RAFAELA SIRTOLI

ASSOCIAÇÃO ENTRE O CONSUMO DE ÁLCOOL E ASPECTOS RELACIONADOS AO SONO

Londrina
2024

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Tese apresentada à Universidade Estadual de Londrina - UEL, como requisito parcial para a obtenção do título de Doutor em Saúde Coletiva

Orientador: Prof. Dr. Camilo Molino Guidoni
Coorientador: Prof. Dr. Arthur Eumann Mesas

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RESUMO

O consumo de álcool permeia toda a história da humanidade, mas o uso nocivo desta substância tem se associado a diversas alterações fisiológicas, como transtornos relacionados ao sono. Embora muito tenha se investigado a respeito do tema, ainda existem lacunas a respeito da influência de características biológicas e sociais em relação a essa associação. **Objetivo:** Investigar a associação entre o consumo de álcool e o sono em adultos. **Métodos:** tese de doutorado elaborada em modelo escandinavo, originando dois artigos científicos como resultados. O primeiro artigo é uma revisão sistemática da literatura com metanálise a respeito da associação entre cronotipo e consumo de álcool. Realizou-se uma busca sistemática de estudos observacionais em cinco bases de dados: *PubMed*, *Scopus*, *Web of Science*, *Cochrane Library* e *PsycINFO*. Modelos de efeitos aleatórios foram utilizados para estimar a odds ratio conjunta (OR) e IC95% de consumo de álcool de acordo com o cronotipo. A revisão foi elaborada de acordo com as recomendações do *Meta-analysis of Observational Studies in Epidemiology* (MOOSE) e do *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA). O segundo artigo é um estudo quantitativo, com dados primários de três bancos de dados de grupos de pesquisa do Brasil, Chile e Espanha. Modelos de regressão logística foram elaborados para analisar de forma independente a associação entre *risk of alcohol-related problems* (RARP) e qualidade e duração de sono nos bancos de dados dos três países. Com base nos resultados dos modelos ajustados de cada país, os valores de cada OR e seus respectivos IC95% foram transformados em escala logarítmica, para possibilitar o cálculo da OR conjunta (p-OR) e IC95%. **Resultados:** No primeiro artigo, um total de 33 estudos envolvendo 28.207 indivíduos foram incluídos na revisão sistemática. De forma geral, os indivíduos vespertinos apresentaram maior frequência e volume de consumo de álcool, quando comparados aos indivíduos de outros cronotipos. Ainda, uma metanálise de 13 estudos evidenciou que indivíduos com cronotipo vespertino apresentam uma chance 41% maior de consumir álcool do que aqueles com outros cronotipos (OR: 1.41; IC95%: 1.16–1.66). No segundo artigo, 1.830 estudantes foram incluídos na análise (31,2% brasileiros, 42,2% chilenos e 26,6% espanhois). De forma geral, 25,0% dos estudantes foram classificados com RARP intermediário, enquanto que 9,9% apresentaram RARP alto. Na análise conjunta dos três países, RARP intermediário a alto se mostrou associado a qualidade de sono subótima (p-OR: 1.24; IC95%: 1.00-1.52). Frequência de consumo de álcool não se mostrou associada à qualidade ou duração do sono. **Conclusão:** O cronotipo vespertino e uma qualidade subótima do sono estão associados ao consumo de álcool. Acredita-se que, devido ao fato de pessoas com cronotipo vespertino apresentarem uma menor quantidade e qualidade do sono, há um aumento da impulsividade e da propensão ao risco, resultando na adoção de comportamentos não saudáveis, e, dentre eles, o consumo de álcool. Em contrapartida, indivíduos com risco de problemas relacionados ao álcool também apresentam uma menor qualidade subjetiva de sono.

Palavras-chave: consumo de álcool; cronotipo; sono; saúde mental; epidemiologia.

