical activity, blood pressure, medications, supplement consumption, socioeconomic classification, nap times, and hours of night sleep [26].

Two studies analyzed post-menopausal women [25,31]. In the first study, they observed no significant association between the dTAC and depressed mood. However, women in the last quartile of ORAC had a 71% lower chance of sleep problems and 62% less chance of anxiety. These findings were independent of age, education, waist circumference, physical activity, use of supplements, fiber consumption, tea and coffee consumption, and total energy intake [31]. In the second study, an inverse association was observed between the ORAC and depression and anxiety scores [25].

Milajerdi et al. (2019) observed that Iranian adults included in the highest quintile of FRAP presented 43% and 38% lower chances of depressive and anxiety symptoms, respectively, when compared to the first FRAP quintile. These associations were independent of age, sex, energy intake, omega-3 fatty acid consumption, marital status, socioeconomic status, smoking, presence of chronic conditions, physical activity, use of supplements, antidepressant drugs, and BMI. In contrast, a Brazilian study found no difference in the mean dTAC values between climacteric women with and without depression [29].

3.3.2 Prospective cohort study

A prospective cohort study investigated the incidence of depressive symptoms in Japanese workers of both sexes, over a period of three years. They noted no association

between the FRAP and ORAC and depressive symptoms in crude and multivariate analyses [27].

3.3.3 Case control study

A case-control study investigated young men with high scores for depressive symptoms and men free of depressive symptoms as the control. They observed no significant differences in the FRAP and TEAC means between the cases and controls. There was no association between the dTAC and the depressive symptom scores [30].

3.4 Quality of studies

Among the analysis of cross-sectional studies, three studies scored seven points. They were classified as fair because they did not report the participation rate in the study and did not justify the sample size [25,26,31]. A cross-sectional study received eight points. This study was considered as good; however, there was no justification for the sample size [28]. In turn, a cross-sectional study with six points was classified as poor. Its outcome was self-reported and not validated; in addition, the confounding factors were not considered [29]. A cohort study obtained 10 points (good); however, there was a loss of follow-up over 20% of the initial population [27]. The case-control study scored seven (poor) because possible confounding variables were not considered in the dTAC comparison between the cases and controls [30] (**Tables 2 and 3**).

4. Discussion

It has been suggested that the ingestion of dietary antioxidants may protect against oxidative damage and related clinical complications [25,26,28,31]. To our knowledge, this study is the first to review the relationship between the dTAC and common mental disorders (depression and anxiety) and sleep disorders. We observed that four cross-sectional studies reported a inverse association between the dTAC and depression or anxiety scores, or sleep disorders in Iranians [25,26,28,31].

In fact, the brain is highly vulnerable to oxidative damage due to the characteristics of the organ itself, such as a high cellular metabolic rate and a constitution rich in lipids and unsaturated fatty acids, which are substrates for oxidation [12,13,35,36]. Brain neurons have a high metabolic demand and lower endogenous levels of antioxidants compared to other cells with an equivalent metabolism [37]. It is noteworthy that the redox imbalance in the brain may be related to risk factors for depression and anxiety, such as increased inflammation,

impaired neuronal plasticity, and reduced neuronal signaling [13,36]. It is important to show that oxidative and inflammatory processes are interconnected in the pathogenesis of depression. During the inflammatory process, increases in interleukins are able to activate the activity of the enzyme indoleamine 2,3-dioxygenase (IDO), which is involved in the synthesis of kynurenine (KYN) from tryptophan, diverting it from its pathway. In addition to reducing the serotonin synthesis, the activation of the KYN pathway generates catabolites called TRYCATS, which induce the influx of calcium, which in turn, generates mitochondrial dysfunction and compromises the cellular antioxidant system [36] (**Figure 2**).

It is highlighted that sleep deprivation can act as a factor that increases the oxidative stress. Thus, in alertness, there is a high neuronal metabolism, a greater requirement for oxygenation, and consequently, a greater formation of ROS. During sleep, there is an increase in the antioxidant state that promotes brain protection [38]. However, it is possible that oxidative stress affects the cellular ability to regulate circadian rhythms [14].

Notably, the diet contributes directly to the composition of the non-enzymatic antioxidant defense and maintenance of the redox balance, in addition to antioxidant enzymes [16]. The consumption of antioxidants, such as carotenoids, flavonoids, and vitamins E and C, can reduce the ROS and consequently, prevent oxidative damage [26]. Thus, a higher dTAC is related to a higher consumption of these antioxidants, which can exert beneficial effects on mental health [26,28]. In this sense, therapies containing antioxidants, such as vitamins C and E, can help in the treatment of psychiatric disorders [13]. Furthermore, a diet rich in antioxidants, such as polyphenols, could be a good strategy for preventing anxiety and depression [18,39] **(Figure 2).**

Furthermore, the anti-inflammatory effect of a high dTAC may explain its inverse association with mental disorders, in addition to antioxidant protection [25,40]. In this sense, studies have shown that a higher dTAC is associated with a lower dietary inflammatory index (DII) and decreased systemic inflammation markers [41–43]. In addition, individuals with a higher dTAC may have a diet with a greater consumption of fruits, vegetables, fibers, and vitamins [20,26,28]. These food groups offer a better quality of the diet, which can offer a potential protective effect against common mental disorders [26,44,45]. In addition to its anti-inflammatory effects, the consumption of certain foods may be related to increased melatonin concentrations. In this sense, a review by Pereira et al. (2020) showed that the consumption of melatonin source foods, such as cherries, grapes, bananas, pineapples, and dark green vegetables was related to the increased urinary excretion of the melatonin metabolite, 6-sulfatoxymelatonin, or circulating melatonin [46]. This indolamine is a potent antioxidant that

coordinates the synchronization of circadian rhythms and controls the onset and quality of sleep [46,47]. Thus, the consumption of food sources of this indoleamine has been related to improvements in the sleep quality and increased urinary antioxidant capacity [48–50].

Of the five studies with Iranian subjects, four studies reported an inverse association between the dTAC and depression and anxiety scores or sleep disorders. Of these, three studies were classified as fair [25,26,31], and only one study was classified as good [28]. Notably, the study that found no association was classified as poor [51]. Upon analyzing the nationality of the studies that found significant associations, it is important to highlight that the cultural and environmental factors, such as planting, cooking methods, and typical culinary, can influence the antioxidant content of the diet [52]. Additionally, three studies analyzed only women [25,26,31]. There is a greater prevalence of depression, anxiety, and sleep disorders among women, which is associated with increasing age and menopause. Menopausal women may experience hormonal, mood, body metabolism, and lifestyle changes [53,54]. Moreover, a case-control study in which no associations were found was conducted with young Iranian men. Confounding variables were not used to investigate the differences in the mean dTAC between the cases and controls [30]. Thus, further investigation of the relationship between the dTAC and mental and sleep disorders according to the sex, age, and ethnicity is necessary. Another point to be considered is the possible reverse causality in cross-sectional studies, since hormonal changes from sleep and mental disorders can lead to worse food choices [55,56].

Unlike the studies on Iranian women, a study with climacteric Brazilians found no association between the dTAC and depression [29]. In this Brazilian study, a self-reported diagnosis of depression was not validated, and adjustments for possible confounding variables were not used. In addition, only a 24-hour food recall was used for the dietary assessment [29]. Thus, it was not possible to accurately measure the dTAC from the diet because the variability in antioxidant food intake on different days was not considered [57].

In turn, no association was found in a prospective cohort of Japanese workers classified as of good quality [27]. Among the studies analyzed here, the one that offered the best level of evidence and some notable points should be highlighted. In this study, the authors made adjustments to the consumption of vitamins and minerals (folate, vitamin B6, vitamin B12, magnesium, and zinc) because they could act as protective factors for depressive symptoms [27]. Another notable point in this study was that the associations between the dTAC and depression by dietary sources (foods and beverages) were investigated. Therefore, there may be a greater bioavailability of antioxidants according to the food sources [27,58].

3.1 Limitations of the Current Research and Challenges Ahead

Although this systematic review supports an inverse association between the dTAC with common mental disorders and sleep disorders, we observed a limited number of available studies on this topic. A low sample size was observed in most studies and the majority of the studies were conducted with Iranian individuals and with women, which can generate a bias when extrapolating the results. We also highlight that some of the studies presented methodological biases, which limit interpretations. Therefore, we reinforce the need to conduct studies with a large sample size, with different nationalities, and with designs that allow the inferring of causality for the relationship of dTAC with common mental disorders and sleep disorders.

5. Conclusion

Most of the reviewed studies reported an inverse association between the dTAC with common mental disorders and sleep disorders. We encourage further research to better understand this relationship and the mechanisms involved, with different assessment methods, additional study countries and with larger sample sizes.

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Conflict of Interest

The authors declare no conflict of interest.

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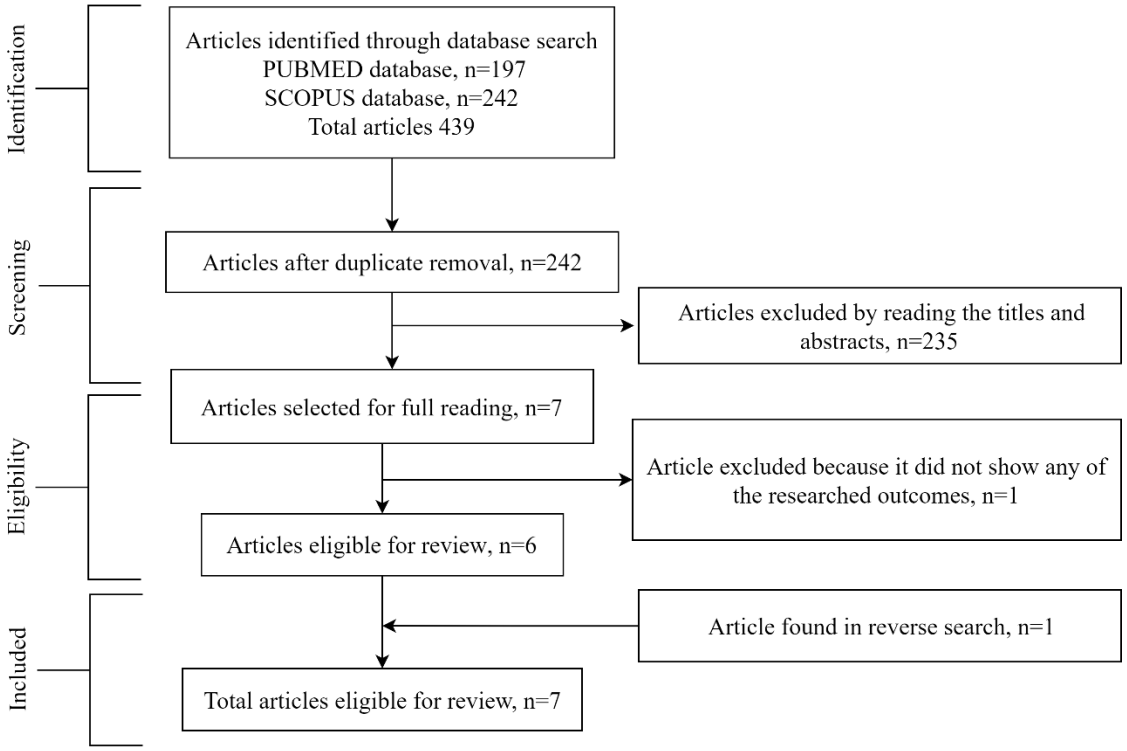

Figure 1: Stages of identification, inclusion, and exclusion of articles in the review.

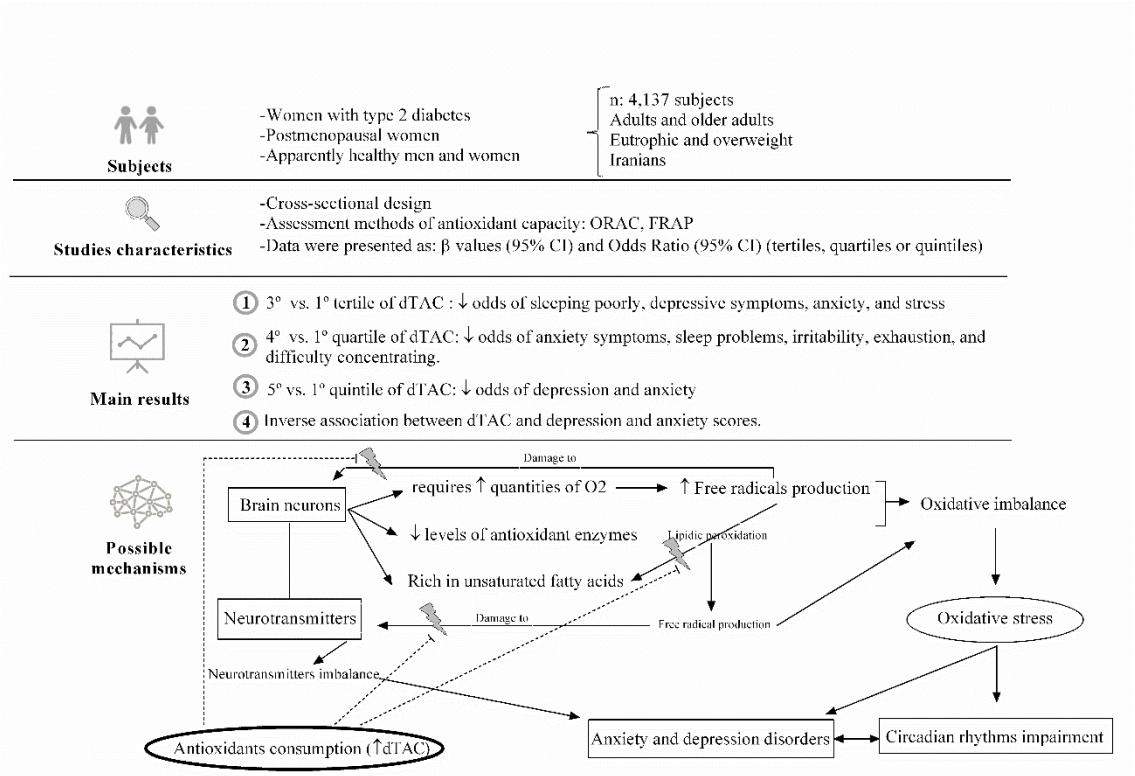

Figure 2: Figure summary of the four studies that observed a significant relationship between the total antioxidant capacity of the diet (dTAC) and the outcomes evaluated in this systematic review. Legend: ↓ = low, ↑ high, dashed lines = cancel the effect.

Table 1: Characteristics of the seven studies included in the systematic review.

Authors / Year of publication / Country	Sample characteristics	Objective of the study	Methodology	Adjustment variables	Main results
Abshirini et al., 2018 Iran	**n:** 400 postmenopausal women (adults and older adults)	To assess the association between dTAC and menopausal symptoms in postmenopausal middle-aged women	**Assay:** ORAC **Assessment of food consumption:** validated semi-quantitative food frequency questionnaire with 147 food items **Outcome assessment:** Menopause Rating Scale (MRS) questionnaire	Age, educational level, waist circumference, physical activity, use of dietary supplements, fiber, tea, coffee, and energy intake	-Higher ORAC quartile was associated with lower chance of anxiety symptoms, sleep problems, irritability, exhaustion / difficulty concentrating. -Absence of association between ORAC and depressed mood.
Abshirini et al., 2019 Iran	**n:** 175 postmenopausal women (adults and older adults)	To evaluate the association between dTAC with scores of depression, stress, anxiety, and oxidative stress in postmenopausal women	**Assay:** ORAC **Assessment of food consumption:** validated semi-quantitative food frequency questionnaire with 147 food items **Outcome assessment:** Stress, Anxiety and Depression Scale (DASS-42)	Age, time of menopause; education level, waist circumference, physical activity, use of dietary supplements, fiber, energy, and coffee intake	-Inverse association between ORAC and depression and anxiety scores -Absence of association between dTAC and stress score

Daneshzad et al., 2020 Iran	**n:** 265 type 2 diabetic women (adults and older adults)	To evaluate the association between dTAC with sleep, stress, anxiety, and depression in women	**Assay:** ORAC and FRAP **Assessment of food consumption:** semi-quantitative food frequency questionnaire validated with 168 food items. **Outcome assessment:** Pittsburgh Sleep Quality Index and Depression, Anxiety and Stress Scale (DASS-21)	Age, BMI, energy intake, physical activity, blood pressure, medication, supplement consumption, socioeconomic classification, nap times, hours of night sleep	-Higher tertile of FRAP and ORAC was associated with lower chances of sleeping poorly, of depressive symptoms and stress -Higher FRAP tertile was associated with lower chance of anxiety
Milajerdi et al., 2018 Iran	**n:** 3.297 men and women, apparently healthy adults	Investigate the association between dTAC and depression and anxiety among Iranian adults	Essay: FRAP **Assessment of food consumption:** validated semi-quantitative food frequency questionnaire with 106 food items. **Outcome assessment:** Hospital Anxiety and Depression Scale	Age, sex, energy consumption, marital status, socioeconomic status, smoking, presence of chronic conditions, physical activity, use of supplements, antidepressant medication use, intake of omega-3 fatty acids and BMI	Higher FRAP quintile was associated with lower chance of higher depression and anxiety scores

Miki et al., 2020 **Japan**	**n:** 911 men and women (youth, adults, and older adults)	To assess the association of dTAC and the incidence of depressive symptoms in Japanese workers	**Assay:** ORAC and FRAP **Assessment of food consumption:** Brief, validated dietary questionnaire with 58 food items **Outcome assessment:** Japanese version of the scale of the Center for Epidemiological Studies of depression **Duration:** 3 years of follow-up	Age, sex, marital status, degree of employment, night work or on a rotating shift, overtime work, Job strain, physical activity at work, household chores, commuting, or leisure, smoking; BMI, consumption of alcohol, total energy intake, antioxidant supplement use, intake of folate, vitamin B6, vitamin B12, n-3 polyunsaturated fatty acids, magnesium, and zinc, and CES-D score	Absence of association between ORAC and FRAP with incidence of depressive symptoms
Oliveira et al., 2019* **Brazil**	**n:** 41 climacteric women	To evaluate the possible relationship between dTAC and polyphenol intake and depression in climacteric women	**Assay:** VCAC **Assessment of food consumption:** 24-hour dietary recall **Outcome assessment:** Medical diagnosis of depression and Beck Depression Inventory (BDI)	No adjustment	Absence of difference in average VCAC values in women with depression or no

Prohan et al., 2014* **Iran**	**n:** 60 men (young) cases: 30 students diagnosed with depression control: 30 healthy students	To evaluate associations between dTAC and serum CAT with depression scales in young university students	**Essay:** TEAC and FRAP **Assessment of food consumption:** Two 24-hour dietary recalls and validated semi-quantitative food frequency questionnaire with 168 food items **Outcome assessment:** Beck-II Depression Inventory	No adjustment	Absence of difference in the average values of TEAC and FRAP between cases and controls

Legend: * did not assess association through regression analyzes, **dTAC**: Dietary Total Antioxidant Capacity **n:** sample size; **BMI:** Body Mass Index; **ORAC**: Oxygen Radical Absorbance Capacity; **FRAP**: Ferric Reducing Ability of Plasma; **VCAC**: Vitamin C Equivalent Antioxidant Capacity; **TEAC:** Trolox Equivalent Antioxidant Capacity; **CES-D:** Center for Epidemiologic Studies Depression Scale.

Table 2. Quality assessment of cross-sectional and cohort studies.

	Questions														
Study	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**Overall Rating**
Daneshzad, et al., 2020	Y	Y	N	Y	N	N	N	Y	Y	N	Y	N	N	Y	Fair
Abshirini, et al., 2018	Y	Y	N	Y	N	N	N	Y	Y	N	Y	N	N	Y	Fair
Abshirini, et al., 2019	Y	Y	N	Y	N	N	N	Y	Y	N	Y	N	N	Y	Fair
Oliveira, et al., 2019	Y	Y	N	Y	N	N	N	Y	Y	N	N	N	N	N	Poor
Milajerdi, et al., 2018	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	N	N	Y	Good
Miki, et al., 2020	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	N	N	Y	Good

Legends: Y: Yes; N: No: no applicable, no reported, no possible to determine.

1. Was the research question or objective in this paper clearly stated?
2. Was the study population clearly specified and defined?
3. Was the participation rate of eligible persons at least 50%?
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?
5. Was a sample size justification, power description, or variance and effect estimates provided?
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
10. Was the exposure(s) assessed more than once over time?
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
12. Were the outcome assessors blinded to the exposure status of participants?
13. Was loss to follow-up after baseline 20% or less?
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

Table 3. Quality assessment of cross-sectional and cohort studies

	Questions												
Study	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**Overall Rating**
Prohan , et al., 2014	Y	Y	N	Y	Y	Y	N	Y	N	Y	N	N	Poor

Legends: Y: Yes; N: No: no applicable, no reported, no possible to determine

Questions

1. Was the research question or objective in this paper clearly stated and appropriate?
2. Was the study population clearly specified and defined?
3. Did the authors include a sample size justification?
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?
6. Were the cases clearly defined and differentiated from controls?
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?
8. Was there use of concurrent controls?
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?
11. Were the assessors of exposure/risk blinded to the case or control status of participants?
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?

3. JUSTIFICATIVA

É possível observar uma grande prevalência e incidência de transtornos mentais como a depressão, da mesma forma, alterações nos padrões adequados do sono são crescentes, com destaque para a diminuição no tempo de sono. A alta prevalência destas morbidades geram grande impacto na vida da população, com complicações biológicas e sociodemográficas, aumento dos gastos em saúde, além de serem fatores de risco para outras doenças crônicas. Esse cenário epidemiológico é influenciado pelo aumento na exposição da população a fatores de risco como sedentarismo, tabagismo, mudanças no padrão alimentar, consumo excessivo de álcool, deficiências nutricionais, entre outros. Em concordância, o estudo CUME mostra, em sua linha de base, alta prevalência de depressão em adultos jovens brasileiros.

O padrão alimentar da população brasileira vem mudando juntamente com a transição epidemiológica. Há diminuição no consumo de refeições completas e ricas em nutrientes e aumento no consumo de alimentos ricos em açúcares e com baixa qualidade nutricional. Juntamente a esses fatores é possível observar um grande nível de inadequação no consumo de antioxidantes na dieta, como vitaminas e minerais. Destaca-se que a carência destes componentes da dieta relaciona-se com o aumento do estresse oxidativo, que por sua vez é considerado fator de risco para alterações no adequado funcionamento do cérebro.

Desde modo um maior aporte antioxidante provindo da dieta poderia atuar como fator de proteção para a depressão e alterações no sono. A análise da CATd é uma técnica eficaz para a mensuração dos antioxidantes da dieta. Entretanto, nota-se a falta de estudos longitudinais avaliando a CATd, sono e depressão na população brasileira.

O presente estudo epidemiológico justifica-se pela necessidade de investigar a relação entre a dieta, medida pela CATd, o sono e a depressão em adultos jovens brasileiros. Dentro do campo da saúde coletiva esses resultados contribuirão para evidenciar a importância da nutrição e dos profissionais nutricionistas como componentes de equipes multidisciplinares. Além disso, gerar subsídios para programas de educação alimentar e nutricional e protocolos que visem a promoção da saúde mental.

4. OBJETIVOS

4.1. OBJETIVO GERAL

Avaliar a relação entre a capacidade antioxidante total da dieta, depressão e sono em participantes da Coorte de Universidades Mineiras-CUME.

4.2. OBJETIVOS ESPECÍFICOS

Estudo Transversal

- ✓ Avaliar a associação entre capacidade antioxidante total da dieta e o tempo de sono;
- ✓ Avaliar a associação entre a capacidade antioxidante total de grupos alimentares específicos com o tempo de sono.

Estudo Longitudinal

- ✓ Avaliar a associação entre capacidade antioxidante total da dieta e o com a incidência de depressão;
- ✓ Avaliar a associação entre a capacidade antioxidante total de grupos alimentares específicos com a incidência de depressão.

5. METODOLOGIA

5.1. COORTE DE UNIVERSIDADES MINEIRAS (ESTUDO CUME)

O Estudo Coorte de Universidades Mineiras (Estudo CUME) trata-se de uma coorte aberta com egressos de instituições federais de ensino superior do estado de Minas Gerais (Brasil). O objetivo principal do estudo CUME é avaliar o impacto do padrão alimentar, de grupos de alimentos e fatores específicos da dieta no desenvolvimento de doenças e agravos não transmissíveis na população de estudo.

A primeira aplicação do questionário de linha de base (Q_0) do estudo CUME ocorreu com egressos da Universidades Federal de Viçosa e Universidade Federal de Minas Gerais no ano de 2016. O acompanhamento da Coorte CUME se dá a cada dois anos (Q_2, Q_4, Q_n...), e novos potenciais participantes recebem o convite para responder o Q_0. Além disso, novas Universidades Federais do estado de Minas Gerais são convidadas a participarem do estudo (**Figura 1**).

O convite para participar do estudo CUME ocorreu através de e-mails enviados para os ex-alunos, disponibilizados pelas instituições de ensino participantes. Além disso, o egresso que tivesse interesse em participar do estudo, entretanto não tivesse recebido o e-mail, pode se cadastrar e participar do estudo através do website da coorte (www.projetocume.com.br).

Atualmente o estudo CUME conta com a participação das seguintes instituições de ensino superior do estado de Minas Gerais: Universidade Federal de Viçosa (UFV), Universidade Federal de Minas Gerais (UFMG), Universidade Federal de Ouro Preto (UFOP), Universidade Federal de Lavras (UFLA), Universidade Federal de Juiz de Fora (UFJF), Universidade Federal de Alfenas (UNIFAL) e da Universidade Federal dos Vales do Jequitinhonha e Mucuri (UFVJM) **(Figura 1**).

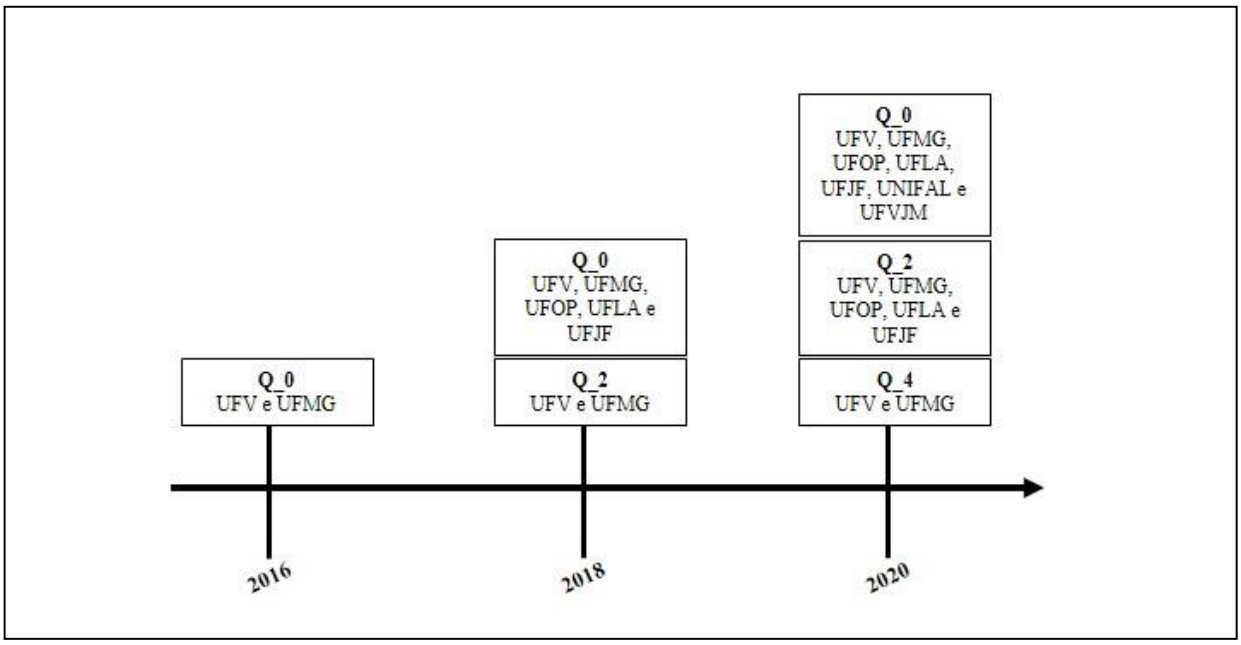

Figura 1. Instituições de ensino superior envolvidas nas coletas de dados do estudo CUME.

5.2. COLETA DE DADOS

Questionário Basal (Q_0)

A primeira coleta de dados online relativa ao questionário basal (Q_0) ocorreu entre março e agosto de 2016 com egressos (1994-2014) da UFV e UFMG. Os potenciais participantes receberam o convite para a participação do projeto via e-mail, onde foram redirecionados à página virtual do CUME e puderam saber mais sobre o estudo, além de ler e assinar o Termo de Consentimento Livre e Esclarecido (TCLE) (**ANEXO II**). Após consentimento, os mesmos puderam seguir como voluntários na pesquisa e então responder o questionário basal.

Vale destacar que o questionário basal passou por validação anterior de fase e conteúdo, onde foram avaliadas sua complexidade de entendimento, sua aplicabilidade e relevância. Além disso, foram realizados estudos piloto para a avaliação da qualidade do instrumento para a coleta de dados (DOMINGOS et al., 2018).

Após as avaliações dos estudos piloto a equipe decidiu pela aplicação do questionário basal em duas fases. A primeira fase continha questões sobre características sociodemográficas, estilo de vida, marcadores bioquímicos e, relativas a desfechos em saúde do indivíduo. Após o intervalo de uma semana da resposta da primeira fase, os participantes foram convidados, por e-mail, para o preenchimento da segunda fase, composta por um

Questionário de Frequência de Consumo Alimentar (QFCA) e perguntas relacionadas a hábitos alimentares.

A segunda coleta de dados relativa ao Q_0 ocorreu de março a julho de 2018 com egressos da instituições de ensino UFOP, UFLA e UFJF, além de egressos dos anos de 2015 à 2017 da UFV e UFMG. Já a terceira coleta de dados relativa ao Q_0 ocorreu entre abril e julho de 2020 e contou com egressos das instituições de ensino superior UFVJM e UNIFAL, além de egressos dos anos de 2018 e 2019 das instituições UFV, UFMG, UFOP, UFLA e UFJF. Atualmente, o estudo CUME conta com 7.710 questionários de linha de base (Q_0) completos, as figuras 1 e 2 exemplificam os resultados da coleta de dados. O questionário basal do estudo CUME encontra-se disponível no seguinte endereço: https://www.projetocume.com.br/questionario.

Questionário de Seguimento (Q_2)

A primeira coleta de dados relativa ao Q_2 ocorreu entre março e julho de 2018. Foram enviados convites para os participantes que preencheram as duas fases do Q_0 de 2016. Já a segunda coleta, relativa ao Q_2, ocorreu entre abril e julho de 2020 onde foram convidados os participantes que completaram o questionário de seguimento Q_0 em 2018 **(Figura 1 e 2).**

O Q_2 foi composto por perguntas relativas às mudanças no estilo de vida, dos hábitos alimentares e das condições de saúde e conta com 3.106 questionários respondidos de forma completa (**Figura 2**). O questionário Q_2 do estudo CUME encontra-se disponível no seguinte endereço: https://www.projetocume.com.br/questionario.

Questionário de Seguimento (Q_4)

A coleta relativa ao questionário de seguimento Q_4 ocorreu entre abril e julho de 2020. Receberam o convite, para o preenchimento do questionário Q_4, participantes que responderam ao Q_2 em 2018. Foram obtidos 1.892 questionários completos (**Figura 1 e 2**).

O questionário de seguimento Q_4 foi composto por perguntas relativas a características sociodemográficas, estilo de vida, marcadores bioquímicos, desfechos em saúde e pelo questionário validado Índice de Gravidade de Insônia. O questionário Q_4 do estudo CUME encontra-se disponível no seguinte endereço: https://www.projetocume.com.br/questionario.

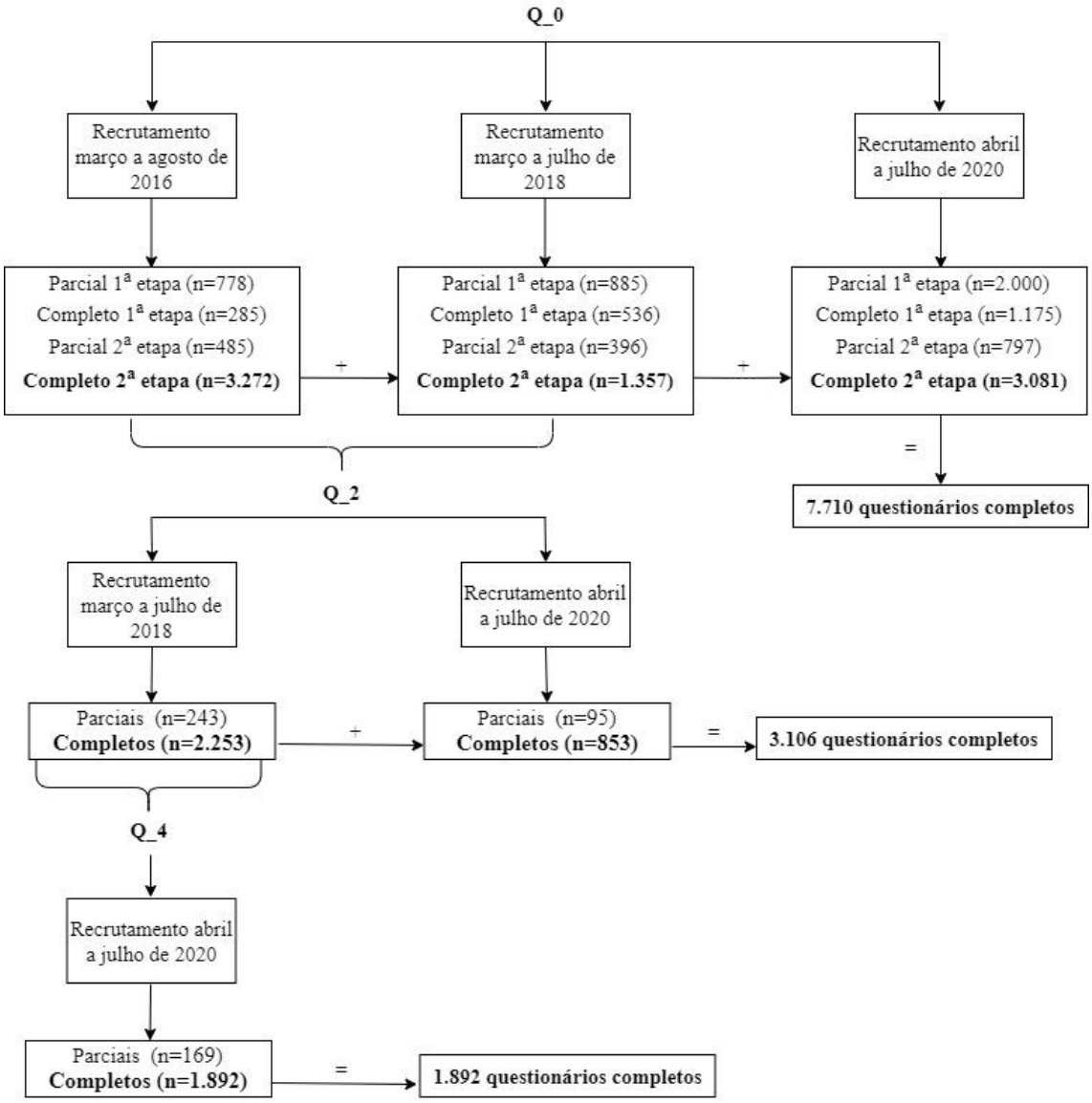

Figura 2. Fluxograma da coleta de dados relativa aos questionários basal Q_0, de seguimento Q_2 e Q_4 do estudo CUME.

5.3. ASPECTOS ÉTICOS

Todos os participantes do estudo CUME manifestam seu aceite no TCLE. O estudo CUME foi aprovado pelos Comitês de Ética em Pesquisa com Seres Humanos de todas as instituições participantes: Universidade Federal de Minas Gerais (registro CAAE: 07223812.3.3001.5153); Universidade Federal de Viçosa (número de registro CAAE: 4483415.5.1001.5149); Universidade Federal de Ouro Preto (número de registro CAAE: 44483415.5.2003.5150); Universidade Federal de Lavras (número de registro do CAAE: 44483415.5.2002.5148); Universidade Federal de Juiz de Fora (número de registro CAAE:

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O retorno aos voluntários é dado de forma contínua através das redes sociais da coorte e do website (www.projetocume.com.br), são fornecidas informações sobre Educação Alimentar e Nutricional assim como resultados dos estudos que vêm sendo desenvolvidos com as bases de dados do estudo CUME.

5.4. POPULAÇÃO DO ESTUDO

Estudo de delineamento transversal

O objetivo principal do estudo transversal foi relacionar a CATd com o tempo de sono dos participantes do estudo CUME. Tal estudo contemplou os dados da linha de base do CUME dos anos 2016, 2018 e 2020, que conta com Q_0 completos de 7.710 participantes. Foram critérios de exclusão: mulheres que relataram estar grávidas ou que estivessem grávidas no último ano (n=282), participantes com consumos extremos de energia < 500 kcal ou > 6,000 kcal por dia (n=229) (SCHMIDT et al., 2015), participantes que não residiram no Brasil no último ano (n= 278), participantes de outras nacionalidades (n=31), participantes que relataram o uso de tranquilizantes ou indutores do sono (n=288), participantes que relataram o diagnóstico médico de apneia do sono (n=142) e participantes que não responderam sobre o tempo de sono (n=73). A amostra final foi composta por 6.387 participantes.

Estudo de delineamento longitudinal

O objetivo principal do estudo longitudinal foi relacionar a CATd com a incidência de depressão em participantes do estudo CUME. Dos 7.710 participantes com dados da linha de base completos foram excluídos 4.084 pois não haviam cumprido pelo menos dois anos de acompanhamento. Também foram excluídas mulheres que estavam grávidas ou tiveram grávidas no último ano (n=430), participantes com consumo de energia < 500 kcal ou > 6.000 kcal por dia (n=79) (SCHMIDT et al., 2015), participantes que relataram não ter residido no Brasil no último ano (n = 135), estrangeiros residentes no Brasil (n = 10) e participantes que relataram diagnóstico de depressão no início do estudo (n = 400). A amostra final foi composta por 2.572 participantes que responderam a pelo menos um questionário de acompanhamento.

5.5. AVALIAÇÃO DO CONSUMO ALIMENTAR

O consumo alimentar habitual foi obtido mediante QFCA previamente validado para a população do estudo (AZARIAS et al., 2021). O QFCA foi composto por 144 itens alimentares, separados pelos seguintes grupos: lácteos, carnes e peixes, cereais e leguminosas, frutas, hortaliças, gorduras e óleos, bebidas e, outros alimentos. Cada participante informou a frequência de consumo de um determinado alimento (diário, semanal, mensal ou anual), a quantidade de vezes que fez este consumo (0 a 9 ou mais vezes) e o tamanho da porção. Com a finalidade de facilitar o preenchimento do tamanho das porções dos itens alimentares e obter informações mais fidedignas possíveis, os voluntários tinham acesso, no momento de resposta do QFCA, a imagens de porções de alimentos e utensílios de servir advindas do álbum fotográfico com 96 imagens elaborado pela equipe do estudo CUME.

O consumo de macro e micronutrientes foi calculado utilizado primeiramente informações da Tabela de Composição Nutricional dos Alimentos Consumidos no Brasil (INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA-IBGE, 2011) e, na ausência de informações, foram consultadas a Tabela de Composição de Alimentos (TACO) (UNIVERSIDADE ESTADUAL DE CAMPINAS - UNICAMP., 2011) e o Banco Nacional de Nutrientes da USDA (GEBHARDT; THOMAS, 2002).

5.6 AVALIAÇÃO DA CAPACIDADE ANTIOXIDANTE DA DIETA

A CATd foi estimada de acordo com o ensaio Ferric Reducing Antioxidant Power (FRAP) o qual mede a capacidade antioxidante do alimento na presença do íon ferro. Assim, a CATd resultou da multiplicação da quantidade em gramas de um alimento com o seu respectivo valor FRAP em mmol por grama (mmol/g) (OKUBO et al., 2014). Para cada item alimentar foi atribuído um valor de FRAP de acordo com estudos previamente publicados (CARLSEN et al., 2010; KOEHNLEIN et al., 2014). Foram adotados os seguintes critérios para atribuição dos valores de FRAP:

- Quando houve mais de um valor de FRAP para o mesmo alimento foi calculado o valor médio;
- Quando não houve valor de FRAP disponível para um determinado alimento, foi utilizado o valor de FRAP de um alimento semelhante do mesmo grupo botânico, ou do mesmo alimento em uma forma de preparo diferente;

- Não foi atribuído valor de FRAP para alimento onde não houve nenhum registro deste valor e não foi possível estimar por alimentos de grupos botânicos semelhantes ou diferentes modos de preparo.