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ABSTRACT

Alcohol consumption permeates the entire history of humanity, but the harmful use of this substance has been associated with several physiological changes, such as sleep disorders. Although much has been investigated on the topic, there are still gaps regarding the influence of biological and social characteristics in relation to this association. **Aim:** To investigate the association between alcohol consumption and sleep in adults. **Methods**: Thesis in Scandinavian model, containing two articles. The first article is a systematic review with meta-analysis about the association between chronotype and alcohol consumption. A systematic search of observational studies on this association was conducted in five databases: PubMed,Scopus, Web of Science, Cochrane Library and PsycINFO. Random-effect models estimated the pooled odds ratio (OR) of alcohol consumption according to chronotype. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were followed. The second article is a quantitative study, with primary data from three databases of research groups from Brazil, Chile and Spain. Independent logistic regression models were performed to analyze the association between risk of alcohol-related problems (RARP) and sleep quality and duration in all three countries. Based on the results of the fully adjusted model obtained for each country, the values of each OR and the lower and upper limits of the CI were transformed into a logarithmic scale for calculating the pooled OR (p-OR) and its 95% CI. **Results:** In the first article, a total of 33 studies involving 28.207 individuals were included in the review. Overall, most studies indicated a higher volume and frequency of alcohol consumptionin evening-type individuals than in individuals with different chronotypes. Additionally, a meta-analysis including 13 studies showed that evening-type individuals were 41% more likely to consume alcohol than those with other chronotypes (OR: 1.41; 95% CI: 1.16–1.66). In the second article, 1.830 students were included in the analysis (31.2% Brazilian, 42.2% Chilean, and 26.6% Spanish). Overall, 25.0% and 9.9% of the students were classified as intermediate and high RARP, respectively. In the combined results for the three countries, intermediate-to-high RARP was associated with a higher likelihood of suboptimal sleep quality (p-OR: 1.24; 95% CI: 1.00-1.52), regardless of sociodemographic and lifestyle covariates and of self-rated health. The frequency of alcohol consumption was not associated with sleep quality or sleep duration. **Conclusion**: Evening chronotype and suboptimal sleep quality are associated with alcohol consumption. It's believed that, due to the fact that people with an evening chronotype have a lower quantity and quality of sleep, there's an increase in impulsivity and greater risk-taking, resulting in the adoption of unhealthy behaviors, such as alcohol consumption. On the other hand, individuals with risk of alcohol-related problems also have poorer subjective sleep quality.

Key-words: alcohol consumption; chronotype; sleep; mental health; epidemiology.

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LISTA DE ABREVIATURAS E SIGLAS

ASSIST   *Alcohol, Smoking and Substance Involvement Screening Test*

AUDIT   *Alcohol Use Disorder Identification Test*

AUDIT-C   *The Alcohol Use Disorders Identification Test — Consumption*

BMI   *Body Mass Index*

BD   *Bipolar Disorder*

CSM   *Composite Scale of Morningness*

CI   *Confidence Interval*

COVID-19   *Coronavirus disease* 2019

DQES   *Dietary Questionnaire for Epidemiological Studies*

DTS   *Diurnal Type Scale*

FFQ   *Food Frequency Questionnaire*

GBD   *Global Burden of Disease*

HED   *Heavy Episodic Drinking*

IC   Intervalo de Confiança

IMC   Índice de Massa Corporal

JLS   *Jet Lag* Social

LDH   *Lifetime Drinking History*

MCTQ   *Munich Chronotype Questionnaire*

MEQ   *Morningness-Eveningness Questionnaire*

MESSi   *The Morningness-Eveningness-Stability-Scale Improved*

MOOSE   *Meta-Analysis of Observational Studies in Epidemiology*

NSQ   Núcleo Supraquiasmático do Hipotálamo

OMS   Organização Mundial da Saúde

OR   *Odds Ratio*

p-OR   *Odds Ratio* conjunta

PRISMA   *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*

PSQI   *Pittsburgh Sleep Quality Index*

RARP   *Risk of Alcohol-Related Problems*

SUD   *Substance Use Disorder*

rMEQ   *Reduced Morningness-Eveningness Questionnaire*

UEL   Universidade Estadual de Londrina

SUMÁRIO

1. INTRODUÇÃO

1.1. CONTEXTUALIZAÇÃO

O consumo de álcool é uma prática comum entre diversas culturas, religiões e círculos sociais ao redor do mundo (WORLD HEALTH ORGANIZATION, 2018). Há seis décadas, Mandelbaum (1965) fez uma afirmação que é pertinente até os dias de hoje. "O álcool consiste em um artefato cultural" (MANDELBAUM, 1965, p. 281). Ou seja, o seu uso e seus muitos significados são definidos pela cultura na qual ele está inserido. Enquanto existem grupos e sociedades que aceitam – e até estimulam – o seu uso de forma libertina, há aqueles que rejeitam completamente o consumo de bebida alcoólica.

Inicialmente utilizado como um alucinógeno, há relatos de uso de álcool como bebida desde 3.500 A.E.C. (HAJAR, 2000). Com exceção da Oceania e de partes da América do Norte, acredita-se que tribos originárias presentes na maioria dos continentes que conhecemos hoje tinham contato com bebidas alcoólicas (MANDELBAUM, 1965; ROOM, 1997).

O simbolismo religioso do álcool é um dos aspectos mais importantes quando consideramos o consumo de bebidas alcoólicas ao longo da história. Para os astecas, o entorpecimento por meio do álcool significava agradar aos deuses (MANDELBAUM, 1965). Para religiões monoteístas, o vinho em particular possui diversos significados ritualísticos e simbólicos. Para o cristianismo, o vinho consiste em um dos elementos centrais da celebração da eucaristia, representando o sangue de Cristo. O vinho também é uma parte importante de diversos rituais judeus, incluindo o Shabat, feriados, casamentos e a Páscoa judaica. Ainda, a despeito da crença islâmica de que o vinho seria uma abominação a ser evitada, os muçulmanos também consomem uma variedade de bebidas intoxicantes (FORSTER, 2021).

Para além das conotações religiosas, outros aspectos culturais também influenciam a relação dos povos com as bebidas. Acredita-se que a maioria dos indivíduos, datando da Era Moderna, não consumiam álcool pelo seu efeito entorpecedor. O álcool é um conhecido "facilitador" de interações sociais, e o seu consumo em tavernas e casas de bebidas na Europa e na Rússia, por exemplo, foi importante na criação de um ambiente no qual diversas classes sociais entravam em contato. Tais locais eram considerados espaços abertos para discussões sobre os mais variados assuntos, de negociações de compra e venda a expressões de oposição à liderança vigente, abrangendo

moradores locais e viajantes. Por esse motivo, esses espaços se tornaram importantes ao ponto de impactar sobre a formação da opinião pública e visão política dessas populações (HOLT, 2006; KÜMIN, 2021).

Ainda, a fim de compreender a significância cultural e social do álcool, Dietler (2020, p. 177) propõe que o álcool consiste no que o autor chama de cultura material incorporada:

> *[...] Like other foods, alcoholic beverages are a kind of material culture made to be destroyed through ingestion into the human body —they become part of our very being. But unlike other foods, they also magically transform consciousness as they enter the body. This means that both alcohol and other foods have an unusually close relationship to the inculcation and the symbolization of concepts of identity and difference in the construction of the self ('you are what you eat'). Moreover, because of their psychotropic properties, alcoholic beverages often have a heightened valuation in ritual contexts, and they frequently even serve as a crucial indexical sign of ritual. Consequently, the consumption of alcohol is usually enveloped by a set of cultural rules and beliefs that are even more emotionally charged than with other foods and drinks.*

A relação da sociedade com as bebidas alcoólicas sempre esteve pautada pelas crenças e valores das populações, os quais refletem sobre as políticas sociais e, consequentemente, sobre a disponibilidade dessa substância para consumo (ROOM, 1997). Atualmente, em adição a todo o simbolismo que permeia a história da humanidade com o álcool, é necessário considerar a normalização do uso de substâncias (SZNITMAN *et al.*, 2013), bem como o crescente prevalência da automedicação e os riscos dessa prática (BEHZADIFAR *et al.*, 2020; ZHENG *et al.*, 2023).

Há uma ampla discussão a respeito do uso de álcool como automedicação, principalmente em condições relacionadas à saúde mental, em detrimento de tratamentos mais adequados e controlados (HAWN *et al.*, 2020; MC HUGH; MCBRIDE, 2020; MENEO *et al.*, 2023). Esse contexto, associado à normalização social do consumo de álcool por parte de amigos, familiares e da mídia – tanto em plataformas sociais, quanto em séries, filmes e propagandas –, e à grande disponibilidade de bebidas alcoólicas em locais como bares, restaurantes e lojas de bebidas contribui para o consumo de álcool (PRABHUGHATE *et al.*, 2020).

Apesar de estar associado ao lazer no imaginário de maior parte das pessoas, o uso nocivo de álcool consiste em um dos principais fatores de risco à saúde da população a nível global, sendo responsável por aproximadamente 3 milhões de mortes por ano (5,3% do total de mortes anuais) (WORLD HEALTH ORGANIZATION, 2018).

Aproximadamente 43% da população mundial com idade igual ou maior a 15 anos, mais de 2,3 bilhões de pessoas, consomem álcool. Em algumas regiões do planeta, como a Europa, as Américas e o Pacífico Ocidental, a proporção de consumidores de álcool é superior à de abstêmios (54,1% nas Américas, 59,9% na Europa e 53,8% no Pacífico Ocidental). Em muitos países, o consumo de álcool tem início precoce, iniciando antes mesmo dos 15 anos de idade, atingindo o pico entre 20 e 24 anos. No que diz respeito à diferença entre os sexos, a proporção de homens que consomem álcool é maior que a proporção de mulheres. Mulheres também consomem menores quantidades e praticam menos *heavy episodic drinking* (HED; definido como o consumo de 60 gramas ou mais de álcool puro em uma única ocasião, ao menos uma vez por mês) (WORLD HEALTH ORGANIZATION, 2018). Apesar disso, a prevalência de transtorno por uso de álcool cresceu 84% em mulheres na última década, comumente associado a estresse e afetos negativos (PELTIER *et al.*, 2019).

Dentre as causas de morte e incapacidade relacionadas ao consumo de álcool estão: diabetes; doenças cardiovasculares; tuberculose; diversos tipos de câncer; acidentes de trânsito; violência interpessoal; pancreatite; cirrose; e epilepsia (WORLD HEALTH ORGANIZATION, 2018). Apesar de alguns autores apontarem os benefícios cardiovasculares do uso moderado de álcool, não há consenso na literatura a respeito do tema (BARBERÍA-LATASA; GEA; MARTÍNEZ-GONZÁLEZ, 2022). Devido ao alto risco associado, e na ausência de evidências mais robustas, recomenda-se a abstenção do consumo (GRISWOLD *et al.*, 2018).