Um total de 133 itens alimentares foram contemplados com os valores de FRAP. A CATd total foi calculada com base no somatório de todos valores de FRAP dos alimentos relatados no QFCA. Para maior sensibilidade das análises também foi calculada da CATd sem o café, uma vez que este é o item alimentar que mais contribuiu para a CATd da população do estudo CUME (SABIÃO et al., 2021), além do seu alto consumo poder estar relacionado com alterações no tempo de sono (CLARK; LANDOLT, 2017; FAWALE et al., 2017). Uma vez que a matriz alimentar em que os antioxidantes estão inseridos pode influenciar em resultados de saúde, a Capacidade Antioxidante Total de Grupos Alimentares (CATga) também foi calculada. Assim foram calculadas a CATga para os seguintes grupos: frutas, hortaliças, feijões e lentilhas, oleaginosas, lácteos, carnes e ovos, massas, pães e cereais, óleos e gorduras, *junk food*, sucos naturais, chás e cafés, sucos artificiais e refrigerantes e bebidas alcoólicas.

5.7. AVALIAÇÃO DO TEMPO DE SONO

Para avaliar o tempo de sono foi utilizada a pergunta número 40 do Q_0 "*Nos últimos 12 meses, quanto tempo em média por dia você se dedicou às seguintes atividades*?" sendo um dos quesitos avaliados o tempo de sono, e as respostas coletadas em números inteiros (1 a 8 e ≥9h). Os participantes foram classificados em sono muito curto (≤ 4 horas) e sono curto (entre 5 e 6 horas), adequado (entre 7 e 8 horas), sono longo (≥ 9 horas), de acordo com pesquisas na literatura epidemiológica existente (KANAGASABAI; ARDERN, 2015; MURPHY et al., 2022; TAMAKOSHI; OHNO, 2004).

5.8. AVALIAÇÃO INCIDÊNCIA DE DEPRESSÃO

A incidência de depressão foi considerada para aqueles participantes que estavam livres do diagnóstico médico de depressão no início do seguimento e foram classificados como portadores da doença durante o acompanhamento Q_2 ou Q_4. Sendo que os casos incidentes foram identificados pela resposta positiva a seguinte questão *"Desde o questionário anterior, você foi diagnosticado clinicamente com depressão pela primeira vez ?"*. Indivíduos que relataram utilizar antidepressivos, porém não confirmaram o diagnóstico de depressão, não foram incluídos como casos de depressão, devido à possibilidade do uso

terapêutico de tais medicamentos em outras doenças. A confiabilidade entre o diagnóstico médico de depressão e o autorrelato, investigado em uma subamostra de participantes, mostrou uma boa concordância (81,0%) com um valor de Kappa de 0,62 (SANTOS et al., 2021).

5.10. DEMAIS VARIÁVEIS

As demais variáveis incluídas no estudo foram obtidas a partir das informações do questionário de linha de base Q_0. Foram elas: Gênero (feminino masculino); Idade; Cor da pele (branca, não branca); Estado civil (solteiro, casado/união estável, viúvo, separado ou divorciado, outros); Situação profissional (aposentado, desempregado, estudante, trabalho em tempo integral, meio período ou informal); Uso de suplementos vitamínicos (sim, não); Condição tabágica (fumante, ex-fumante, não fumante); Tempo diário de uso do computador (1 a 8 e ≥9h); Ano de coleta (2016, 2018, 2020). A frequência de consumo episódico pesado de bebida alcoólica também foi avaliada (1 a 2 dias/mês, 3 a 4 dias/mês e 5 ou mais dias/mês), o consumo episódico pesado foi considerado como 4 ou mais doses de bebida alcoólica em uma única ocasião para mulheres e 5 ou mais doses de bebida alcoólica em uma única ocasião para homens (NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM, 2022). A atividade física foi avaliada por meio de uma lista de 24 atividades e expressa em minutos por semana. Foram considerados ativos participantes com ≥ 150 minutos/semana de atividade de intensidade moderada ou ≥ 75 minutos/semana de atividade de intensidade vigorosa; foram classificados como insuficientemente ativos aqueles participantes com < 150 minutos/semana de atividade de intensidade moderada ou < 75 minutos/semana de atividade de intensidade vigorosa e inativos aqueles que relataram ausência de atividade física no lazer (WORLD HEALTH ORGANIZATION, 2010). O Índice de Massa Corporal (IMC) foi obtido a partir do peso e estatura autorrelatados no questionário linha de base, dividindo-se o peso (quilogramas) pela altura (metros) elevada ao quadrado. Valores de IMC ≥ 30 kg/m^2 foram classificados como obesidade (WORLD HEALTH ORGANIZATION/WHO., 1998). O IMC a partir do peso e altura autorrelatados também foi validado, em estudo prévio, para a população participante do estudo CUME, indicando uma concordância excelente com o aferido, coeficiente de correlação intraclasse-CCI: 0,989 (MIRANDA et al., 2017).

5.11. ANÁLISES ESTATÍSTICAS

As análises estatísticas foram realizadas no *software* estatístico Stata, versão 15.0. Foi adotado um nível de significância (α) de 5%, sendo todos os testes de hipóteses propostos em nível bilateral. Para avaliar a normalidade das variáveis quantitativas foi realizado o teste de Kolgomorov Smirnoff. As variáveis quantitativas foram apresentadas como média e desvio padrão e as variáveis qualitativas foram apresentadas em valores absolutos e relativos.

Para controlar o efeito da ingestão calórica sobre o consumo de nutrientes e sobre a CATd e CATga os mesmos foram ajustados pela ingestão calórica total pelo método residual (WILLETT, 1998).

Análises transversais

As características sociodemográficas, de estilo de vida e de saúde foram descritas de forma categórica conforme as classificações do tempo de sono, sendo o *p* valor calculado a partir do teste qui-quadrado de Pearson.

Foi realizada análise multivariada com procedimentos de regressão logística multinomial, a variável dependente foi o tempo de sono, como categoria de referência foi considerada classificação do sono "adequada" (7-8 horas de sono). Foram analisadas as razões de chances de sono muito curto/curto e também de sono longo de acordo com os quartis de CATd. Através de busca na literatura epidemiológica foram consideradas as seguintes variáveis de ajuste para o modelo: sexo, idade, cor da pele (branco, não branco), condição tabágica (não fumante, fumante, ex-fumante), frequência de consumo episódico pesado de bebida alcoólica (nenhum, de 1 a 2 vezes/mês, 3 a 4 vezes/mês, 5 ou mais vezes/mês), atividade física (inativo, insuficientemente ativo, ativo), situação profissional (empregado, estudante, desempregado e aposentado), estado civil (solteiro, casado/união estável, Separado/divorciado/viúvo/outros), tempo diário de uso de computador ($\leq$5, >5 e > 9, $\geq$9 horas), IMC, autorrelato de diagnóstico médico de depressão (sim, não) e ano de coleta (2016, 2018, 2022).

Foi realizada uma análise de sensibilidade, performando-se a regressão logística multinomial para as chances de se ter sono muito curto/curto ou sono longo, de acordo com os quartis de CATd sem o FRAP do café e também de acordo com quartis da CATga.

Análises longitudinais

As características sociodemográficas, de estilo de vida e de consumo alimentar foram descritas de acordo com os quartis de CATd, sendo o *p* valor para variáveis categóricas obtido pelo teste qui-quadrado de Pearson e para variáveis contínuas pelo teste ANOVA.

O cálculo do tempo de acompanhamento de cada participante se deu por anos-pessoa. Desta forma, foi obtido pela diferença entre a data de preenchimento do questionário de acompanhamento no qual a depressão foi diagnosticada e a data de preenchimento do questionário de linha de base. A partir do tempo de acompanhamento foram criados modelos de regressão de COX, utilizando a CATd em quartis como variável de exposição (primeiro quartil como referência) e a incidência de depressão como variável desfecho. Para selecionar as variáveis que fariam parte do modelo de ajuste foi construído um gráfico acíclico direcionado (DAG) usando o programa DAGitty. O modelo final foi ajustado para os seguintes fatores de confusão: sexo, idade (contínua), condição tabágica (não fumante/fumante/ex-fumante), frequência de consumo episódico pesado de bebida alcoólica (nunca/de 1 a 2 dias por mês/ de 3 a 4 dias por mês/5 ou mais dias por mês), estado civil (solteiro/casado ou união estável/separado ou divorciado ou viúvo), cor da pele (branca/não branca), situação profissional (empregado, estudante, desempregado e aposentado), atividade física (inativo /insuficientemente ativo/ativo), uso de suplementos vitamínicos (sim/não), IMC (contínuo) e ingestão calórica (kcal/dia) e consumo de vitamina D (μg/dia). A tendência linear foi testada utilizando os valores da mediana de cada quartil da variável de exposição no modelo final da regressão de Cox. Para maior sensibilidade das análises foi realizada a regressão de Cox com quartis da CATd sem o café e com os quartis da CATga.

6. RESULTADOS

Os resultados e discussão da presente tese estão apresentados no formato de dois artigos científicos originais, a saber:

Artigo 1. Capacidade antioxidante total da dieta e de grupos de alimentos e sua relação com o tempo de sono de graduandos brasileiros (Estudo CUME).

Artigo 2. Associação entre capacidade antioxidante total da dieta e de grupos de alimentos e incidência de depressão em uma coorte de graduados brasileiros (Projeto CUME). O presente artigo foi publicado na **Revista British Journal of Nutrition** (doi: 10.1017/S0007114523000181). A formatação do segundo artigo encontra-se de acordo com as normas contidas nas instruções aos autores da revista.

6.1. ARTIGO 1. CAPACIDADE ANTIOXIDANTE TOTAL DA DIETA E DE GRUPOS DE ALIMENTOS E SUA RELAÇÃO COM O TEMPO DE SONO DE GRADUANDOS BRASILEIROS (ESTUDO CUME)

Total dietary antioxidant capacity and food groups and their relationship with the sleep time of Brazilian graduates (CUME Study).

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Abstract

Introduction: Sleep is characterized as an essential process of human life. The reduction in sleep time has occurred due to the modern lifestyle of society. Oxidative stress can contribute to sleep alterations; in this sense, a higher Total Antioxidant Capacity of the Diet (dTAC) could act as a protective factor.

Objective: To investigate the association between the dTAC and the Total Antioxidant Capacity of food groups (fgTAC) with the sleep time of Brazilian graduates participating in the Cohort of Universities of Minas Gerais (CUME Study).

Methodology: This cross-sectional study analyzed 6,387 graduates (2,052 men, 4,335 women, 35.3 ± 9.3 years old) from the CUME Study. Data was collected online, and dTAC was obtained by the Ferric Reduction Antioxidant Power (FRAP) method. Daily sleep time was classified as very short/short sleep, normal sleep, and long sleep (≤ 6, 7–8, and ≥ 9 hours, respectively). Multinomial logistic regression models were used to estimate the Odds Ratio (OR) and its 95% Confidence Interval (95% CI) between very short/short sleep and long sleep with quartiles of dTAC and the fgTAC.

Results: Lower odds of very short/short sleep was observed only for the second quartile of dTAC (OR: 0.83; 95% CI: 0.71-0.96). Lower odds of very short/short sleep were observed for fourth quartile of fgTAC of fruits (OR: 0.84; CI: 0.71-0.99), beans, and lentils (OR: 0.77; CI0.65-0.90) and for the third quartile of fgTAC of vegetables (OR: 0.84; CI: 0.71-0.98) and oils and fats (OR: 0.83; CI: 0.70-0.97). Higher odds of very short/short sleep for the fourth quartile of fgTAC of teas and coffees (OR: 1.24; CI: 1.06-1.45). For long sleep, inverse associations were observed for the fourth quartile of fgTAC of oilseeds (OR: 0.66; CI: 0.46-0.93) and the third quartile of fgTAC of teas and coffees (OR: 0.67; CI: 0.48-0.94).

Conclusion: We cannot independently assert an association between higher dTAC and sleep time. In turn, the associations between sleep time and fgTAC show the importance of the food matrix that antioxidants are inserted, requiring longitudinal studies to observe the direction of associations.

Keywords: Sleep, Dietary Total Antioxidant Capacity, Epidemiology, Oxidative Stress

Introduction

Sleep is characterized as an essential process of human life under neurobiological regulation, which impacts the functioning of physiological systems (GRANDNER, 2017). Although sleep characteristics are inherent to the genetic constitution, they are strongly influenced by the environment, interpersonal and social factors (GRANDNER, 2017). In this sense, a reduction in sleep time has occurred due to the modern lifestyle of society (DENG et al., 2017).

According to the National Sleep Foundation (NSF), the sleep time from 7 to 9 hours is adequate for adults is, and shorter or longer sleep durations have been associated with increased morbidity and mortality (HIRSHKOWITZ et al., 2015) as well as with higher incidence of obesity, arterial hypertension and metabolic syndrome (DENG et al., 2017; GOZAL; DUMIN; KOREN, 2016). Likewise, inadequate sleep duration may be associated with cognitive changes, anxiety, and depression (WINER et al., 2021).

Among the factors that may be related to changes in sleep time, we highlight oxidative stress, which can lead to changes in the circadian cycle (KANAGASABAI; ARDERN, 2015; WILKING et al., 2013). Furthermore, it can induce a pro-inflammatory state, with an emphasis on neuroinflammation, which is related, in turn, to poorer sleep quality (BALMUS et al., 2016; CLARK; VISSEL, 2014; LIU et al., 2020). In this perspective, oxidative stress and inflammation biomarkers have been associated with inadequate sleep duration (KANAGASABAI; ARDERN, 2015; PETROV et al., 2020).

On the other hand, diet is highlighted when it comes to non-drug therapeutic forms that are beneficial for sleep time and quality (GODOS et al., 2019; JANSEN et al., 2021; PEREIRA; GOMES DOMINGOS; AGUIAR, 2022). For example, nutrients and antioxidants present in fruits and vegetables can help both in initiating and maintaining sleep, either because they are sources of melatonin or because of their role in controlling oxidative stress and inflammation (GODOS et al., 2019; JANSEN et al., 2021; PEREIRA; GOMES DOMINGOS; AGUIAR, 2022). Dietary-nutritional interventions with antioxidants can improve the circadian rhythm, quality and duration of sleep (OSEGUERA-CASTRO et al., 2019). In turn, anti-inflammatory and antioxidant dietary patterns such as those offered by the Mediterranean diet or the greater consumption of fruits may improve sleep quality (CASTRO-DIEHL et al., 2018; GODOS et al., 2019).

A metric widely used to measure diet quality, especially with regard to the amount of antioxidants, is the Dietary Total Antioxidant Capacity (dTAC) (CARLSEN et al., 2010),

which has proven to be very useful to investigate associations between diet and health outcomes (HERMSDORFF et al., 2011; NASCIMENTO-SOUZA et al., 2018; SABIÃO et al., 2021). However, only two cross-sectional studies have assessed the association of dTAC with sleep disorders (ABSHIRINI et al., 2018; DANESHZAD et al., 2020), whereas, until now, studies that investigated dTAC and its relationship with sleep time in the Brazilian adult population have not been reported. Thus, the present study investigated the association between dTAC and the Total Antioxidant Capacity of food groups (fgTAC) with the sleep time of Brazilian graduates participating in the Cohort of Universities of Minas Gerais (CUME Study).

Methods

Cohort of Universities of Minas Gerais: CUME Study

The CUME Study is an open cohort with graduates from federal institutions of higher education in the state of Minas Gerais (Brazil), whose objective is to assess the impact of dietary patterns, food groups and specific dietary factors on the development of noncommunicable diseases and conditions in the study population. The sample design and the recruitment and communication strategies with the participants were previously reported (DOMINGOS et al., 2018).

The first application of the baseline questionnaire (Q_0) of the CUME Study occurred in 2016, with graduates from the Federal University of Viçosa and Federal University of Minas Gerais, who received an invitation to participate via available emails. The CUME Study is monitored every two years (Q_2, Q_4, Q_n...), and new potential participants are invited to answer Q_0. Similarly, new Federal Universities in Minas Gerais state are invited to participate in the study.

Questionnaire Q_0 is answered in a virtual environment in two phases. In the first phase, participants answer questions related to sociodemographic and lifestyle characteristics, biochemical markers, and health outcomes. After a week of response to the first phase, participants receive the second part of the questionnaire with questions related to eating habits and a Food Frequency Questionnaire (FFQ).

All participants expressed their acceptance of the Informed Consent Form (ICF). The CUME Study was approved by the Human Research Ethics Committees of all participating institutions: Federal University of Minas Gerais (CAAE registration: 07223812.3.3001.5153); Federal University of Viçosa (CAAE registration number: 4483415.5.1001.5149); Federal University of Ouro Preto (CAAE registration number: 44483415.5.2003.5150); Federal

University of Lavras (CAAE registration number: 44483415.5.2002.5148); Federal University of Juiz de Fora (CAAE registration number: 4483415.5.5133); Federal University of Vale do Jequitinhona and Mucuri (CAAE registration: 44483415.5.2005.5103) and Federal University of Alfenas (CAAE registration: 4.501.344).

Study population

We developed this cross-sectional analysis with baseline data from 7,710 participants of the CUME Study who completed the Q_0 in 2016, 2018 and 2020. Therefore, we excluded women who reported being pregnant or who had been pregnant in the last year (n=282); participants with extreme energy intakes < 500 kcal or > 6,000 kcal per day (n=229) (SCHMIDT et al., 2015); participants who did not live in Brazil in the last year (n= 278); participants from other nationalities (n=31); participants who reported the use of tranquilizers or sleep inducers (n=288); participants who reported the medical diagnosis of sleep apnea (n=142) and participants who did not respond about sleep time (n=73). The final sample consisted of 6,387 participants.

Outcome variable: sleep time

To assess sleep time, we used the question number 40 of Q_0, "*In the last 12 months, how much time on average per day did you dedicate to the following activities*?" one of the items assessed was sleep time, and responses were collected in whole numbers (1 to 8 and ≥9h). We classified participants into very short sleep (≤ 4 hours) and short sleep (between 5 and 6 hours), adequate (between 7 and 8 hours), long sleep (≥ 9 hours), according to existing epidemiological literature (KANAGASABAI; ARDERN, 2015; MURPHY et al., 2022; TAMAKOSHI; OHNO; JACC STUDY GROUP, 2004).

Food consumption and dTAC estimation variables

We assessed food consumption using the FFQ previously validated for the CUME Study population (AZARIAS et al., 2021). This has 144 food items distributed in the following groups: dairy products, meat and fish, cereals and legumes, fruits, vegetables, oils and fats, beverages, and other foods. In a virtual environment, participants had access to the description of the food. They could inform the frequency they consumed this food in the previous year (daily, weekly, monthly or yearly), the number of times this consumption was done (0 to 9 or more times), and the portion size of the food (specific for each food). In order to obtain greater reliability in the responses on portion sizes, the participants had access, at the

time of the response, to images of food portions from the FFQ and serving utensils from an album with 96 photos prepared by the CUME Study team. We conducted the assessment of the consumption of macro and micronutrients by first consulting information from the Table of Nutritional Composition of Foods consumed in Brazil (INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA-IBGE, 2011). In the absence of information, we consulted the Brazilian Table of Food Composition (UNIVERSIDADE ESTADUAL DE CAMPINAS - UNICAMP., 2011) and the USDA National Nutrient Database (GEBHARDT; THOMAS, 2002).

We used the values related to the Ferric Reducing Antioxidant Power (FRAP) assay from previously published databases to calculate the dTAC (CARLSEN et al., 2010; KOEHNLEIN et al., 2014). FRAP results for each food were expressed in mmol per gram (mmol/g). In this sense, the TAC of each food was obtained by multiplying the average amount of grams consumed per day of the respective food and its corresponding value of FRAP in mmol. We summed all the FRAP values of the items consumed by each participant to obtain the individual dTAC.

A total of 133 FFQ food items were covered with FRAP values. We used the following criteria to attribute the FRAP value to a food: 1) For foods with more than one FRAP value, we considered the mean of these values; 2) For foods that did not have the FRAP value, we used that of a similar food from the same botanical group or the value of the same food in a different way of preparation; 3) For foods that did not meet the aforementioned criteria, we did not assign FRAP values.

We calculated the dTAC values without FRAP of coffee for greater sensitivity of our analyses since coffee is a beverage that most contributes to the dTAC value in our study population (SABIÃO et al., 2021), in addition to its high consumption being related to changes in sleep time (CLARK; LANDOLT, 2017; FAWALE et al., 2017). We also calculated fgTAC values for food groups by summing all FRAP values for the following food groups: fruits, vegetables, beans and lentils, oilseeds, dairy products, meats and eggs, pasta, breads and cereals, oils and fats, junk food, natural juices, teas and coffees, artificial juices and alcoholic beverages (**Table 1**).

Covariates

We obtained the other variables based on information from the Q_0 questionnaire: Year of collection (2016, 2018 and 2020); Gender (female, male); Age; Skin color (white, non-white); Marital status (single, married/stable union, widowed, separated or divorced,

others); Professional status (retired, unemployed, student, full-time, part-time or informal job); Use of vitamin supplements (yes, no); Smoking status (smoker, ex-smoker, non-smoker); Daily time of computer use (1 to 8 and ≥9h). We also included the frequency of binge drinking [heavy episodic alcohol consumption (1 to 2 days/month, 3 to 4 days/month, and 5 or more days/month)], with binge drinking being considered 4 or more doses on a single occasion for women and 5 or more doses on a single occasion for men (NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM, 2022). We assessed physical activity using a list of 24 activities expressed in minutes per week. Those participants with 150 minutes/week of moderate-intensity activity or ≥ 75 minutes/week of vigorous-intensity activity were considered active, those participants with < 150 minutes/week of moderate-intensity activity or < 75 minutes/week of vigorous-intensity activity were considered insufficiently active and those participants who reported no physical activity were considered inactive (WORLD HEALTH ORGANIZATION, 2010). We also assessed the prevalence of depression through self-report of medical diagnosis of depression. The reliability between the medical diagnosis and the self-report of depression was validated for the population of this cohort, showing good agreement (81.0%) with a Kappa value of 0.62 (SANTOS et al., 2021). We obtained the Body Mass Index (BMI) from self-reported weight (kilograms) and height (meters) in the baseline questionnaire Q_0. BMI values ≥ 30 kg/m2 were classified as obesity (WORLD HEALTH ORGANIZATION/WHO., 1998). BMI obtained by self-reported weight and height was validated for CUME Study participants in a previous study, obtaining excellent agreement (measured intraclass correlation coefficient: 0.989) (MIRANDA et al., 2017).

Statistical analyzes

We performed all analyzes using the Stata SE 15.0 software. A two-tailed p-value less than 0.05 was considered statistically significant. We adjusted all food consumption variables for daily caloric intake using the residual method (WILLETT, 1998).

For analytical purposes, we grouped the short and very short sleep categories, and we analyzed the following categories: very short/short sleep (≤ 6 hours/day), adequate sleep (7-8 hours/day) and long sleep (≥ 9 hours). Thus, sociodemographic, lifestyle and health characteristics were categorically described according to sleep time classifications, with the p-value calculated from Pearson's chi-square test.

We also performed the multivariate analysis with multinomial logistic regression procedures, with sleep time being the dependent variable, whose classification considered

adequate (7-8 hours of sleep) was the reference category. In this sense, we analyzed the Odds Ratio (OR) of very short/short sleep and also of long sleep according to the dTAC quartiles. As adjustment variables for the models, we considered the following: gender, age, skin color (white, non-white), smoking status (non-smoker, smoker, ex-smoker), frequency of binge drinking (none, from 1 to 2 times/month, 3 to 4 times/month, 5 or more times/month), physical activity (inactive, insufficiently active and active), professional status (employed, student, unemployed and retired), marital status (single, married/stable union, Separated/divorced/widowed/other), daily time of computer use (≤5, >5 and < 9, ≥9 hours), BMI, depression (yes, no) and year of collection (2016, 2018, 2022). We have chosen the adjustment variables from a search in the epidemiological literature.

Also, we conducted a sensitivity analysis, performing the multinomial logistic regression for the odds of having very short/short sleep or long sleep, according to the dTAC quartiles without coffee FRAP and also according to the fgTAC (fruits, vegetables, beans and lentils, oilseeds, dairy products, meat and eggs, bread, pasta and cereals, oils and fats, junk food, natural juices, teas and coffees, artificial juices and sodas and alcoholic beverages).

Results

The mean age of the participants was 35.32 ± 9.29 years, with 67.87% of the participants being female (n=4,335). Regarding the participants' sleep time, 1.4% (n=87) were classified as “very short sleep” (≤ 4 h); 30.5% (n=1,947) as “short sleep” (5-6 hours); 63.2% (n=4037) as “normal sleep” (7-8 hours) and 4.9% (n=316) as “long sleep” (≥ 9 hours). The mean dTAC of the participants was 11.2 ± 5.1 (mmol/d). The mean TAC according to the food groups and their respective consumption quartiles are shown in **Table 1**.

Among participants with adequate sleep time, there was a higher prevalence of white people, non-smokers, with computer use up to 5 hours a day, without reports of binge drinking, eutrophic and with no medical diagnosis of depression compared to the participants with very short/short or long sleep. In turn, among individuals with very short/short sleep time, there was a higher prevalence of men, married participants or in a stable relationship, and employed individuals compared to the other classifications. Curiously, compared to the different classifications, for individuals with long sleep time, there was a higher prevalence of unemployed, students, young, smokers and participants who use the computer ≥ 9 hours/day (**Table 2**).

Regarding the relationship between dTAC and sleep time, a lower chance of very short/short sleep was observed only for the second quartile of dTAC compared to the first, after all adjustments. For dTAC analysis without coffee, there was a lower chance of very short/short sleep in the highest dTAC quartiles, but these associations did not remain after the final adjustments. No associations were observed for the chance of long sleep and dTAC and dTAC without coffee (**Table 3**).

When analyzing the fgTAC, there was less chance of having very short/short sleep in the highest fgTAC quartile, after all adjustments, for fruits (OR: 0.84; IC: 0.71-0.99) and beans/lentils (OR: 0.77; CI: 0.65-0.90). Those participants in the third fgTAC quartile for the vegetables group (OR: 0.84; CI: 0.71-0.98) and for the oils and fats group (OR: 0.83; CI: 0.70-0.97) had less chance to have very short/short sleep, regardless of the adjustment variables (**Table 4**). Regarding the fgTAC of the beverage groups, participants had a greater chance of having very short/short sleep when included in the last fgTAC quartile of teas and coffees (OR: 1.24; CI: 1.06-1.45). For the fgTAC of alcoholic beverages and natural juices, there was an inverse association only in the first adjustments (**Table 5**).

Regarding to long sleep time, lower odds were observed for the highest quartile of fgTAC in the oilseed group (OR: 0.66; CI: 0.46-0.93) after all adjustments. For the beans and lentils group, inverse associations with long sleep time, after all adjustments, were maintained only for the second quartile (**Table 3**). In turn, there was less chance of long sleep in the third fgTAC quartile of teas and coffees (OR: 0.67; CI: 0.48-0.94) after all adjustments (**Table 5**).

Discussion

The present study investigated, to our knowledge, for the first time, associations between dTAC, dTAC without coffee and fgTAC with sleep time in adults with a high level of education. We observed associations between dTAC and dTAC without coffee for very short/short sleep time only. Also, the fgTAC of the fruits, vegetables, beans and lentils, oils and fats and teas and coffee groups were associated with very short/short sleep time, while fgTAC of oilseeds, beans and lentils and teas and coffees were associated with long sleep time.

In this context, two cross-sectional studies with Iranian women also investigated the relationship between dTAC and sleep (ABSHIRINI et al., 2018; DANESHZAD et al., 2020). The first observed, in 265 women with type 2 diabetes, for the highest tertiles of FRAP, compared to the lowest tertile, a lower risk of poor sleep quality (DANESHZAD et al., 2020).

The second study, with 400 postmenopausal women, used the Menopause Rating Scale Questionnaire to assess menopausal symptoms and their relationship with sleep quality. The authors observed that dTAC was inversely associated with sleep problems in the studied population (ABSHIRINI et al., 2018). In addition to food consumption, plasma levels of antioxidant vitamins are also related to sleep time (KANAGASABAI; ARDERN, 2015). Thus, a cross-sectional study, with 2,079 participants of the National Health and Nutrition Examination Survey (NHANES) aged over twenty years, observed lower serum levels of vitamin C and carotenoids in individuals with a short (5 to 6h) or very short time (≤4h) in relation to adequate sleep time (7 to 8h) (KANAGASABAI; ARDERN, 2015).

Some mechanisms could explain the relationship between dietary antioxidant consumption and sleep time. Thus, high oxidative stress is closely related to changes in the circadian rhythm, which may compromise the expression of genes related to circadian control. Therefore, the orphan nuclear receptor REV-ERBβ, an important regulator of the circadian cycle, may have its activity reduced according to the plasma redox state (WILKING et al., 2013). It is also important to highlight that oxidative stress can induce neuroinflammation, which is related to changes in adequate sleep patterns (CLARK; VISSEL, 2014).

There was a lower chance of very short/short sleep for the highest fgTAC quartile of the fruit group and for the third fgTAC quartile of the vegetables group. Such results show the importance of the food matrix in which antioxidants are inserted. A cross-sectional study with 1,444 Americans aged between 21 and 30 years old found that individuals with better sleep quality reported 37% higher consumption of daily fruit servings compared to those with lower sleep quality (JANSEN et al., 2021). In an American study with 2,951 pregnant women, the highest consumption of fruits and vegetables was associated with greater chances of adequate or long sleep (DUKE et al., 2017). On the other hand, a study with 823 young people from Bangladesh found that a 1-hour increase in sleep duration was related to an increase in the consumption of 7% of a daily portion of fruits and vegetables (SALWA et al., 2021). In fact, the micronutrients and antioxidants present in fruits and vegetables control oxidative stress and inflammation (COCATE et al., 2015; HERMSDORFF et al., 2010, 2012; ROCHA et al., 2017). Besides, many groups of fruits and vegetables may contain melatonin (GOMES DOMINGOS; HERMSDORFF; BRESSAN, 2019). This substance can improve sleep quality by its natural antioxidant potential (AMARAL; CIPOLLA-NETO, 2018; PEREIRA; GOMES DOMINGOS; AGUIAR, 2022) and by modulating the circadian cycle (AMARAL; CIPOLLA-NETO, 2018). In a recent review, our study group analyzed the relationship between food consumption and the increase in circulating melatonin in humans, so that the

consumption of foods such as cherries, grapes, bananas, pineapple, dark green vegetables are related to higher circulating melatonin or increased urinary excretion of its metabolite 6-sulfoxymelatonin (PEREIRA; GOMES DOMINGOS; AGUIAR, 2022).

Individuals in the highest fgTAC quartile of the beans and lentils groups were less likely to have very short/short sleep. We also observed inverse associations with long sleep for the second quartile. For example, for 440 medical students, the chance of good quality sleep was 6.57 times greater, with a bean intake greater than or equal to 1 time per week when compared to intake less than once a week or no intake (NISAR et al., 2019). In turn, in a survey of 80 Japanese women between 18 and 27 years old, there was a higher consumption of beans among those women with high subjective sleep quality compared to those with low quality (HASHIMOTO; INOUE; KUWANO, 2020). The authors highlight that beans are an important source of tryptophan, the precursor of serotonin and melatonin, both important for sleep quality. (HASHIMOTO; INOUE; KUWANO, 2020). Notably, the consumption of beans, in addition to offering polyphenols, folate, potassium, magnesium and tryptophan, is related to better dietary patterns (DA SILVA; ROCHA; BRAZACA, 2009; SHANG et al., 2021; SILVEIRA et al., 2019). In fact, consuming legumes within a dietary pattern rich in fruits and vegetables and poor in ultra-processed foods is related to reducing oxidative stress markers (ALEKSANDROVA; KOELMAN; RODRIGUES, 2021; HERMSDORFF et al., 2009).

Unexpectedly, we observed lower chances of very short/short sleep for the third quartile of fgTAC for oils and fats. It is important to emphasize that excess energy from dietary fat consumption could increase oxidative stress, leading to greater inflammation and worsening of cognitive function (TAN; NORHAIZAN, 2019). With regard to saturated fat, its higher consumption in the diet could be related to worse sleep quality. Thus, a randomized clinical trial with 26 adults observed that the higher consumption of saturated fat was associated with less time of slow wave sleep (ST-ONGE et al., 2016). Similarly, the study by Gander et al. observed a negative correlation between sleep duration, measured by actigraphy, and saturated fat consumption in women (GRANDNER et al., 2010). On the other hand, it is noteworthy that the metabolism of omega-6 fatty acids, especially arachidonic acid, is a precursor of pair-series prostaglandins. Thus, prostaglandin derivatives (PGD2) are important factors in sleep regulation (ZHAO et al., 2020). However, direct information on the relationship between omega-6 fatty acids and their role in sleep is still scarce (ZHAO et al., 2020). In turn, a meta-analysis with 12 cohort studies observed a lower chance of long sleep ≥ 9 hours for higher plasma concentrations of long-chain PUFA fatty acids (MURPHY et al.,

2022). In this sense, the relationship between the higher fgTAC of oils and fats should be interpreted cautiously since the type of fat and the dietary profile in which they are inserted can interfere with the inflammatory and oxidative profile and consequently in the neurodegeneration (TAN; NORHAIZAN, 2019).

We observed that for the higher fgTAC of oilseeds, there was a lower chance of long sleep. We also observed inverse associations with very short/short sleep for first adjustments. It is noteworthy that, in addition to being a source of antioxidants, oilseeds provide magnesium, fiber, MUFA, α-linolenic acid, and several other compounds that help control oxidative stress and inflammation (CASAS-AGUSTENCH; BULLÓ; SALAS-SALVADÓ, 2010). In addition, oilseeds can be considered good sources of melatonin (MENG et al., 2017). Given its anti-inflammatory and antioxidant potential, we could infer that higher consumption of antioxidants from oilseeds could be beneficial since changes in sleep time, especially increased sleepiness, may be related to greater inflammation (CLARK; VISSEL, 2014).

There was a greater chance of very short/short sleep for the highest fgTAC quartile of teas and coffees and for the third quartile, we observed lower chances of long sleep. It is noteworthy that coffee, nowadays, is one of the main suppliers of phenolic acids and polyphenols (KOLB; KEMPF; MARTIN, 2020). It is possible that coffee polyphenols and those from vegetables and fruits activate responses involved in increasing the expression of antioxidants and other cytoprotective genes (KOLB; KEMPF; MARTIN, 2020). In fact, coffee is an important contributor to the increase in dTAC in our population, as demonstrated in a previous study (SABIÃO et al., 2021). Despite its beneficial antioxidant effects, coffee is the main dietary source of caffeine, one of the main stimulant psychoactive substances consumed worldwide (CLARK; LANDOLT, 2017). Caffeine acts to promote wakefulness by being an antagonist of adenosine receptors, which plays a role in regulating sleep, and can reduce both total sleep time and its efficiency (CLARK; LANDOLT, 2017). Corroborating our findings, a study with 183 university students showed lower sleep quality for higher coffee consumption (SAWAH et al., 2015). On the other hand, a study with 814 individuals aged over 18 years, participants of the Bavarian Food Consumption Survey II, observed a higher average coffee consumption in individuals who slept less than 6 hours a night compared to longer sleep times (KLEISER et al., 2017). Likewise, an investigation with 428 Nigerian women showed a greater chance of sleeping less than 7 hours for higher daily coffee consumption (FAWALE et al., 2017).

Some limitations of the present study must be considered. Although using dTAC measurements using FRAP has a good association with health outcomes, there is a lack of national tables with FRAP values, which would contribute to greater rigor in our analyses. Besides, we did not assess other aspects of sleep quality, such as sleep latency, number of awakenings, bedtimes, sleep consistency, perceived sleep quality and sleep architecture, which may also be related to dTAC and fgTAC. However, sleep time has been linked to several health outcomes such as type 2 diabetes, obesity, depression and cognitive function (CHAPUT et al., 2020). Thus, both duration and bedtime represent an important dimension to measure sleep (HIRSHKOWITZ et al., 2015). It is also noteworthy that the correlations between self-reported sleep duration and that assessed by actigraphy may be moderate, with characteristics such as gender, age, efficiency and sleep variability influencing these associations (CESPEDES et al., 2016).

As strength, we used of the quantitative FFQ validated for our study population, which has good validity and reproducibility in food consumption analyses (AZARIAS et al., 2021). Also, the sample size and the high level of education of the participants are sample characteristics can lead to obtaining more reliable results (SEGUÍ-GÓMEZ et al., 2006). Finally, we controlled several sociodemographic and behavioral variables, according to literature review as adjustment factors for the investigated associations.

Conclusion

According to our findings, we cannot assert an association between dTAC and sleep time independently. However, a higher fgTAC such as fruits, vegetables, beans and lentils, oilseeds, and oils and fats is related to adequate sleep time, while a higher fgTAC from coffee and teas is related to short sleep time. Our results indicate the importance of the food matrix in which antioxidants are inserted, and longitudinal studies are still needed to confirm the direction of these associations.

Conflict of Interest

The authors declare no conflict of interest.

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Contribution of the authors

Conceptualization, methodology, formal analysis, investigation, data curation, writing, Pereira-Sol GA, Hermsdorff HHM, Pimenta AM, Bressan J, Moreira APB, Aguiar AS. All authors read and approved the final manuscript. All authors critically reviewed the manuscript and approved the final version submitted for publication.

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Table 1 - Food groups TAC (mmol/d) according to fgTAC quartiles, CUME Study (n=6,387)

Groups	Quartiles from TAC				Total TAC
Fruits	**Q1** 0.41±0.91	**Q2** 1.84± 0.25	**Q3** 2.77 ±0.30	**Q4** 5.63 ± 3.77	2.66 ± 2.73
	Avocado, pineapple, açaí pulp, acerola cherry, banana, guava, kiwi, orange, tangerine, apple, papaya, mango, watermelon, melon, strawberry, cherry, peach, plum, grape, pass grape, tropical fruits, fruit salad				
Vegetables	**Q1** 0.25± 0.17	**Q2** 0.52± 0.05	**Q3** 0.73± 0.07	**Q4** 1.32± 0.58	0.70 ± 0.50
	Pumpkin, courgette, chayote, chard, lettuce, cress, green cabbage, arugula, spinach, cassava, yam, baroa potato, fried cassava, baked potato, french fries, beetroot, eggplant, carrot, cauliflower, cabbage, green corn, cucumber, bell pepper, green beans, tomato, vegetables soup.				
Beans and lentils	**Q1** 0.01 ± 0.07	**Q2** 0.15 ± 0.02	**Q3** 0.25 ± 0.03	**Q4** 0.62 ± 0.39	0.26 ± 0.30
	Bean, lentil, chickpea.				
Oilseeds	**Q1** 0.17 ± 0.23	**Q2** 0.19 ± 0.06	**Q3** 0.41 ± 0.08	**Q4** 1.78 ± 1.39	0.55 ± 1.02
	Peanuts, walnut, chestnuts.				
Dairy	**Q1** 0.02 ± 0.02	**Q2** 0.08 ± 0.01	**Q3** 0.14 ± 0.02	**Q4** 0.28 ±0.11	0.13 ± 0.11
	Whole milk, skimmed milk, semi-skimmed milk, soy milk, whole yogurt, low-fat yogurt, cream cheese, cream cheese light, cheese, cottage cheese, ricotta cheese.				
Meat and eggs	**Q1** 0.05 ± 0.07	**Q2** 0.16 ± 0.01	**Q3** 0.22 ± 0.01	**Q4** 0.41 ± 0.21	0.21 ± 0.17
	Mortadella, soy meat, turkey breast, beef, chicken with skin, skinless chicken, pork, sheep meat, viscera, sausage, egg, bacon and pork rinds, sardines and tuna, shrimp, salmon, and other fishes.				
Breads, pasta and cereals	**Q1** 0.19 ± 0.12	**Q2** 0.37 ± 0.03	**Q3** 0.53 ± 0.05	**Q4** 0.94 ± 0.34	0.51 ± 0.33
	French bread, loaf bread, toast bread, wheat bread, light bread, sweet bread, cheese bread, breakfast cereals, oatmeal, granola, cereal bar, rice, brown rice, noodle, lasagna, gnocchi, polenta, fried polenta, hominy, pizza, cassava flour, cornflour.				
Oils and Fats	**Q1** 0.02 ± 0.03	**Q2** 0.07 ± 0.01	**Q3** 0.13 ± 0.01	**Q4** 0.29 ± 0.14	0.13 ± 0.12

	Butter, margarine, mayonnaise, light margarine and light mayonnaise, olive oil, canola oil, sunflower oil, corn oil, soy oil, pork fat.				
Junk food	**Q1** 0.04± 0.24	**Q2** 0.42 ± 0.06	**Q3** 0.67 ± 0.08	**Q4** 1.94 ± 1.35	0.77 ± 0.99
	Sugar, brown sugar, sweetener, dark chocolate, milk chocolate, bonbon, candies, honey, popcorn, hot dog, hambúrguer, snack chips, pepper sauce, pudding, milk cream, mustard, chocolate milk, pie, quiche, ice cream, light ice cream, fruit in syrup, guava paste, compote fig, compote peach, fruits jam, noodle soups.				
Natural Juices	**Q1** 0.02 ± 0.12	**Q2** 0.25 ± 0.05	**Q3** 0.54 ± 0.12	**Q4** 1.31 ± 0.70	0.53 ± 0.60
	Natural fruit juice.				
Teas and Coffee	**Q1** 0.42 ± 0.66	**Q2** 2.20 ± 0.48	**Q3** 4.15 ± 0.71	**Q4** 9.27 ± 4.12	4.01 ± 3.93
	Mate, black tea, green tea, coffee.				
Artificial juices and sodas	**Q1** 0.03 ± 0.04	**Q2** 0.04 ± 0.01	**Q3** 0.12 ± 0.04	**Q4** 0.66 ± 0.54	0.20 ± 0.38
	Soda, light soda, sugar-free soda, artificial juice.				
Alcoholic beverages	**Q1** 0.04 ± 0.09	**Q2** 0.14 ± 0.04	**Q3** 0.35 ± 0.09	**Q4** 1.34 ± 1.31	0.44 ± 0.85
	Liquor, distilled drinks, beer, red wine, and other types of wines.				

fgTAC: Total Antioxidant Capacity of Food Groups.
TAC: Total Antioxidant Capacity

Table 2 - Sociodemographic and health characteristics according to sleep time, CUME Study (n=6,387).