A despeito dessa recomendação, o consumo abusivo de álcool continua sendo um dos principais fatores de risco para a saúde em todo mundo (WORLD HEALTH ORGANIZATION, 2018), em partes devido aos seus efeitos de reforço positivo (efeitos hedônicos) e reforço negativo (alívio de desconfortos), bem como pela falta de opções de reforço não alcoólicas (MACKILLOP *et al.*, 2022). Cooper (1994) propôs um modelo de quatro motivos para o consumo de álcool: 1) motivos de intensificação (beber para intensificar sentimentos positivos); 2) motivos sociais (beber para facilitar ou melhorar as interações sociais); 3) motivos de *coping* (beber para esquecer ou reduzir sentimentos negativos); e 4) motivos de conformidade (beber para evitar a rejeição social ou para se encaixar em um grupo). Em adição a esse modelo, há ampla discussão na literatura a respeito do uso de álcool como auxílio para dormir (GOODHINES *et al.*, 2019; GRAUPENSPERGER *et al.*, 2023; RICHTER *et al.*, 2020; SCHWEIZER *et al.*, 2019).

Nesses casos, indivíduos com problemas relacionados ao sono e/ou dificuldade para dormir ingerem álcool com o objetivo de indução do sono (GOODHINES *et al.*, 2019).

Distúrbios relacionados ao sono também são considerados importantes problemas de saúde pública, visto que o sono é essencial para o bom funcionamento de inúmeros processos biológicos (LIM *et al.*, 2023). A curta duração do sono está associada a uma pior saúde mental, maior risco de eventos cardiovasculares e um pior estado de saúde de modo geral (GREENLUND *et al.*, 2022), além de ser considerada um fator de risco para mortalidade por todas as causas (ROBBINS *et al.*, 2021). Adicionalmente, a deficiência do sono representa custos econômicos, relacionados a desfechos negativos em saúde, bem-estar, segurança e produtividade, traduzidos em forma de gastos financeiros (ex.: atendimentos em saúde, acidentes de trânsito e de trabalho, queda de produtividade, etc) e gastos não financeiros (perda de qualidade de vida e mortes prematuras) (LIM *et al.*, 2023).

A prevalência de má qualidade subjetiva do sono em adultos em idade ativa é de 32,8%, aumentando para 33,4% em idosos (SIMONELLI *et al.*, 2019). No que se refere à curta duração do sono (ponto de corte considerado: < 6 horas), há uma grande diferença de acordo com os métodos utilizados nos estudos. A prevalência de curta duração subjetiva do sono em adultos é de 7,5-9,6%, enquanto que os dados subjetivos reportam prevalências de até 53,3% (MATSUMOTO; CHIN, 2019). Ainda, evidências sugerem que cerca de um terço dos adultos (30-36%) relatam ao menos um sintoma de insônia, sendo o sintoma mais frequente a dificuldade para o início do sono (MORIN; JARRIN, 2022).

Conforme afirmado anteriormente, o consumo de álcool e a saúde do sono estão relacionados. Problemas relacionados ao sono aumentam o consumo de álcool, em uma tentativa de automedicação para dormir, enquanto que o consumo exacerbado de álcool diminui a qualidade e a duração do sono, exigindo maiores doses de álcool para dormir. Trata-se de uma relação recíproca, que se potencializa com o passar do tempo (BROWER, 2003; EDWARDS; REEVES; FISHBEIN, 2015; GOODHINES *et al.*, 2019; HE; HASLER; CHAKRAVORTY, 2019).

Diante do exposto, este trabalho pretende investigar a relação entre consumo de álcool e aspectos relacionados ao sono. Serão abordadas as variáveis: cronotipo, qualidade subjetiva do sono, consumo ou abstenção de álcool e problemas relacionados ao álcool.

1.2. RITMO CIRCADIANO

O estado de sono e vigília de um indivíduo é determinado por um sistema intrínseco, denominado ritmo circadiano – ou relógio biológico –, o qual dita mudanças fisiológicas e comportamentais ao longo das 24 horas do dia. Dentre os efeitos, pode-se citar alterações na temperatura corporal, nos níveis de cortisol, na produção de urina, na capacidade cognitiva e no humor. Ademais, o ritmo circadiano também garante que os processos biológicos do corpo sigam uma sequência temporal apropriada e ocorram sintonizados uns aos outros (FOSTER, 2020; FOSTER; KREITZMAN, 2014).

Apesar de intrínseco, o rimo circadiano funciona sincronizado a estímulos externos, conhecidos como *zeitgebers* (do alemão *zeit*, tempo; *geben*, dar, doar), sendo o mais predominante deles a atividade luminosa resultante do movimento de rotação da Terra (BROWN, 1976; FOSTER, 2020). Por meio de estímulos captados por fotorreceptores da retina, as oscilações claro-escuro do meio ambiente são transmitidas para o núcleo supraquiasmático (NSQ), localizado no hipotálamo. O NSQ projeta o estímulo para aproximadamente 35 regiões do cérebro, em sua maioria também hipotalâmicas e associadas à produção de hormônios (FOSTER, 2020).