	Very short /short sleep (n=2,034)	**Adequate sleep (n=4,037)**	**Long sleep (316)**	***P value***
Year collection [n (%)]				
2016	902 (44.3)	1,712 (42.4)	116 (36.7)	
2018	392 (19.3)	690 (17.1)	52 (16.5)	**0.001**
2020	740 (36.4)	1,635 (40.5)	148 (46.8)	
Age [n (%)]				
< 40 years	1,393 (68.5)	3,038 (75.3)	265 (83.9)	
40-59 years	589 (29.0)	918 (22.7)	47 (14.9)	**<0.001**
≥60 years	51 (2.5)	81 (2.0)	4 (1.3)	
Gender [n (%)]				
Male	719 (35.3)	1,257 (31.1)	76 (24.1)	
Female	1,315 (64.7)	2,780 (68.9)	240 (75.9)	**<0.001**
Skin color [n (%)]				
White	1,221 (60.0)	2695 (66.8)	199 (63.0)	
Non-white	813 (40.0)	1,342 (33.2)	117 (37.0)	**<0.001**
Marital status [n (%)]				
Single	939 (46.2)	1,980 (49.0)	188 (59.5)	
Married/stable union	953 (46.9)	1,840 (45.6)	111 (35.1)	**<0.001**
Separated/divorced/widower/other	142 (7.0)	217 (5.4)	17 (5.4)	
Professional Situation [n (%)]				
Employee	1,559 (76.6)	2,908 (72.0)	199 (63.0)	
Student	321 (15.8)	722 (17.9)	71 (22.5)	
Retired	40 (2.0)	80 (2.0)	7 (2.2)	**<0.001**
Unemployed	114 (5.6)	327 (8.1)	39 (12.3)	
Suplementes Use [n (%)]				
No	938 (73.1)	1,722 (72.2)	126 (75.0)	0.656
Yes	345 (26.9)	663 (27.8)	42 (25.0)	
Smoking status [n (%)]				
No	1,591 (78.2)	3,264 (80.9)	230 (72.8)	
Past	268 (13.2)	438 (10.8)	39 (12.3)	**<0.001**
Current	175 (8.6)	335 (8.3)	47 (14.9)	
Computer time frequency [n (%)]				
Ate 5 horas	990 (48.7)	2,004 (49.6)	111 (35.1)	
>5 and <9 hours	665 (32.7)	1,400 (34.7)	52 (16.5)	**<0.001**
<=9 hours	379 (18.6)	633 (15.7)	153 (48.4)	
Binge drinking [n (%)]				
None	1,187 (58.7)	2,463 (61.0)	165 (52.2)	
1 to 2 times a month	458 (22.5)	751 (18.6)	68 (21.5)	

3 to 4 times a month	229 (11.3)	482 (11.9)	38 (12.0)	**<0.001**
5 or more times a month	160 (7.9)	341 (8.4)	45 (14.2)	
Physical activity [n (%)]				
Inactive	526 (25.9)	856 (21.2)	62 (19.6)	
Insufficiently active	391 (19.2)	829 (20.5)	63 (19.9)	**0.001**
Active	1,117 (54.9)	2,352 (58.3)	191 (60.2)	
Obesity [n (%)]				
No	1,756 (86.3)	3,615 (89.5)	275 (87.0)	**0.001**
Yes	278 (13.7)	422 (10.5)	41 (13.0)	
Depression [n (%)]				
Yes	230 (11.3)	409 (10.1)	45 (14.2)	**0.043**
No	1,804 (88.7)	3,628 (89.9)	271 (85.8)	

P-values according to trend chi-squared test.

Table 3 - Crude and adjusted Odds Ratios (OR) and their 95% Confidence Intervals (95% CI) of sleep time according to dTAC and dTAC without coffee, CUME Study (n=6,387).

	Very short and short sleep		**Long sleep**	
Total dTAC	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	**0.81 (0.69-0.94)**	**0.83 (0.71-0.96)**	0.81 (0.58-1.14)	0.89 (0.63-1.26)
Q3	**0.85 (0.73-0.99)**	0.85 (0.73-1.00)	0.92 (0.66-1.28)	1.02 (0.72-1.44)
Q4	0.91 (0.78-1.06)	0.86 (0.74-1.01)	1.13 (0.82-1.56)	1.13 (0.81-1.57)
	Very short and short sleep		**Long sleep**	
dTAC without coffee	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	0.89 (0.76-1.04)	0.98 (0.83-1.15)	0.85 (0.60-1.19)	1.08 (0.75-1.55)
Q3	**0.80 (0.69-0.94)**	0.89 (0.76-1.05)	0.93 (0.67-1.30)	1.14 (0.80-1.63)
Q4	**0.82 (0.70-0.96)**	0.90 (0.76-1.05)	1.02 (0.74-1.41)	1.16 (0.82-1.63)

Model 1: Sex, age, smoking status (never, current, former) and alcohol consumption (binge drinking).
Model 2 = Model 1 + physical activity (active/insufficiently active/active), professional situation, marital status (single or married), skin color (white and not white), energy intake (continuous, kcal/day), baseline BMI (continuous kg/m²), depression (yes, no), computer usage time per day, year of data collection (2016, 2018 or 2020).
dTAC: Total Dietary Antioxidant Capacity.

Table 4- Crude and adjusted Odds Ratios (OR) and their 95% Confidence Intervals (95% CI) of sleep time according to fgTAC, CUME Study (n=6,387).

	Very short and short sleep		**Long sleep**	
fgTAC from fruits	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	0.86 (0.74-1.00)	0.94 (0.80-1.11)	0.80 (0.58-1.12)	0.95 (0.66-1.36)
Q3	**0.82 (0.71-0.96)**	0.93 (0.79-1.10)	0.80 (0.57-1.12)	1.05 (0.72-1.52)
Q4	**0.77 (0.66-0.90)**	**0.84 (0.71-0.99)**	0.96 (0.70-1.33)	1.08 (0.76-1.51)
	Very short and short sleep		**Long sleep**	
fgTAC from vegetables	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	**0.85 (0.73-0.98)**	0.90 (0.77-1.06)	1.00 (0.72-1.39)	1.26 (0.88-1.78)
Q3	**0.79 (0.68-0.92)**	**0.84 (0.71-0.98)**	0.84 (0.60-1.18)	1.06 (0.74-1.51)
Q4	0.93 (0.80-1.08)	0.95 (0.82-1.11)	1.12 (0.81-1.55)	1.21 (0.87-1.70)
	Very short and short sleep		**Long sleep**	
fgTAC from beans and lentils	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	**0.81 (0.69-0.94)**	0.86 (0.74-1.01)	**0.40 (0.28-0.56)**	**0.47 (0.32-0.68)**
Q3	0.86 (0.74-1.00)	0.94 (0.80-1.11)	0.76 (0.56-1.03)	0.95 (0.68-1.32)
Q4	**0.72 (0.62-0.84)**	**0.77 (0.65-0.90)**	**0.62 (0.45-0.85)**	0.72 (0.52-1.00)
	Very short and short sleep		**Long sleep**	
fgTAC from oilseeds	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	**0.81 (0.69-0.94)**	0.86 (0.73-1.02)	**0.65 (0.47-0.88)**	0.75 (0.52-1.08)
Q3	**0.79 (0.68-0.92)**	0.89 (0.74-1.07)	**0.56 (0.40-0.78)**	0.68 (0.45-1.02)
Q4	**0.79 (0.68-0.93)**	0.86 (0.73-1.01)	**0.59 (0.43-0.82)**	**0.66 (0.46-0.93)**
	Very short and short sleep		**Long sleep**	
fgTAC from dairy	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	1.01 (0.86-1.16)	1.05 (0.90-1.23)	0.81 (0.58-1.12)	0.87 (0.62-1.22)
Q3	1.03 (0.88-1.20)	1.08 (0.93-.1.27)	0.71 (0.51-1.01)	0.75 (0.53-1.08)
Q4	1.03 (0.88-1.20)	1.06 (0.91-1.24)	1.15 (0.85-1.57)	1.16 (0.84-1.60)
	Very short and short sleep		**Long sleep**	
fgTAC from meat and eggs	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	1.01 (0.87-1.18)	1.07 (0.91-1.25)	0.74 (0.53-1.03)	0.82 (0.58-1.18)
Q3	0.93 (0.80-1.09)	1.00 (0.85-1.18)	0.75 (0.54-1.04)	0.91 (0.63-1.31)
Q4	1.06 (0.91-1.23)	1.07 (0.92-1.26)	0.98 (0.71-1.33)	1.01 (0.73-1.41)
	Very short and short sleep		**Long sleep**	
fgTAC from bread, pasta and cereals	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	0.99 (0.85-1.16)	1.03 (0.88-1.21)	0.92 (0.67-1.26)	1.04 (0.74-1.45)
Q3	0.94 (0.81-1.10)	0.98 (0.83-1.14)	0.82 (0.60-1.14)	0.95 (0.68-1.33)
Q4	0.97 (0.84-1.13)	0.98 (0.84-1.15)	0.75 (0.54-1.05)	0.80 (0.57-1.13)
	Very short and short sleep		**Long sleep**	
fgTAC from oils and fats	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	0.98 (0.85-1.14)	1.04 (0.88-1.21)	1.07 (0.77-1.47)	1.19 (0.85-1.67)
Q3	**0.80 (0.68-0.93)**	**0.83 (0.70-0.97)**	0.81 (0.58-1.13)	0.86 (0.60-1.22)
Q4	0.95 (0.81-1.10)	0.94 (0.80-1.09)	0.97 (0.70-1.35)	1.02 (0.73-1.44)
	Very short and short sleep		**Long sleep**	
fgTAC from junk food	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	0.86 (0.74-1.01)	0.92 (0.78-1.08)	0.75 (0.54-1.05)	0.88 (0.62-1.26)
Q3	0.92 (0.79-1.07)	1.00 (0.84-1.18)	0.77 (0.55-1.07)	0.94 (0.65-1.35)
Q4	0.88 (0.76-1.03)	0.95 (0.81-1.11)	0.76 (0.55-1.06)	0.84 (0.60-1.19)

Model 1: Sex, age, smoking status (never, current, former) and alcohol consumption (binge drinking)

Model 2 = Model 1 + physical activity (active/insufficiently active/active), professional situation, marital status (single or married), skin color (white and not white), energy intake (continuous, kcal/day), baseline BMI (continuous kg/m²), depression (yes, no), computer usage time per day, year of data collection (2016, 2018 or 2020).
fgTAC: Total Antioxidant Capacity of Food Groups.

Table 5 - Crude and adjusted Odds Ratios (OR) and their 95% Confidence Intervals (95% CI) of sleep time according to consumption of fgTAC by beverages, CUME Study (n=6.387).

	Very short and short sleep		**Long sleep**	
fgTAC from natural juices	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	0.92 (0.79-1.07)	1.01 (0.85-1.20)	0.81 (0.59-1.11)	0.94 (0.65-1.36)
Q3	0.90 (0.77-1.05)	0.99 (0.83-1.18)	**0.66 (0.47-0.92)**	0.77 (0.52-1.15)
Q4	**0.81 (0.70-0.95)**	0.84 (0.70-1.01)	0.83 (0.60-1.14)	0.81 (0.55-1.21)
	Very short and short sleep		**Long sleep**	
fgTAC from teas and coffee	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	0.89 (0.77-1.05)	0.93 (0.79-1.08)	**0.62 (0.45-0.86)**	**0.70 (0.50-0.97)**
Q3	0.95 (0.82-1.11)	0.99 (0.85-1.16)	**0.63 (0.45-0.86)**	**0.67 (0.48-0.94)**
Q4	**1.22 (1.04-1.42)**	**1.24 (1.06-1.45)**	0.73 (0.53-1.01)	0.72 (0.52-1.00)
	Very short and short sleep		**Long sleep**	
fgTAC from artificial juices and sodas	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	**0.83 (0.71-0.97)**	0.90 (0.76-1.07)	0.89 (0.64-1.25)	1.23 (0.84-1.79)
Q3	1.00 (0.86-1.16)	1.05 (0.88-1.25)	1.04 (0.75-1.44)	1.48 (1.01-2.16)
Q4	1.12 (0.96-1.30)	1.12 (0.95-1.31)	1.13 (0.82-1.57)	1.38 (0.97-1.98)
	Very short and short sleep		**Long sleep**	
fgTAC from alcoholic beverages	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Q1	1	1	1	1
Q2	**0.90 (0.77-1.04)**	1.01 (0.85-1.20)	**0.77 (0.55-1.06)**	0.94 (0.65-1.36)
Q3	**0.87 (0.74-1.02)**	0.99 (0.83-1.18)	**0.64 (0.45-0.92)**	0.77 (0.52-1.15)
Q4	**0.74 (0.62-0.88)**	0.84 (0.70-1.01)	**0.67 (0.47-0.97)**	0.81 (0.55-1.21)

Model 1: Sex, age, smoking status (never, current, former), and alcohol consumption (binge drinking)
Model 2 = Model 1 + physical activity (active/insufficiently active/active), professional situation, marital status (single or married), skin color (white and not white), energy intake (continuous, kcal/day), baseline BMI (continuous kg/m²), depression (yes, no), computer usage time per day, year of data collection (2016, 2018 or 2020).
fgTAC: Total Antioxidant Capacity of Food Groups.

Supplementary Table 1. Mean and standard deviation of consumption in grams per day (g/d) of food groups according to their respective fgTAC quartiles.

Groups (g/d)	**Quartiles from TAC**			
Fruits	**Q1** 135.15 ± 169.23	**Q2** 351.11 ± 119.03	**Q3** 495.61 ± 142.03	**Q4** 827.14 ± 379.65
Vegetables	**Q1** 93.40 ± 66.57	**Q2** 181.84 ± 37.59	**Q3** 242.58 ± 54.73	**Q4** 418.20 ± 185.38
Beans and lentils	**Q1** 5.61 ± 24.5	**Q2** 48.35 ± 9.80	**Q3** 82.80 ± 12.56	**Q4** 197.58 ± 127.06
Oilseeds	**Q1** 1.77 ± 2.96	**Q2** 2.43 ± 3.47	**Q3** 4.80 ± 4.53	**Q4** 44.64 ± 36.24
Dairy	**Q1** 59.60 ± 56.58	**Q2** 143.38 ± 74.47	**Q3** 253.65 ± 92.52	**Q4** 490.68 ± 239.30
Meat and eggs	**Q1** 107.36 ± 110.81	**Q2** 196.38 ± 67.92	**Q3** 242.33 ± 73.76	**Q4** 358.02 ± 165.88
Breads, pasta and cereals	**Q1** 183.08±113.77	**Q2** 195.06±103.64	**Q3** 227.85±112.89	**Q4** 314.05±172.65
Oils and Fats	**Q1** 5.00±5.90	**Q2** 14.14± 3.89	**Q3** 21.57± 5.92	**Q4** 38.58±18.41
Junk food	**Q1** 34.93±48.87	**Q2** 78.10±45.68	**Q3** 98.53±55.90	**Q4** 133.34±115.55
Natural Juices	**Q1** 4.19± 26.36	**Q2** 52.83±11.52	**Q3** 111.77±25.13	**Q4** 267.45±142.90
Teas and Coffee	**Q1** 23.88±41.50	**Q2** 108.41±45.70	**Q3** 201.41±112.19	**Q4** 450.58±306.98
Artificial juices and sodas	**Q1** 22.74±39.43	**Q2** 28.31±46.98	**Q3** 71.16±82.84	**Q4** 250.03±219.60
Alcoholic beverages	**Q1** 14.06±31.78	**Q2** 29.50±47.51	**Q3** 106.06±87.98	**Q4** 227.47±222.67

6.2. ARTIGO 2. ASSOCIAÇÃO ENTRE CAPACIDADE ANTIOXIDANTE TOTAL DA DIETA E DE GRUPOS DE ALIMENTOS E INCIDÊNCIA DE DEPRESSÃO EM UMA COORTE DE GRADUADOS BRASILEIROS (PROJETO CUME)

Association between total dietary antioxidant capacity and food groups and incidence of depression in a cohort of Brazilian graduates (CUME Project)

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Abstract

This study aims to evaluate the association between Total Dietary Antioxidant Capacity (dTAC) and Total Antioxidant Capacity of food groups (fgTAC) with the incidence of depression in Brazilian graduates participating in the Cohort of Universities of Minas Gerais (CUME Study). The sample consisted of 2,572 participants without a medical diagnosis of depression at baseline who responded to at least one follow-up questionnaire from the CUME project. The Ferric Reducing Antioxidant Power (FRAP) assay was used to determine dTAC. Incidence of depression was estimated by self-reported medical diagnosis of depression during the years of cohort follow-up. Cox regression models were used to relate dTAC and fgTAC to the incidence of depression. The mean follow-up time was 2.96 (1.00) years and 246 cases of depression were observed (32.3/1,000 person years). The mean dTAC was 11.03 (4.84) mmol/d. We found no associations between higher dTAC and lower risk of developing depression after adjusting for possible confounders. The incidence of depression was inversely associated with fgTAC of the beans and lentils group (HR: 0.61; IC0.41 - 0.90). The fgTAC of the Junk food group was positively associated with higher incidence of depression after all adjustments (HR:1.57; IC:1.08-2.26). Our findings do not support an association between dTAC and the incidence of depression in a highly educated Brazilian population. However, associations of fgTAC show the importance of analyzing the food matrix in which these antioxidants are inserted. We highlight the need for more prospective studies with different nationalities to confirm these results.

Keywords: Dietary Total Antioxidant Capacity, Depression, Epidemiology, Oxidative Stress.

Introduction

Depression is a chronic mental illness with great worldwide prevalence [1]. Data indicate that 3.8% of the world population is affected by depression, affecting about 5% of the adult population and 5.7% of the population over 60 years old [1]. The main characteristics of depressive disorder are depressed mood, feelings of guilt or low self-esteem, changes in sleep and appetite, lack of disposition, and poor concentration. In many cases, these symptoms can be accompanied by feelings of anxiety [2]. In moderate or severe intensities, depression can greatly affect an individual's daily life in work, studies, and family relationships, and in its most severe forms, it can lead to suicide [1,2].