Além dos estímulos luminosos, também são considerados *zeitgebers* – ou sincronizadores –, variações de temperatura e umidade do ambiente, horários de alimentação ou jejum e interações sociais (SHARMA; CHANDRASHEKARAN, 2005; STEPHAN, 2002). No que se trata das interações sociais, evidências apontam uma bidirecionalidade na associação com o relógio biológico, visto que o ritmo circadiano influencia a propensão ao engajamento social, enquanto que as interações sociais auxiliam na regulação do sistema endógeno (TUTEK; GUNN; HASLER, 2019).

O ajuste do ritmo circadiano por parte dos sincronizadores exógenos reflete em alterações no organismo que garantem o funcionamento do mesmo de forma adequada ao ambiente externo e à rotina desejada (MONK, 2010). Contudo, algumas circunstâncias causam uma dessincronização entre o relógio biológico e o ciclo dia e noite. Um dos exemplos mais conhecidos desse desalinhamento é o *jet lag*. Tal condição ocorre quando um indivíduo percorre mais de três fusos horários em um curto período, sem tempo hábil para que o sistema circadiano ressincronize com o ambiente. Os sintomas incluem fadiga, insônia, sonolência diurna, desorientação, falta de apetite, distúrbios gastrointestinais e mudanças de humor. Quanto maior a distância percorrida, e, consequentemente, quando

maior o número de fusos horários atravessados, mais tempo o organismo demora para se adaptar (FOSTER; KREITZMAN, 2014; SACK, 2009).

Outro exemplo de desalinhamento entre o ritmo interno e externo consiste no *jet lag* social (JLS). Apesar da nomenclatura similar, o JLS difere do *jet lag* por não ser uma condição episódica, mas sim crônica. Ainda, o JLS não envolve uma mudança espacial, e sim um descompasso entre a propensão individual a acordar mais tarde (controlada pelo relógio biológico endógeno) e as rotinas habituais de trabalho e estudo, as quais iniciam mais cedo (controladas pelo relógio social exógeno). Tal cenário resulta em um maior débito de sono e menor qualidade de sono para esses indivíduos, quando comparados àqueles que apresentam propensão diferente (ex.: se sentem bem dispostos pela manhã) (WITTMANN *et al.*, 2006).

1.3. CRONOTIPO

Os indivíduos podem ser classificados de acordo com sua preferência circadiana, ou seja, de acordo com o período do dia no qual se sentem mais bem dispostos (RANDLER, 2019). Pessoas do cronotipo matutino acordam mais cedo e atingem o pico de sua performance física e mental ao final da manhã, enquanto que aquelas que preferem acordar mais tarde e atingem pico de energia ao final da tarde ou à noite são classificadas como cronotipo vespertino (ADAN *et al.*, 2012; NATALE; CICOGNA, 2002).

O primeiro instrumento desenvolvido para avaliação de cronotipo foi o *Morningness-Eveningness Questionnaire* (MEQ), o qual consiste em um questionário de 19 questões, que geram um escore final de 16 a 86 pontos, possibilitando a classificação dos respondentes em cinco diferentes categorias: definitivamente vespertino; vespertino moderado; intermediário; matutino moderado; e definitivamente matutino (HORNE; OSTBERG, 1976). Apesar de apresentar algumas limitações no que diz respeito à extensão do questionário – por vezes considerado muito longo – e ao baixo poder discriminatório de algumas de suas perguntas, o MEQ é o instrumento de avaliação de cronotipo mais utilizado na literatura, e é considerado uma ferramenta confiável em diversos países (ADAN *et al.*, 2012). A fim de contornar essas limitações, Adan e Almirall (1991) desenvolveram uma versão reduzida, o *Reduced Morningness–Eveningness Questionnaire* (rMEQ), com apenas cinco questões, as quais focam exclusivamente na detecção de cronotipos matutinos.

Cerca de 60% da população apresenta cronotipo intermediário, ou seja, encontra-se em meio a dois extremos (matutino e vespertino), e segue distribuição normal (ADAN

et al., 2012). Por essa razão, autores apontam que o cronotipo pode ser visto como uma variável contínua (NATALE; CICOGNA, 2002).

O cronotipo de um indivíduo não é permanente e pode sofrer alterações ao longo da vida. Crianças, em sua maioria, apresentam inclinação ao cronotipo matutino, o que muda na adolescência, período no qual se observa um aumento na frequência de cronotipos vespertinos. Observa-se que o pico de "vespertinidade" ocorre aos 19 anos para mulheres e aos 21 anos para homens. Após o fim da adolescência e o início da vida adulta, a tendência é o cronotipo se tornar mais matutino com o passar do tempo (DRUIVEN *et al.*, 2021; ROENNEBERG *et al.*, 2004).