In this sense, much has been investigated about the pathogenesis of depression, and oxidative stress has stood out among the risk factors [3,4]. Oxidative stress can be characterized as an imbalance between the antioxidant defenses of the organism and the presence of free radicals, a pathogenic process related to cell injury and death [3–5]. It is noteworthy that the brain, compared to other organs, is highly vulnerable to oxidative stress due to its high metabolism [5,6]. Thus, redox imbalance may be related to depression through mechanisms such as inflammation and neurodegeneration, impairing neuronal and neurotransmitter function [3,4,7].

Due to the need for new approaches to treat and prevent depression, antioxidants such as vitamins C, E, and zinc have been associated with improvements in neurocognitive function, bringing therapeutic benefits to depression [8]. A recent cross-sectional study with 14,737 individuals participating in the Brazilian Longitudinal Study of Adult Health (ELSA) reported, for Brazilian women, an inverse association of the consumption of zinc, selenium, vitamin A and C with depression [9]. Inverse associations of zinc and selenium consumption with depression were also found for 14,834 adults participating in the National Health and Nutrition Examination Survey (NHANES) 2009–2014 [10].

Despite the results obtained so far between nutrient intake and the occurrence of depression, the isolated assessment of antioxidants may not be as effective as the assessment of the interaction of different dietary antioxidants [11]. Therefore, the Dietary total antioxidant capacity (dTAC), an index capable of measuring the global content of dietary antioxidants [12], has proved to be a helpful tool for investigating the interaction between dietary antioxidants and health outcomes [13–15]. However, investigations into the relationship between dTAC and depression are still limited, mostly being cross-sectional studies with the Iranian population [16–19]. Unfortunately, as far as we know, no prospective study has investigated the association between dTAC and depression in Brazilians, nor has it analyzed this relationship through the

Total Antioxidant Capacity of food groups (fgTAC) [16]. Thus, the present study aimed to assess the association between dTAC and fgTAC with the incidence of depression in Brazilian graduates participating in the Cohort of Universities of Minas Gerais (CUME Study).

Methodology

Cohort of Universities of Minas Gerais (CUME Study)

The CUME Study is an open, prospective cohort conducted with alumni from universities located in the state of Minas Gerais (Brazil), whose main objective is to assess the impact of the Brazilian dietary pattern, specific diet factors, and the nutritional transition in the incidence of chronic non-communicable diseases (NCDs), as previously detailed [20].

The CUME study questionnaires were developed on the Alchemer (www.alchemer).com online interface by specialists. The team conducted pilot studies with the baseline questionnaire to assess its applicability[20]. The CUME Study began in 2016 with the application of the baseline questionnaire Q_0, and its recruitment has been periodic since then. Invitations to participate were sent to all volunteers who had emails available. Thus, every two years, the participants are invited to answer follow-up questionnaires (Q_2, Q_4...Q_n) to update their information about lifestyle, the emergence of new diseases, and changes in dietary patterns, among others, while new potential participants are recruited and invited to answer the baseline cohort questionnaire (Q_0). Characteristics related to project design and recruitment of the first volunteers were described in a previous study[20].

The questionnaires are answered in a virtual environment of the CUME Study. Q_0 is divided into two phases: the first phase with questions about sociodemographic characteristics, lifestyle, biochemical markers (triglyceride concentrations, total cholesterol, HDL cholesterol, LDL cholesterol, blood glucose concentration), and related to the individual's health outcomes; the second phase is answered after one week, contains a Food Frequency Questionnaire (FFQ) and questions related to dietary practices. On the other hand, Q_2 is composed of questions related to changes in lifestyle, eating habits, and health conditions. Finally, the follow-up questionnaire Q_4 has questions related to sociodemographic characteristics, lifestyle, biochemical markers, health outcomes, and insomnia severity.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Human Research Ethics Committees of all participating institutions: Federal University of Minas Gerais

(CAAE registration number: 07223812.3.3001.5153); Federal University of Viçosa (CAAE registration number: 4483415.5.1001.5149); Federal University of Ouro Preto (CAAE registration number: 44483415.5.2003.5150); Federal University of Lavras (CAAE registration number: 44483415.5.2002.5148); Federal University of Juiz de Fora (CAAE registration number: 4483415.5.5133); Federal University of Vale do Jequitinhona e Mucuri (CAAE registration number: 44483415.5.2005.5103) and Federal University of Alfenas (CAAE registration number: 4.501.344). Written informed consent was obtained from all subjects[20].

Data collection

Information from the Q_0 questionnaires for the years 2016, 2018, and 2020 composed the baseline of the present study. We used data from the two-year follow-up Q_2 and the four-year follow-up Q_4 to investigate the incidence of the depression outcome.

The first collection related to the two-year follow-up occurred in 2018, answered by participants who started the baseline (Q_0) in 2016. The second collection, associated with Q_2, occurred in 2020 when we invited participants who completed the Q_0 follow-up questionnaire in 2018. Finally, the collection related to the Q_4 follow-up questionnaire occurred in 2020. Participants who answered Q_2 in 2018 were invited to fill it out.

Study population

The CUME Study has responses from 7,710 participants. For the present study, of the total number of respondents, we excluded 4,084 participants who had not accomplished at least the two-year follow-up. We also excluded women who were pregnant or had been pregnant in the last year (n=430), participants with energy consumption < 2092 or > 25104 kJ per day (< 500 kcal or > 6000 kcal) (n 79) [21], participants who reported not having lived in Brazil in the last year (n = 135) and foreigners living in Brazil (n=10) and participants who reported a diagnosis of depression at baseline (n=400). The final sample consisted of 2,572 participants who answered at least one follow-up questionnaire (**Figure 1**).

Outcome variable: Incidence of depression

We considered incident cases of depression in those participants who were disease-free at the beginning of the follow-up and were classified as having the disease during Q_2 or Q_4 follow-up. For it, we considered incident depression when participants answered yes to

the following question: “Since the previous questionnaire, were you clinically diagnosed with depression for the first time?”. Individuals who reported using antidepressants but did not confirm the diagnosis of depression were not included due to the possibility of the therapeutic use of such drugs in diseases other than depression. The reliability between medical diagnosis and self-report depression in this cohort was validated in a subsample of participants showing good agreement (81.0%) with a Kappa value of 0.62 [22].

Food consumption and estimation of dTAC

We assessed habitual food consumption using FFQ, previously validated for the study population [23], which includes 144 food items presented in the following groups: dairy, meat and fish, cereals and legumes, fruits, vegetables, oils and fats, beverages, and other foods. Each participant reported the frequency of consumption of a particular food (daily, weekly, monthly, or yearly), the number of times they consumed it (0 to 9 or more times), and the portion size. To facilitate filling in the portion sizes of food items and obtain the most reliable information possible, participants had access, at the time of answering the FFQ, to images of portions of food and serving utensils from the photo album with 96 pictures prepared by the CUME Study team[20]. The consumption of macro and micronutrients were calculated using primarily data from the Table of Nutritional Composition of Foods consumed in Brazil [24] and, in the absence of information in this table, we consulted the Brazilian Table of Food Composition [25] and the USDA National Nutrient Database [26].

We used the values from the Ferric Reducing Antioxidant Power (FRAP) assay to estimate dTAC, which measures the antioxidant capacity of food in the presence of iron. We consulted previously published databases to obtain the FRAP values [12,27]. Thus, the dTAC of each food item resulted from the multiplication between the amount in grams of food consumed and its corresponding FRAP value in mmol per gram of food (mmol/g).

We used the following criteria to assign the FRAP value to a portion of food: when there was more than one FRAP analysis value for the same food, we considered the mean value; in the absence of a FRAP value for a particular food, when possible, we used the value of a similar food from the same botanical group, or the same food in a different way of preparation. We did not assign FRAP values to foods where there was no record of this value, and it was not possible to estimate for foods from similar botanical groups or different methods of preparation

A total of 133 food items were covered with FRAP values. We summed all FRAP values of foods reported in the FFQ to estimate the total dTAC of each participant. In order to

perform a sensitivity analysis, we also calculated dTAC values, excluding coffee values, as this is a beverage that greatly contributes to dTAC values in our population [13]. We also calculated fgTAC values according to food groups (fruits, vegetables, beans and lentils, oilseeds, dairy products, meats and eggs, pasta, breads and cereals, oils, junk food, natural juices, teas and coffees, artificial juices, and alcoholic beverages) (**Supplementary Table 1**).

We adjusted all food consumption variables for daily caloric intake using the residual method [28], including dTAC.

Covariates

We obtained the other variables from self-reported information in the baseline questionnaire Q_0, including sociodemographic variables (gender, skin color, marital status, professional status), use of vitamin supplements, and smoking habits (non-smoker, smoker, or ex-smoker). The frequency of heavy episodic consumption of alcoholic beverages (1 to 2 days/month, 3 to 4 days/month, and 5 or more days/month) was also a variable included in this study, with heavy episodic consumption considered as 4 or more doses of alcoholic beverage on a single occasion for women and 5 or more doses of alcoholic beverage on a single occasion for men [29]. We also assessed physical activity using a list of 24 activities expressed in minutes per week. Participants with ≥ 150 minutes/week of moderate-intensity activity or ≥ 75 minutes/week of vigorous-intensity activity were considered active; participants with < 150 minutes/week of moderate-intensity activity or < 75 minutes/week of vigorous-intensity activity were classified as insufficiently active, and those who reported no leisure-time physical activity were classified as inactive [30]. We obtained the Body Mass Index (BMI) from the self-reported weight and height in the baseline questionnaire, dividing weight (kilograms) by height (meters) squared. BMI values ≥ 30 kg/m^2 were classified as obesity [31,32]. The BMI based on self-reported weight and height was also validated, in a previous study, for the population participating in the CUME project, indicating excellent agreement with the measured intraclass correlation coefficient- ICC: 0.989 [33].

Statistical analysis

We performed the analyzes with Stata SE 15.0. A two-tailed p-value less than 0.05 was considered statistically significant.

We described sociodemographic, lifestyle, health, and food consumption characteristics in absolute or relative frequency or as mean and standard deviation according to the dTAC quartiles baseline. We calculated the p-value using Person's chi-square tests for categorical variables and ANOVA for continuous variables to compare the categories.

The follow-up time was calculated in person-years for each participant: difference between the date of completion of the follow-up questionnaire in which depression was diagnosed and the date of completion of the baseline questionnaire. In this sense, we created cox regression models to assess the association between dTAC in quartiles and the incidence of depression. We used the lowest quartile as the reference category to compare the incidence of depression among the dTAC categories (exposure variable). As a guide for selecting the covariates included in the analyses, we constructed a directed acyclic graph (DAG) using the DAGitty program. DAGs are a strategy that helps identify a minimum set of confounding covariates in the analysis of causal relationships, helping to estimate less biased measures of effect [34,35] (**Supplementary Figure 1**). Thus, we adjusted the final model for potential confounders such as gender, age (continuous), smoking habit (non-smoker/smoker/ex-smoker), frequency of heavy episodic alcohol consumption (never/from 1 to 2 days per month/from 3 to 4 days per month/5 or more days per month), marital status (single/married or stable union/separated or divorced or widowed), skin color (white/non-white), professional status, physical activity (inactive/ insufficiently active/active), use of vitamin supplements (yes/no), BMI (continuous) and caloric intake (kcal/day) and vitamin D consumption (μg/day). Linear trends were tested using the median values of each quartile of the exposure variable ordered in Cox regression models. We also performed a sensitivity analysis excluding coffee items from the dTAC computation. In addition, we analyzed the relationship between fgTAC and the incidence of depression (fruits, vegetables, beans and lentils, oilseeds, dairy, meat and eggs, breads, pasta and cereals, oils, "junk food", natural juices, teas and coffees, artificial and soda and alcoholic beverages), considering that antioxidants present in diet may be inserted in different proportions in food matrices [15,36].

Results

During the average time of 2.96 (1.00) years of monitoring of the present study, 246 new cases of depression (32.3/1,000 person-years) were observed and the mean age of the participants was 36.09 (SD 9.63). The mean dTAC was 11.03 (4.84 mmol/d).

Participants included in the highest quartile for dTAC (> 13.32 mmol/d) are mostly older, married or in a stable union, employed workers, smokers, and physically active, in

addition to having a higher frequency of heavy episodic alcohol consumption (**Table 1**). Regarding food consumption, individuals belonging to the fourth quartile of dTAC, when compared to the first quartile (< 7.92mmol/d), had a higher intake of carbohydrates, omega 3, alcohol, vitamins A, E, C, and B9, magnesium, fiber, as well as higher consumption of fruits and vegetables (**Table 2**).

There was no association between dTAC and incidence of depression (**Table 3**), regardless of adjustment for confounding variables. The results of the analysis of dTAC without coffee and incidence of depression remained similar. When we assessed the associations between fgTAC and the incidence of depression (**Tables 4 and 5**), we observed a lower incidence of depression according to the quartiles of fgTAC of natural juices in the model adjusted by age and gender (HR:0.70; CI: 0.49-0.99). Still, the significance of this association was lost after the total adjustment of the model. On the other hand, the TAC of the beans and lentils were inversely associated with the incidence of depression in our cohort (HR: 0.61; IC: 0.41 - 0.90) (**Table 4**). Interestingly, a higher fgTAC from the junk food group was positively associated with a higher incidence of depression among participants after all adjustments (HR:1.57; IC:1.08-2.26).

Discussion

In the present study, we found no association between total dTAC and incidence of depression. Still, fgTAC from specific food groups, such as natural juice, beans and lentils, and junk foods, showed associations. As far as we know, this is the first prospective study to investigate the association between dTAC and fgTAC by different food groups with the incidence of depression in Brazilian graduates.

When analyzing the fgTAC, we observed an inverse association between the fgTAC of the beans and lentils group with the incidence of depression. A study from the National Health Survey in Brazil with 46,785 adults showed an inverse association between bean consumption and depression [37]. Bean consumption was also inversely associated with mental disorders in a study with 712 Brazilian pregnant women [38]. It is noteworthy that beans, besides being sources of antioxidants such as polyphenols, are sources of B vitamins and minerals such as iron, potassium, and magnesium, in addition to dietary fiber [39,40]. In a previous study, beans proved to be an important contributor to folate consumption in part of the CUME project baseline population [41]. In fact, in addition to antioxidants, folate consumption has been inversely associated with depression [42,43]. Another point worth mentioning is the fact that the regular consumption of beans may be related to a higher quality

dietary pattern, characterized by a diversity of in natura and minimally processed foods, while low intake may be associated with an increase in the consumption of ultra-processed foods [40,44,45]. We emphasize that the dietary pattern rich in ultra-processed foods is positively related to the incidence of depression [37,46].

We observed that higher fgTAC of junk food was positively associated with higher incidence of depression in our cohort. This fact raises the question of the importance of the food matrix in which antioxidants are inserted. Although some ultra-processed foods have vitamins and minerals with antioxidant potential added to their composition to increase their shelf life, these are generally rich in simple sugars, fats, flavorings, and preservatives that can contribute to a pro-oxidant and inflammatory state, closely related to depression [47–49]. In addition, a diet rich in fast food can contain a lower amount of vitamins and minerals than in natura or minimally processed foods. The deficient consumption of several nutrients is related to depression [50,51].

We did not observe any association between total dTAC and incidence of depression. These findings agree with a prospective study with 911 Japanese workers, with no associations between dTAC and incidence of depressive symptoms after three years of monitoring [52]. In the same way, two cross-sectional articles, one with climacteric women and another with 60 Iranian men, found no association between dTAC, depressive symptoms, or diagnosed depression [53,54]. Contrary to our findings, three cross-sectional Iranian studies observed positive associations between dTAC and the prevalence of depressive symptoms [17–19]. In a recent systematic review, our group analyzed existing studies that linked dTAC and depression, concluding that consumption of an antioxidant-rich diet characterized by high dTAC scores appears to be inversely associated with depression, anxiety, and sleep disorders. However, we emphasize that there are few studies available in the literature, and most have a cross-sectional design and methodological limitations, as they were conducted with Iranian individuals and, most of them, with women [16].

Contrary to our expectations, we did not find associations between the fgTAC of the fruit and vegetables group and the incidence of depression. On the other hand, for the fgTAC of the natural juices group, the inverse association with depression remained only for the first adjustments (gender, age), not being maintained for total adjustments. A longitudinal study with Add Health Study data, which monitored 3,696 17-year-old participants for 12 years, found no association between fruit and vegetables consumption and the incidence of depression either [55]. In turn, another longitudinal study with 8,353 Canadians that observed inverse associations between fruit and vegetable consumption and depression being attenuated

after adjusting variables such as smoking and physical activity [56]. Although the results of the consumption of fruits and vegetables are contradictory, a meta-analysis with observational studies found a reduction in the risk of depression with the increase in the consumption of fruits and vegetables [57]. It is worth mentioning that fruits and vegetables and natural juices are sources of antioxidants that modulate oxidative stress, and their consumption is related to mental health [56,57]. In addition, they are related to healthier eating patterns [45]. However, the association between the consumption of fruits and vegetables and other behavioral factors in the incidence of depression can be complex [56]. Thus, some behavioral factors such as physical activity, use of supplements, BMI, and professional situation may have a more important impact on depression when compared to, fruits, vegetables and natural juices consumption.

The strengths of this study are its prospective design and the use of the quantitative FFQ previously validated for the study population, with good validity and reproducibility, ensuring good consistency in food consumption analyzes [23]. In addition, we highlight that the self-report of depression was previously validated for the study population [22]. Another point is the high level of education of the participants, which can result in more reliable answers and greater adherence to the study [58]. Finally, we highlight the use of several confounding factors for our adjustments, carefully chosen after literature reviews and with the help of a directed acyclic graph [34,35].

As limitations, we highlight that although the FFQ has good reproducibility, we cannot guarantee that the baseline FRAP values represent the habitual long-term dietary intake precisely. Another point is the lack of national tables for FRAP values, requiring the use of values arranged in international tables for most calculations. Such factors may mediate the results observed here. Nor can we discard the possibility of residual confounding by some unmeasured or not precisely measured factors. We highlight the non-assessment of plasma TAC, but it is worth mentioning that plasma TAC may not be reflected in long-term diets, which limits its comparison with dTAC [14,59]. In addition, dTAC proves to be a handy tool in assessing the relationship between diet and health outcomes [14,59]. Finally, although the collection of data from the follow-up questionnaire Q_4 was carried out in the initial months of the COVID 19 pandemic, we cannot guarantee that this short period of time had an influence on the increase in medical diagnosis of depression. However, future analyzes carried out with the next years of follow-up of the cohort may provide answers about the impact of the pandemic on the incidence of depression.

Conclusion

Our findings do not support an association between dTAC and the incidence of depression after an average of 2.96 (1.00) years of follow-up in a highly educated Brazilian population. However, the inverse association of fgTAC from beans and lentils and the direct association of junk food with the incidence of depression in the population indicate that not only the presence of antioxidants but the food matrix in which these antioxidants are inserted should be considered to explain the associations between diet and health outcomes. We highlight the need for further prospective studies with different nationalities to confirm these results.

Conflict of Interest

The authors declare no conflict of interest.

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Contribution of the authors

Conceptualization, methodology, formal analysis, investigation, data curation, writing, Pereira-Sol GA, Hermsdorff, HHM, Leal ACG, Pimenta AM, Bressan J, Moreira, APB, Aguiar AS. All authors read and approved the final manuscript. All authors critically reviewed the manuscript and approved the final version submitted for publication.

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Figure 1 – Flow chart of participant selection

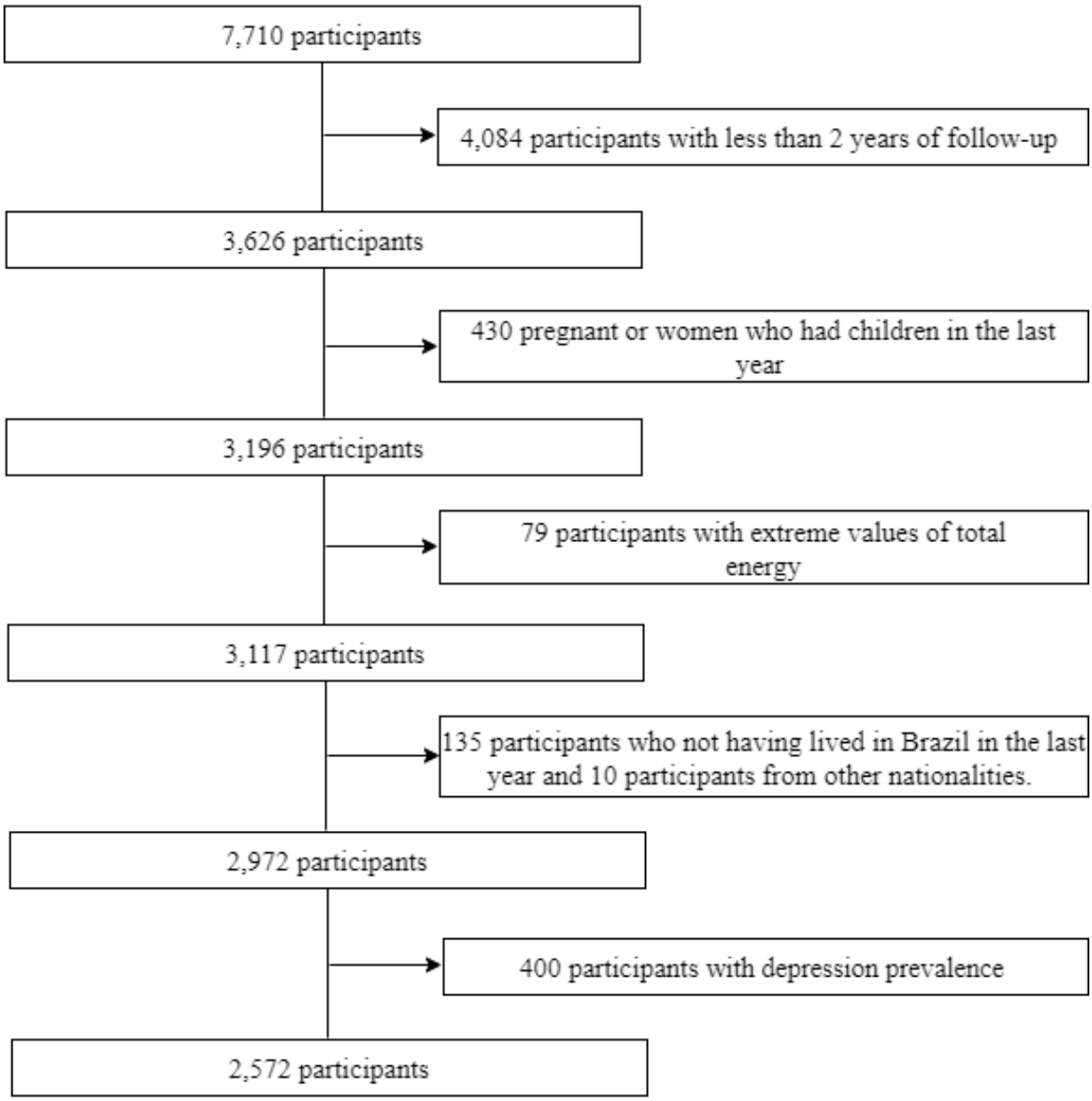


Table 1 - Baseline sociodemographic and health characteristics according to energy-adjusted dTAC (mmol/d) quartiles, CUME project (n=2,572).

	Q1 6.02 (SD 1.80)	**Q2** 9.09 (SD 0.67)	**Q3** 11.69 (SD 0.85)	**Q4** 17.33 (SD4.49)	*P value*
Age [n (%)]					
< 40 years	517 (80.4)	476 (74.0)	421 (65.5)	393 (61.1)	**<0.001**
40-59 years	115 (17.9)	152 (23.6)	200 (31.1)	231 (35.9)	
≥60 years	11 (1.7)	15 (2.4)	22 (3.4)	19 (3.0)	
Gender [n (%)]					
Male	251 (39.0)	214 (33.3)	219 (34.1)	252 (39.2)	**0.040**
Female	392 (61.0)	429 (66.7)	424 (65.9)	391 (60.8)	
Skin color [n (%)]					
White	406 (63.1)	403 (62.7)	418 (65.0)	434 (67.5)	0.257
Non-white	237 (36.9)	240 (37.3)	225 (35.0)	209 (32.5)	
Marital status [n (%)]					
Single	370 (57.5)	315 (49.0)	281 (43.7)	277 (43.1)	
Married/stable union	250 (38.9)	296 (46.0)	322 (50.1)	313 (48.7)	**<0.001**
Separated/divorced/widower/other	23 (3.6)	32 (5.0)	40 (6.2)	53 (8.2)	
Professional Situation [n (%)]					
Employee	445 (69.2)	506 (78.7)	495 (77.0)	508 (79.0)	
Student	126 (19.6)	87 (13.5)	92 (14.3)	86 (13.4)	**<0.001**
Retired	9 (1.4)	9 (1.4)	17 (2.6)	18 (2.8)	
Unemployed	63 (9.8)	41 (6.4)	39 (6.1)	31 (4.8)	
Smoking status [n (%)]					
No	565 (87.9)	533 (82.9)	502 (78.1)	475 (73.9)	
Past	38 (5.9)	69 (10.7)	86 (13.4)	91 (14.2)	**<0.001**
Current	40 (6.2)	41 (6.4)	55 (8.6)	77 (12.0)	
Binge frequency [n (%)]					
None	401 (62.4)	402 (62.5)	370 (57.5)	327 (50.9)	
1 to 2 times a month	124 (19.3)	130 (20.2)	148 (23.0)	147 (22.9)	**<0.001**
3 to 4 times a month	75 (11.7)	75 (11.7)	69 (10.7)	89 (13.8)	
5 or more times a month	43 (6.7)	36 (5.6)	56 (8.7)	80 (12.4)	
Physical activity [n (%)]					
Inactive	204 (31,7)	156 (24,3)	128 (19,9)	110 (17,1)	
Insufficiently active	134 (20,8)	141 (21,9)	130 (20,2)	118 (18,4)	**<0.001**
Active	305 (47,4)	346 (53,8)	385 (59,9)	415 (64,5)	
Use of supplements [n (%)]					
Yes	149 (23.2)	157 (24.4)	181 (28.1)	182 (28.3)	0.078
No	494 (76.8)	486 (75.6)	462 (71.9)	461(71.7)	
Obesity [n (%)]					

No	561 (87.2)	574 (89.3)	582 (90.5)	579 (90.0)	0.242
Yes	82 (12.8)	69 (10.7)	61 (9.5)	64 (10.0)	

P values according to trend chi-squared test.
dTAC: Total Dietary Antioxidant Capacity

Table 2 - Baseline dietary intake according to the energy-adjusted dTAC (mmol/d) quartiles, CUME project (n=2,572).

	Q1 6.02(1.80)	**Q2** 9.09(0.67)	**Q3** 11.69(0.85)	**Q4** 17.33(4.49)	*P value**
Total energy intake, Kcal/d	2662.50 (1027.93)[a]	2091.645 (761.19)[b]	2200.05 (793.04)[b]	2504.59 (986.68)[c]	< **0.001**
Carbohydrates, g/d	241.54 (67.05)[a]	259.92(44.43)[b]	265.17(54.59)[b,c]	272.72(69.11)[c]	< **0.001**
Protein, g/d	113.17(36.38)[a]	105.92(23.26)[b]	103.60(28.00)[b]	99.39(30.82)[c]	< **0.001**
Lipids g/d	101.63(23.60)[a]	96.14(16.13)[b]	93.93(19.02)[b,c]	90.99(24.36)[c]	< **0.001**
SFA, g/d	36.09(10.28)[a]	33.58(6.80)[b]	32.51(8.94)[b,c]	30.93(9.62)[c]	< **0.001**
MUFA, g/d	36.15(10.46)[a]	35.07(7.52)[a,b]	34.48(9.25)[b,c]	33.28(11.11)[c]	< **0.001**
PUFA, g/d	18.36(6.99)[a]	19.24(5.08)[a]	19.33(5.40)[a]	19.15(7.38)[a]	**0.021**
TRANS, g/d	1.41(1.27)[a]	1.22(0.73)[b]	1.10(0.70)[b]	0.93(0.80)[c]	< **0.001**
Omega-3 fatty acids, g/d	2.09(0.73)[a]	2.30(0.55)[b,c]	2.38(0.55)[c]	2.60(0.87)[d]	< **0.001**
Alcohol intake, g/d	4.43(9.89)[a]	5.14(6.46)[a,b]	6.31(7.97)[b]	8.17(11.92)[c]	< **0.001**
Vitamin C, mg/d	161.34(134.79)[a]	236.67(151.71)[b]	277.50(196.60)[c]	335.43(286.27)[d]	< **0.001**
Vitamin A, µg/d	761.89(324.25)[a]	835.82(291.15)[b]	869.10(280.26)[b,c]	912.19(546.31)[c]	< **0.001**
Vitamin E, mg/d	7.39(3.16)[a]	8.51(2.64)[b]	9.11(3.16)[c]	9.95(4.75)[d]	< **0.001**
Folic acid, µg/d	450.31(179.77)[a]	497.34(113.24)[b]	497.45(124.52)[b]	509.58(142.11)[b]	< **0.001**
Vitamin B12, µg/dc	4.55(3.13)[a]	4.22(1.81)[b,a]	4.05(1.65)[b]	3.84(3.11)[b]	< **0.001**
Vitamin D, µg/d	4.22 (3.57)[a]	4.20 (2.82)[a]	4.04 (2.57)[a,b]	3.73 (2.67)[b]	**0.008**
Magnesium, mg/d	324.88(81.93)[a]	366.15(72.53)[b]	391.66(77.50)[c]	424.95(98.65)[d]	< **0.001**
Fiber g/d	21.06(9.70)[a]	25.88(7.07)[b]	28.10(8.59)[c]	30.80 (12.22)[d]	< **0.001**
Fruit g/d	267.45(248.88)[a]	414.15(218.94)[b]	491.77(290.02)[c]	598.97(441.48)[d]	< **0.001**
Vegetables g/d	188.75(142.55)[a]	222.26(121.12)[b]	245.91(132.15)[c,d]	262.90(178.20)[d]	< **0,001**
Legumes g/d	93.46(120.75)[a]	80.65(83.50)[a,b]	75.78(83.46)[b]	80.15(84.14)[a,b]	**0.005**

Data expressed as mean (standard deviation)
*P values by ANOVA test. Different letters show statistically significant differences between groups according to Bonferroni's post hoc test.

Table 3 - Hazard ratios and 95% CI of depression incidence according to dTAC and dTAC without coffee, CUME project (n=2,572).

	Total dTAC				
	Q1 6.02 (SD 1.80)	**Q2** 9.09 (SD 0.67)	**Q3** 11.69 (SD 0.85)	**Q4** 17.33 (SD 4.49)	*P for trend*
Crude	1.00	0.98 (0.68 -1.41)	1.15 (0.81-1.63)	1.07 (0.75 -1.52)	0.591
Model 1[a]	1.00	0.98 (0.68 -1.41)	1.16 (0.81-1.67)	1.10 (0.77-1.59)	0.460
Model 2[b]	1.00	0.97 (0.67-1.40)	1.14 (0.79 -1.64)	1.09 (0.75-1.58)	0.521
Model 3[c]	1.00	1.10 (0.75-1.62)	1.29 (0.88-1.87)	1.18 (0.81 -1.72)	0.342
	dTAC without coffee				
	Q1 4.08 (SD 1.42)	**Q2** 6.29 (SD 0.39)	**Q3** 7.76 (SD 0.49)	**Q4** 11.79 (SD 3.85)	*P for trend*
Crude	1.00	1.16 (0.81 -1.65)	0.94 (0.65-1.36)	1.23 (0.86 -1.76)	0.370
Model 1[a]	1.00	1.12 (0.78 -1.59)	0.88 (0.61 -1.29)	1.15 (0.79 -1.66)	0.605
Model 2[b]	1.00	1.11 (0.78-1.59)	0.88 (0.60-1.28)	1.16 (0.80 -1.68)	0.562
Model 3[c]	1.00	1.29 (0.89 -1.87)	1.02 (0.69-1.50)	1.32 (0.91-1.91)	0.246

[a]Adjusted – Sex and age

[b]Adjusted - Model 1 + smoking status (never, current, former), alcohol consumption (BINGE frequency) and vitamin D consumption (mcg)

[c]Adjusted – Model 2 + marital status (single/married or stable union/separated or divorced or widowedd), skin color (white and not white), physical activity (inactive/insufficiently active/active), use of supplements (yes or no), energy intake (continuous, kcal/day), baseline BMI (continuous kg/m²), professional situation.

dTAC: Total Dietary Antioxidant Capacity

Table 4. Hazard ratios and 95% CI of depression incidence according to fgTAC from food groups, CUME project (n=2,572).

	fgTAC from fruits				
	Q1 0.49 (SD 0.79)	**Q2** 1.76 (SD 0.25)	**Q3** 2.68 (SD 0.30)	**Q4** 5.39 (SD 3.32)	*P for trend*
Crude	1.00	1.14 (0.80-1.62)	0.97 (0.67-1.40)	1.13 (0.79-1.61)	0.668
Model 1[a]	1.00	1.06 (0.74 -1.51)	0.87 (0.60 -1.26)	1.03 (0.71-1.49)	0.962
Model 2[b]	1.00	1.06 (0.74-1.51)	0.87 (0.60-1.27)	1.04 (0.72-1.50)	0.996
Model 3[c]	1.00	1.26 (0.87-1.83)	1.03 (0.70-1.53)	1.23 (0.84-1.80)	0.473
	fgTAC from vegetables				
	Q1 0.26 (SD 0.15)	**Q2** 0.53 (SD 0.05)	**Q3** 0.72 (SD 0.06)	**Q4** 1.29 (SD 0.60)	*P for trend*
Crude	1.00	0.84 (0.59-1.18)	0.96 (0.68-1.36)	0.75 (0.53-1.08)	0.187
Model 1[a]	1.00	0.79 (0.56-1.11)	0.89 (0.63-1.25)	0.72 (0.50-1.14)	0.135
Model 2[b]	1.00	0.78 (0.55-1.11)	0.88 (0.62-1.25)	0.71 (0.49-1.03)	0.121
Model 3[c]	1.00	0.86 (0.60-1.23)	0.96 (0.67-1.37)	0.77 (0.53-1.11)	0.216
	fgTAC from beans and lentils				
	Q1 0.02 (SD 0.07)	**Q2** 0.15 (SD 0.03)	**Q3** 0.26 (SD 0.03)	**Q4** 0.60 (SD 0.35)	*P for trend*
Crude	1.00	1.09 (0.79-1.49)	**0.63 (0.44-0.90)**	**0.56 (0.38-0.81)**	**0.001**
Model 1[a]	1.00	1.06 (0.77 -1.45)	**0.63 (0.44-0.90)**	**0.59 (0.40-0.86)**	**0.001**
Model 2[b]	1.00	1.03 (0.75 -1.43)	**0.61 (0.42-0.88)**	**0.57 (0.38-0.83)**	**0.001**
Model 3[c]	1.00	1.14 (0.81-1.60)	0.68 (0.46 -1.00)	**0.61 (0.41 - 0.90)**	**0.002**
	fgTAC from oilseeds				
	Q1 0.01 (SD 0.24)	**Q2** 0.19 (SD 0.07)	**Q3** 0.43 (SD 0.08)	**Q4** 1.73 (SD 1.47)	*P for trend*
Crude	1.00	0.71 (0.49-1.03)	0.96 (0.67-1.36)	1.08-0.76-1.51)	0.216
Model 1[a]	1.00	**0.65 (0.44-0.94)**	0.84 (0.59-1.21)	0.98 (0.69-1.39)	0.353
Model 2[b]	1.00	**0.65 (0.45-0.95)**	0.85 (0.60-1.23)	0.99 (0.69-1.40)	0.351
Model 3[c]	1.00	0.76 (0.50-1.15)	1.05 (0.69-1.60)	1.13 (0.79-1.61)	0.183
	fgTAC from dairy				
	Q1 0.03 (SD 0.03)	**Q2** 0.09 (SD 0.01)	**Q3** 0.15 (SD 0.02)	**Q4** 0.29 (SD 0.11)	*P for trend*
Crude	1.00	0.92 (0.63-1.34)	1.03 (0.72-1.48)	1.19 (0.83-1.70)	0.215

Model 1[a]	1.00	0.90 (0.62-1.30)	0.99 (0.69-1.42)	1.15 (0.80-1.64)	0.296
Model 2[b]	1.00	0.92 (0.63-1.34)	1.02 (0.70-1.48)	1.20 (0.83-1.75)	0.217
Model 3[c]	1.00	0.96 (0.66-1.39)	1.05 (0.73-1.52)	1.22 (0.84-1.78)	0.204
			fgTAC from meat and eggs		
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.06 (SD 0.06)	0.15 (SD 0.01)	0.21 (SD 0.09)	0.39 (SD 0.18)	
Crude	1.00	0.94 (0.66-1.34)	0.86 (0.60-1.24)	1.06 (0.75-1.49)	0.777
Model 1[a]	1.00	0.88 (0.62-1.25)	0.82 (0.57-1.18)	1.00 (0.71-1.42)	0.948
Model 2[b]	1.00	0.90 (0.63-1.27)	0.84 (0.58-1.21)	1.01 (0.69-1.47)	0.929
Model 3[c]	1.00	0.98 (0.67-1.42)	0.92 (0.62-1.36)	1.03 (0.70-1.52)	0.872
			fgTAC from bread, pasta and cereals		
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.21 (SD 0.12)	0.40 (SD 0.03)	0.56 (SD 0.06)	0.97 (SD 0.35)	
Crude	1.00	0.81 (0.56-1.16)	0.87 (0.62-1.24)	0.89 (0.63-1.26)	0.753
Model 1[a]	1.00	0.79 (0.55-1.13)	0.84 (0.59-1.19)	0.87 (0.61-1.24)	0.676
Model 2[b]	1.00	0.78 (0.54-1.12)	0.84 (0.59-1.19)	0.87 (0.61-1.24)	0.706
Model 3[c]	1.00	0.85 (0.59-1.23)	0.88 (0.61-1.26)	0.92 (0.65-1.31)	0.822
			fgTAC from oils		
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.01 (SD 0.04)	0.07 (SD 0.01)	0.13 (SD 0.02)	0.30 (SD 0.14)	
Crude	1.00	0.89 (0.62-1.29)	1.22 (0.87-1.73)	1.06 (0.75-1.52)	0.499
Model 1[a]	1.00	0.84 (0.58-1.22)	1.17 (0.83-1.65)	1.03 (0.72-1.46)	0.587
Model 2[b]	1.00	0.86 (0.60-1.24)	1.17 (0.82-1.65)	1.01 (0.71-1.46)	0.683
Model 3[c]	1.00	0.96 (0.66-1.40)	1.24 (0.86-1.77)	1.04 (0.72-1.51)	0.704
			fgTAC from junk food		
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.04 (SD 0.24)	0.39 (SD 0.06)	0.62 (SD 0.08)	1.74 (SD 1.22)	
Crude	1.00	1.25 (0.86-1.81)	1.01 (0.68-1.49)	**1.63 (1.15-2.31)**	**0.007**
Model 1[a]	1.00	1.15 (0.79- 1.67)	0.91 (0.61-1.35)	**1.46 (1.02-2.09)**	**0.031**
Model 2[b]	1.00	1.15 (0.79-1.69)	0.91 (0.61-1.35)	**1.46 (1.01-2.10)**	**0.034**
Model 3[c]	1.00	1.31 (0.88-1.95)	1.06 (0.69-1.62)	**1.57 (1.08-2.26)**	**0.020**

[a]Adjusted – Sex and age

[b]Adjusted - Model 1 + smoking status (never, current, former), alcohol consumption (BINGE frequency) and vitamin D consumption (mcg)

[c]Adjusted – Model 2 + marital status (single/married or stable union/separated or divorced or widowedd), skin color (white and not white), physical

activity (inactive/insufficiently active/active), use of supplements (yes or no), energy intake (continuous, kcal/day), baseline BMI (continuous kg/m²), professional situation.
dTAC: Total Dietary Antioxidant Capacity
fgTAC: Total Antioxidant Capacity of Food Groups.