Além da idade, outros fatores intrínsecos também influenciam a preferência circadiana, como fatores genéticos, gênero e raça (EASTMAN; TOMAKA; CROWLEY, 2017; HU *et al.*, 2016; RANDLER; ENGELKE, 2019). Quanto a fatores ambientais, sabe-se que o cronotipo sofre interferência do fotoperíodo ao nascimento (duração da luz do dia), as estações do ano, oscilações na temperatura e a posição geográfica da residência do indivíduo (LEHMANN *et al.*, 2012; LEOCADIO-MIGUEL *et al.*, 2017; MONGRAIN; PAQUET; DUMONT, 2006; SHAWA; RAE; RODEN, 2018). De forma simplificada, todos os fatores ambientais influenciam o cronotipo por meio da influência que exercem sobre a exposição à luz solar, o *zeitgeber* mais importante na natureza.

Uma das motivações por trás da cronobiologia, ou seja, do estudo dos ritmos biológicos, se deve às repercussões práticas dos cronotipos, principalmente no que se refere ao ambiente de trabalho (NATALE; CICOGNA, 2002). Sabe-se que o trabalho por turnos exerce impacto sobre a saúde do sono dos trabalhadores, sendo associado a uma menor qualidade e quantidade de sono, bem como distúrbios do sono e disfunção diurna (LIM, Yin Cheng *et al.*, 2020). Isso se deve ao fato de o trabalho por turno exigir que o indivíduo se mantenha alerta em um horário habitual de sono, gerando um desalinhamento com o ritmo circadiano endógeno (JAMES *et al.*, 2017).

Para além do trabalho por turnos, conforme mencionado anteriormente, esse desalinhamento – ou JLS – também está presente em indivíduos classificados como vespertinos, os quais enfrentam uma privação crônica de sono por dormirem mais tarde e acordarem cedo para cumprir demandas sociais (WITTMANN *et al.*, 2006). As consequências do JLS são diversas, incluindo parâmetros metabólicos desfavoráveis, como alta glicemia e alto colesterol, maior risco cardiovascular, distúrbios de humor, comprometimento cognitivo e uso de substâncias (BEAUVALET *et al.*, 2017; ZHANG *et al.*, 2022).

1.4. O Sono e o Consumo de Álcool

A privação parcial e gradual do sono interfere sobre o processo de tomada de decisões, diminuindo o tempo de deliberação e aumentando a propensão ao risco (SALFI *et al.*, 2020). De acordo com o modelo proposto Hofmann e colaboradores (2009), a forma como um indivíduo se comporta é o resultado da batalha entre o sistema impulsivo e o sistema de autocontrole, sendo que certas circunstâncias e fatores – nesse caso, a privação do sono – contribuem para a predominância de um sistema sobre o outro. Dentre os comportamentos de risco associados à menor qualidade e quantidade do sono estão: consumo de álcool, de substâncias ilícitas e de tabaco; comportamentos de risco sexual; violações de segurança rodoviária; e participação em jogos de aposta (MASSAR, 2021).

Além da impulsividade e a propensão ao risco, há outros fatores envolvidos na relação entre saúde do sono e o consumo de substâncias. Conforme descrito anteriormente, o álcool é utilizado como tentativa de automedicação para dormir (GOODHINES *et al.*, 2019). Ainda, o álcool também é utilizado para minimizar a tensão e outros sentimentos negativos associados à ansiedade (BULLEY *et al.*, 2016). Considerando a relação bidirecional entre ansiedade e insônia (ALVARO; ROBERTS; HARRIS, 2013), é possível dizer que o álcool é utilizado para reduzir a ansiedade e facilitar o processo de adormecer.

No que concerne os cronotipos, estudos apontam a impulsividade como mediadora da relação entre vespertinidade e o consumo de álcool (EVANS; NORBURY, 2021). A vespertinidade também está associada à busca por novidades ("*novelty-seeking*") (HSU *et al.*, 2012), sintomas de ansiedade e depressão (MERIKANTO; PARTONEN, 2021), todos previamente associados ao uso de álcool (BODEN; FERGUSSON, 2011; BULLEY *et al.*, 2016; KOVÁCS *et al.*, 2022). Ademais, evidências sugerem que a vontade de consumir álcool ocorre frequentemente no período noturno (PIASECKI *et al.*, 2011). Finalmente, a denominada "*pub hypothesis*", proposta por Wittmann e colaboradores (2010), defende que o consumo de álcool é um hábito noturno, e, por conseguinte, indivíduos com cronotipo vespertino simplesmente têm mais oportunidade para beber, quando comparados aos indivíduos matutinos, os quais dormem mais cedo.

A ocorrência concomitante da privação do sono e o alcoolismo é clinicamente relevante pois se trata de um círculo vicioso, no qual o uso de álcool agrava os sintomas da insônia (ex.: ansiedade, disfunção diurna, sintomas depressivos), enquanto que a

insônia está relacionada a episódios subsequentes de consumo e a recaídas em pacientes alcoólatras (BROWER, 2003).