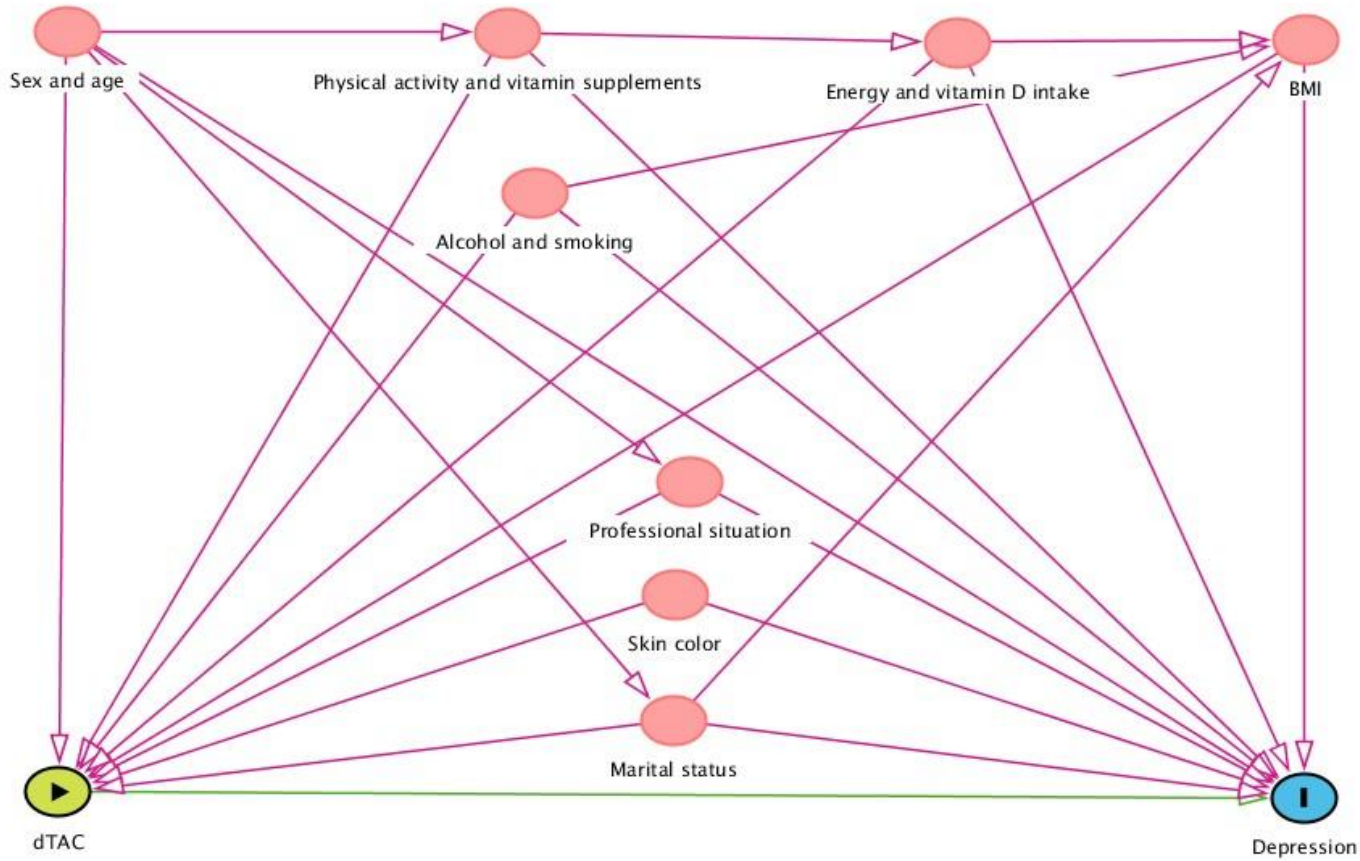
Table 5. Hazard ratios and 95% CI of depression incidence according to consumption of fgTAC by beverages, CUME project (n=2,572).

	fgTAC from natural juices				
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.02 (SD 0.13)	0.26 (SD 0.05)	0.54 (SD 0.12)	1.33(SD 0.75)	
Crude	1.00	0.78 (0.55-1.11)	0.80 (0.57-1.12)	0.71 (0.50-1.01)	0.099
Model 1[a]	1.00	0.74 (0.52-1.05)	0.78 (0.55-1.10)	**0.70 (0.49-0.99)**	0.100
Model 2[b]	1.00	0.74 (0.52-1.05)	0.78 (0.55-1.09)	0.70 (0.50-1.00)	0.114
Model 3[c]	1.00	0.82 (0.57-1.19)	0.85 (0.60-1.22)	0.77 (0.54-1.11)	0.235
	fgTAC from teas and coffee				
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.42 (SD 0.68)	2.25 (SD 0.48)	4.19 (SD 0.72)	9.14 (SD 3.90)	
Crude	1.00	0.88 (0.61-1.25)	0.89 (0.63-1.27)	1.01 (0.71-1.42)	0.807
Model 1[a]	1.00	0.85 (0.59-1.21)	0.91 (0.63-1.30)	1.06 (0.74-1.51)	0.533
Model 2[b]	1.00	0.83 (0.58-1.18)	0.88 (0.61-1.27)	1.02 (0.71-1.45)	0.678
Model 3[c]	1.00	0.85 (0.59-1.22)	0.93 (0.64-1.34)	1.03 (0.72-1.48)	0.636
	fgTAC from artificial juices and sodas				
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.01 (SD 0.04)	0.05 (SD 0.01)	0.16 (SD 0.05)	0.72 (SD 0.53)	
Crude	1.00	1.00 (0.70-1.45)	1.00 (0.70-1.43)	1.12 (0.79-1.58)	0.443
Model 1[a]	1.00	0.94 (0.66-1.36)	0.93 (0.65-1.34)	1.10 (0.78-1.55)	0.389
Model 2[b]	1.00	0.95 (0.66-1.38)	0.94 (0.65-1.35)	1.09 (0.77-1.55)	0.426
Model 3[c]	1.00	1.09 (0.73-1.63)	1.02 (0.69-1.51)	1.12 (0.79-1.61)	0.568
	fgTAC from alcoholic beverages				
	Q1	**Q2**	**Q3**	**Q4**	*P for trend*
	0.01 (SD 0.10	0.13 (SD 0.03)	0.34 (SD 0.09)	1.32 (SD 1.11)	
Crude	1.00	0.82 (0.57-1.17)	0.81 (0.58-1.14)	0.85 (0.60-1.20)	0.596
Model 1[a]	1.00	0.77 (0.54-1.11)	0.82 (0.58-1.16)	0.91 (0.64-1.29)	0.996
Model 2[b]	1.00	0.79 (0.55-1.14)	0.85 (0.59-1.23)	0.98 (0.67-1.43)	0.694
Model 3[c]	1.00	0.93 (0.60-1.43)	1.02 (0.67-1.55)	1.16 (0.75-1.77)	0.323

[a]Adjusted – Sex and age

[b]Adjusted - Model 1 + smoking status (never, current, former), alcohol consumption (BINGE frequency) and vitamin D consumption (mcg)

[c]Adjusted – Model 2 + marital status (single/married or stable union/separated or divorced or widowedd), skin color (white and not white), physical activity (inactive/insufficiently active/active), use of supplements (yes or no), energy intake (continuous, kcal/day), baseline BMI (continuous kg/m²), professional situation.



dTAC: Total Dietary Antioxidant Capacity.
fgTAC: Total Antioxidant Capacity of Food Groups.

Supplementary figure 1. Direct acyclic graph (DAG) derived from previous literature search. Nodes represent variables, and arrows represent causal associations. Dietary Antioxidant Capacity (dTAC) is the exposure, and depression is the outcome. BMI (Body Mass Index).

Supplementary Table 1. Food groups and their respective TAC (mmol/d) averages.

Group	Foods	TAC
Fruits	Avocado, pineapple, açaí pulp, acerola cherry, banana, guava, kiwi, orange, tangerine, apple, papaya, mango, watermelon, melon, strawberry, cherry, peach, plum, grape, pass grape, tropical fruits, fruit salad	2.58 (SD 2.49)
Vegetables	Pumpkin, courgette, chayote, chard, lettuce, cress, green cabbage, arugula, spinach, cassava, yam, baroa potato, fried cassava, baked potato, french fries, beetroot, eggplant, carrot, cauliflower, cabbage, green corn, cucumber, bell pepper, green beans, tomato, vegetables soup.	0.70 (SD 0.49)
Beans and lentils	Bean, lentil, chickpea.	0.25 (SD 0.28)
Oilseeds	Peanuts, walnut, chestnuts.	0.54 (SD 1.04)
Dairy	Whole milk, skimmed milk, semi-skimmed milk, soy milk, whole yogurt, low-fat yogurt, cream cheese, cream cheese light, cheese, cottage cheese, ricotta cheese.	0.14 (SD 0.11)
Meat and eggs	Mortadella, soy meat, turkey breast, beef, chicken with skin, skinless chicken, pork, sheep meat, viscera, sausage, egg, bacon and pork rinds, sardines and tuna, shrimp, salmon, and other fishes.	0.20 (SD 0.15)
Breads, pasta and cereals	French bread, loaf bread, toast bread, wheat bread, light bread, sweet bread, cheese bread, breakfast cereals, oatmeal, granola, cereal bar, rice, brown rice, noodle, lasagna, gnocchi, polenta, fried polenta, hominy, pizza, cassava flour, cornflour.	0.53 (SD 0.37)
Oils	Butter, margarine, mayonnaise, light margarine and light mayonnaise, olive oil, canola oil, sunflower oil, corn oil, soy oil, pork fat.	0.13 (SD 0.14)
Junk food	Sugar, brown sugar, sweetener, dark chocolate, milk chocolate, bonbon, candies, popcorn, hot dog, hambúrguer, snack chips, pepper sauce, pudding, milk cream, mustard, chocolate milk, pie, quiche, ice cream, light ice cream, fruit in syrup, guava paste, compote fig, compote peach, fruits jam, noodle soups.	0.70 (SD 0.90)
Natural Juices	Natural fruit juice.	0.54 (SD 0.64)
Teas and Coffee	Mate, black tea, green tea, coffee.	4.00 (SD 3.83)
Artificial juices and sodas	Soda, light soda, sugar-free soda, artificial juice.	0.23 (SD 0.40)
Alcoholic beverages	Liquor, distilled drinks, beer, Red wine, and other types of wines.	0.43 (SD 0.78)

7. CONCLUSÕES GERAIS

O presente estudo foi realizado com egressos de universidades públicas do estado de Minas Gerais, uma amostra com alto nível de instrução o que permitiu o fornecimento de dados mais fidedignos e, consequentemente uma observação mais confiável das relações entre os fatores de exposição e os desfechos de saúde.

Os achados do presente estudo mostram uma considerável incidência de depressão e prevalência de tempo de sono inadequado na população de estudo, evidenciado que esses são desfechos de saúde de grande impacto para a saúde pública e qualidade de vida.

Entre os fatores de risco modificáveis para a depressão e alterações no tempo de sono, a dieta vem se destacando. Sendo que os antioxidantes presentes na dieta podem atuar como fatores externos importantes no combate ao estresse oxidativo, que por sua vez relaciona-se a fisiopatologia dos desfechos investigados. No presente estudo, não foi possível afirmar uma associação independente entre uma maior CATd com a incidência de depressão e prevalência de inadequação no tempo de sono da população estudada.

Ao analisar a Capacidade Antioxidante de grupo alimentares, uma maior CATga de leguminosas associou-se a menor incidência de depressão, por sua vez, uma maior CATga de "*Junk Food*" associou-se a maior incidência de depressão. Houve menor chance de sono muito curto/curto para o maior quartil CATga de frutas e de feijões e lentilhas, assim como para o terceiro quartil de CATga de hortaliças e óleos e gorduras. Além disso, o maior quartil de CATga de chás e cafés se associou positivamente ao menor tempo de sono. Para o tempo de sono logo, associações inversas foram observadas para o maior quartil CATga de oleaginosas e o para o terceiro quartil de chás e cafés. Tais resultados mostram que as fontes em que os antioxidantes estão inseridos podem influenciar na sua relação com os desfechos estudados.

Os achados apresentados nesta tese têm importância para políticas de alimentação e nutrição e para saúde coletiva, evidenciando a necessidade da nutrição e de profissionais nutricionistas no cuidado integral da saúde mental. Além disso, por salientar a importância da matriz alimentar em que os antioxidantes estão inseridos, reforçam as recomendações do Guia Alimentar para a População Brasileira, destacando os alimentos *in natura* como importantes fontes de antioxidantes da dieta.

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ANEXO I. Artigo de revisão: Association of dietary total antioxidant capacity with depression, anxiety, and sleep disorders: A systematic review of observational studies.

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REVIEW ARTICLE

Association of dietary total antioxidant capacity with depression, anxiety, and sleep disorders: A systematic review of observational studies

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ABSTRACT

Background and Aim: We aimed to systematically review observational studies that evaluated the potential association of the dietary total antioxidant capacity (dTAC) with common mental disorders (depression and anxiety) and sleep disorders.
Methods: Studies with an observational design that evaluated the association between the dTAC and common mental disorders and sleep disorders were identified using the PubMed and Scopus databases. The meta-analysis guideline of observational studies in epidemiology and the preferred reporting items for systematic reviews and meta-analysis were used to conduct and report the data of this systematic review.
Results: Of the 439 records, seven studies were included in this review. There was a sample variation of 41-3297 participants. We highlight that five of the studies analyzed were conducted in the Iranian population. Four studies analyzed only women, and three studies were conducted with postmenopausal or climacteric women. Four cross-sectional studies showed inverse associations between the dTAC and depression, anxiety, and sleep disorders in Iranians.
Conclusion: The consumption of a diet rich in antioxidants, characterized by high dTAC scores, seems to be inversely associated with depression, anxiety, and sleep disorders. However, further studies with different populations and designs are necessary for a better understand this relationship.
Relevance to Patients: This review assesses the association of the dTAC with common mental disorders (depression and anxiety) with sleep disorders. This will help guide further studies on the relationship between diet and mental disorders and sleep disorders. Knowledge about these relationships is essential for the creation of non-pharmacological practices for the prevention of these disorders.

1. Introduction

Depression and anxiety are common mental disorders due to their high prevalence in the contemporary society [1]. Depression has been diagnosed in more than 322 million individuals worldwide and is one of the major contributors to the global burden of disease [1,2]. Anxiety disorders have affected approximately 264 million people worldwide. Although anxiety is an important and necessary feeling in certain situations, it may be indicative of mental disorders when observed to be in an uncontrolled degree [1]. This condition can be classified into generalized anxiety disorders, panic syndrome, and obsessive-compulsive disorder among others [1,3].

Sleep disorders can be characterized as manifestations that cause impairment in the sleep quality, among which changes in the circadian rhythm and insomnia stand

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ANEXO II. Termo de Consentimento Livre e Esclarecido

Estimado (a) ex-aluno (a) da Universidade Federal de Minas Gerais (UFMG) ou da Universidade Federal de Viçosa (UFV), vimos por meio deste, convidá-lo (a) a participar de uma pesquisa intitulada "Coorte de Universidades MinEiras (CUME), cujo objetivo é avaliar o impacto do padrão alimentar brasileiro, de grupos de alimentos e fatores dietéticos específicos no desenvolvimento de Doenças e Agravos Não Transmissíveis (DANT), tais como obesidade, hipertensão arterial, cânceres, doenças intestinais, pulmonares e cardiovasculares, entre outras. Este estudo será desenvolvido em parceria entre a Escola de Enfermagem da UFMG e o Departamento de Nutrição e Saúde da UFV, e é de responsabilidade dos seguintes professores: Dra. Josefina Bressan (Coordenadora/UFV), Dra. Helen Hermana Miranda Hermsdorff (Colaboradora/UFV) e Dr. Adriano Marçal Pimenta (Colaborador/UFMG). Caso concorde em participar, você responderá a um questionário, autoaplicável, com 55 perguntas sobre dados demográficos, socioeconômicos, antropométricos, bioquímicos, hábitos de vida, consumo alimentar e histórico de saúde. Esse questionário será nosso questionário basal (Q_0). Posteriormente, a cada dois anos, você deverá responder a outros questionários de seguimento (Q_2, Q_4, ..., Q_n), também autoaplicáveis, normalmente com um número menor de perguntas, com o intuito de avaliar modificações em relação aos parâmetros basais. Sua colaboração é voluntária e o seu anonimato será garantido. Firmamos o compromisso de que os seus dados serão utilizados, apenas, para fins da pesquisa e divulgados, somente, em eventos e periódicos científicos. O seu consentimento em participar deste estudo também deve considerar que o projeto foi aprovado pelos Comitês de Ética e Pesquisa da UFMG e da UFV. Em qualquer fase da pesquisa, você poderá fazer perguntas, caso tenha dúvidas, e retirar o seu consentimento, além de não permitir a posterior utilização de seus dados, sem nenhum ônus ou prejuízo. Se os esclarecimentos feitos forem satisfatórios e se estiver de acordo, favor assinar o presente termo, dando seu consentimento para a participação da pesquisa em questão.

Atenciosamente,
Profa. Dra. Josefina Bressan
Profa. Dra. Helen Hermana Miranda Hermsdorff
Prof. Dr. Adriano Marçal Pimenta

Nome: _____ R.G_____
Assinatura: _____
Local_____ Data: _____/ _____/ _____

Nome do coordenador da pesquisa: Josefina Bressan. Tel.: (31) 3899-2692 Comitê de Ética e Pesquisa da UFMG: Av. Presidente Antônio Carlos, nº 6627. Prédio da Reitoria, 7º andar, sala 7018, Bairro Pampulha, Belo Horizonte/MG. CEP: 31270-901. Tel.: (31) 3499-4592. Comitê de Ética em Pesquisa com Seres Humanos da UFV: Av. PH Rolfs, s/n, Divisão de Saúde, Universidade Federal de Viçosa. Viçosa/MG. CEP: 36570-001 Tel.: (31) 3899-3783.

ANEXO III. Artigo original II: Association between total dietary antioxidant capacity and food groups and incidence of depression in a cohort of Brazilian graduates (CUME Project)

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Association between total dietary antioxidant capacity and food groups and incidence of depression in a cohort of Brazilian graduates (CUME Project)

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Abstract

This study aims to evaluate the association between Dietary Total Antioxidant Capacity (dTAC) and Total Antioxidant Capacity of food groups (fgTAC) with the incidence of depression in Brazilian graduates participating in the Cohort of Universities of Minas Gerais (CUME Study). The sample consisted of 2572 participants without a medical diagnosis of depression at baseline who responded to at least one follow-up questionnaire from the CUME Project. The Ferric Reducing Antioxidant Power assay was used to determine dTAC. Incidence of depression was estimated by self-reported medical diagnosis of depression during the years of cohort follow-up. Cox regression models were used to relate dTAC and fgTAC to the incidence of depression. The mean follow-up time was 2·96 (1·00) years, and 246 cases of depression were observed (32·3/1000 person-years). The mean dTAC was 11·03 (4·84) mmol/d. We found no associations between higher dTAC and lower risk of developing depression after adjusting for possible confounders. The incidence of depression was inversely associated with fgTAC of the beans and lentils group (hazard ratio (HR): 0·61; 95 % CI 0·41, 0·90). The fgTAC of the junk food group was positively associated with higher incidence of depression after all adjustments (HR: 1·57; 95 % CI 1·08, 2·26). Our findings do not support an association between dTAC and the incidence of depression in a highly educated Brazilian population. However, associations of fgTAC show the importance of analysing the food matrix in which these antioxidants are inserted. We highlight the need for more prospective studies with different nationalities to confirm these results.

Key words: **Dietary Total Antioxidant Capacity: Depression: Epidemiology: Oxidative stress**

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ANEXO IV. Artigo de revisão: Relationship between food consumption and improvements in circulating melatonin in humans: an integrative review

Esta é uma revisão desenvolvida durante o doutorado, publicada na Revista Critical Reviews in Food Science and Nutrition, a qual teve como objetivo avaliar a relação entre o consumo de alimentos e melhorias na melatonina circulante em humanos.

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REVIEW

Relationship between food consumption and improvements in circulating melatonin in humans: an integrative review

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ABSTRACT

Melatonin is an important hormone in the regulation of circadian rhythms and has great antioxidant power. Recent studies have demonstrated the benefits of its supplementation in the metabolic profile. Food sources have also been studied for complementary therapies. However, information on the bioavailability of food sources of melatonin is still scarce. Thus, the objective of this review is to gather in the literature studies that evaluate the relationship between food consumption and improvements in circulating melatonin in humans. In total, 178 studies were found, of which 11 were included in this review. The results show increases in the excretion of the melatonin metabolite (6- sulfatoxymelatonin) or circulating melatonin for foods such as cherries, grapes, bananas, pineapples, dark green vegetables, Japanese vegetables and beer. Significant increases in melatonin were observed even after ingesting cultivars with low concentrations of this hormone. It was possible to assume that other nutrients that precede their synthesis (serotonin and tryptophan) could also have led to this increase. Although consumption of the foods found is beneficial in increasing circulating melatonin, further confirmatory studies are needed.

KEYWORDS

Foods; melatonin; 6-sulfatoxymelatonin and bioavailability