1.5. ESTUDANTES UNIVERSITÁRIOS

Diante do exposto, uma população particularmente em risco são os jovens adultos, e, mais especificamente, os estudantes universitários. A transição da adolescência para a vida adulta é marcada por alterações no ritmo circadiano, no cronotipo e na saúde do sono. Durante esse período, observa-se um aumento da prevalência de cronotipos vespertinos e uma redução constante da duração do sono dos 16 aos 30 anos de idade, com o horário do sono se tornando mais tardio dos 16 aos 24 anos, atingindo o pico aos 22 anos (KARAN *et al.*, 2021; KUULA *et al.*, 2022).

Esse cenário é refletido no contexto acadêmico, no qual a maioria dos estudantes universitários apresenta cronotipo vespertino, uma pior qualidade do sono e maiores escores de disfunção diurna (NÚÑEZ *et al.*, 2019). Estudos também apontam uma associação entre má qualidade do sono, menor duração do sono e/ou cronotipo vespertino e impulsividade – por vezes como mediadora – e comportamentos não saudáveis, como o uso nocivo de smartphones, comportamentos de risco no trânsito e o uso de substâncias (EVANS; NORBURY, 2021; RUSNAC; SPITZENSTETTER; TASSI, 2016; SAKSVIK-LEHOUILLIER *et al.*, 2020; SAMBOU *et al.*, 2021).

Diversos outros fatores contribuem para o consumo exacerbado de álcool durante a graduação, dentre eles: uma maior independência quando comparado à adolescência e ao ensino médio; a inserção em novos círculos sociais; o desenvolvimento de uma nova identidade, contextos que permitem e/ou incentivam o consumo, estressores e sentimentos negativos relacionados à rotina acadêmica, (BORSARI; MURPHY; BARNETT, 2007; CRAWFORD; NOVAK; JAYASEKARE, 2019; SKIDMORE; KAUFMAN; CROWELL, 2016). Alguns desses fatores são ainda mais preponderantes no primeiro ano na universidade, período no qual os estudantes estão se adaptando ao seu novo papel perante à sociedade e muitos acreditam que o consumo exagerado de substâncias é sinônimo com a experiência universitária (CRAWFORD; NOVAK; JAYASEKARE, 2019), resultando em um aumento no consumo de álcool e de HED, quando comparado aos anos anteriores à graduação (CHO *et al.*, 2015; HULTGREN *et al.*, 2019).

Nos Estados Unidos, o consumo de álcool está envolvido em cerca de 1.500 mortes de estudantes universitários por ano (HINGSON; ZHA; SMYTH, 2017). No

Brasil, 86,2% dos universitários referem o uso de álcool em algum momento da vida e 72,0% relatam o uso no último ano (ANDRADE; DUARTE; OLIVEIRA, 2010).

1.6. JUSTIFICATIVA

Considerando a magnitude e a abrangência das consequências do consumo de álcool para a saúde pública, é fundamental elucidar populações e fatores de risco, com a finalidade de nortear estratégias de prevenção e enfrentamento. Ainda, embora existam estudos a respeito da associação entre cronotipo e o uso de substâncias, pouco ainda se sabe sobre as especificidades dessa relação, e se faz necessário sumarizar sistematicamente as evidências disponíveis, a fim de identificar padrões inexplorados e possíveis lacunas na literatura.

Ainda, os estudos acerca da associação entre consumo de álcool e qualidade do sono em adultos jovens não avaliam de modo amplo as diferenças socioculturais e econômicas presentes em diversas partes do mundo. Desta forma, considera-se necessária a realização de um estudo que avalie a qualidade do sono e o consumo de álcool em diferentes países, visando explorar as associações que se mantém significativas, independente do contexto sociocultural e econômico.

2. OBJETIVOS

2.1. OBJETIVO GERAL

- Investigar a associação entre o consumo de álcool e o sono em adultos.

2.2. OBJETIVOS ESPECÍFICOS

- Sintetizar as evidências referentes à associação entre o cronotipo vespertino e o consumo de álcool;
- Estudar a associação entre problemas relacionados ao álcool e sono em estudantes do primeiro ano de universidades do Brasil, Chile e Espanha.

3. MÉTODOS

A presente tese de doutorado foi elaborada em modelo escandinavo, originando dois artigos científicos como resultados. O primeiro artigo é uma revisão sistemática da literatura com metanálise. O segundo artigo é um estudo quantitativo, com dados primários de três bancos de dados de grupos de pesquisa do Brasil, Chile e Espanha. A seguir, estão expostos os métodos científicos adotados nos respectivos artigos.

3.1. ARTIGO 1

Para o artigo 1, a metodologia desenvolvida será apresentada em duas partes: passo a passo para a realização da revisão sistemática e, posteriormente, para a metanálise.

3.1.1. Desenho do estudo

A revisão sistemática buscou responder às seguintes perguntas: 1) "Existe associação entre cronotipo vespertino e consumo de álcool em adultos?"; e 2) "Adultos que apresentam cronotipo vespertino consomem mais álcool que aqueles que apresentam cronotipo não-vespertino?". Com base nessas perguntas, realizou-se uma busca por artigos que relacionavam cronotipo com o consumo de bebidas alcoólicas. A revisão foi elaborada de acordo com as recomendações do *Meta-analysis of Observational Studies in Epidemiology* (MOOSE) (STROUP *et al.*, 2000) e do *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) (MOHER *et al.*, 2009).

A pesquisa foi registrada no *International Prospective Register of Systematic Reviews* (CRD42022343778).

3.1.1.1. Estratégia de busca

Dois pesquisadores independentes conduziram a busca em cinco bases de dados: *PubMed*; *Scopus*; *Web of Science*; *Cochrane Library*; e *PsycINFO*. Buscou-se artigos originais, com dados primários, os quais disponibilizassem dados a respeito da relação entre cronotipo e consumo de álcool, publicados até o dia 30 de abril de 2023. Não foi estabelecido um limite de idioma ou de ano de publicação.

A estratégia de busca utilizada em cada base de dados está descrita no **Quadro 1**.

Quadro 1. Palavras-chave e operadores booleanos utilizados em cada base de dados.

Base de dados	Estratégia de busca
PubMed	(alcohol*[Title/Abstract] OR "binge drinking"[Title/Abstract] OR "heavy drinking"[Title/Abstract] OR Alcohols[MeSH Terms] OR Binge Drinking[MeSH Terms]) AND (chronotype[Title/Abstract] OR chronotype[MeSH Terms] OR morningness[Title/Abstract] OR eveningness[Title/Abstract] OR "Munich Chronotype Questionnaire"[Title/Abstract] OR "Horne Östberg Questionnaire"[Title/Abstract])
Scopus	(TITLE-ABS-KEY (alcohol* OR "binge drinking" OR "heavy drinking") AND TITLE-ABS-KEY (chronotype OR morningness OR eveningness OR "Munich Chronotype Questionnaire" OR "Horne Östberg Questionnaire"))
Web of Science	TS=(alcohol* OR "binge drinking" OR "heavy drinking") AND TS=(chronotope OR morningness OR eveningness OR "Munich chronotope Questionnaire" OR "Horne Östberg Questionnaire")
Cochrane Library	(alcohol* OR "binge drinking" OR "heavy drinking") AND (chronotype OR morningness OR eveningness OR "Munich Chronotype Questionnaire" OR "Horne Östberg Questionnaire")
PsycINFO	(alcohol* OR "binge drinking" OR "heavy drinking") AND ((chronotype OR morningness OR eveningness OR "Munich Chronotype Questionnaire" OR "Horne Östberg Questionnaire"))

Fonte: Próprio autor.

3.1.1.2. Seleção dos estudos

Os artigos identificados por meio da busca nas bases de dados foram todos inseridos em uma biblioteca no programa *Mendeley*, sendo possível, inicialmente excluir aqueles duplicados. Em seguida, dois pesquisadores independentes analisaram os títulos e resumos, avaliando a pertinência dos mesmos ao tema, e selecionando os trabalhos que seriam lidos na íntegra. Em casos de discordâncias, um terceiro pesquisador foi consultado.

Estabeleceu-se os seguintes critérios de inclusão: participantes com idade maior ou igual a 18 anos; estudos observacionais (ex.: transversal, caso-controle ou estudo de coorte);   variável de exposição: vespertinidade ou cronotipo predominantemente vespertino; comparação: cronotipo não-vespertino (matutino, intermediário ou nenhum cronotipo); desfecho: consumo de bebidas alcoólicas, independentemente da frequência, quantidade ou tipo de bebida.

Ainda, foram aplicados os seguintes critérios de exclusão: publicações não elegíveis (ex.: estudos de caso, editoriais, cartas ao editor, outras); revisões; estudos os quais as populações consistiam apenas de indivíduos diagnosticados com condições que poderiam afetar os resultados (ex.: diabetes, distúrbio bipolar, transtornos por uso de substâncias); dados indiretos a respeito do cronotipo (ex.: variantes genéticas, horário do meio do sono ou horário de acordar como proxy para cronotipo); falta de informações a respeito da associação entre cronotipo e consumo de álcool.

3.1.1.3. Extração dos dados

Realizou-se o fichamento das seguintes informações em planilha do Excel, extraídas dos artigos originais: sobrenomes dos autores e o ano de publicação; país; tamanho da amostra; média de idade, desvio padrão e faixa etária; população do estudo e proporção de mulheres; método de avaliação do cronotipo; método de avaliação do consumo de álcool; variáveis de ajuste; e principais resultados referentes à relação entre cronotipo e consumo de álcool.

3.1.1.4. Avaliação de qualidade

A qualidade dos estudos foi analisada com base na *Quality Assessment tool for Observational Cohorts and Cross-sectional Studies*, do *National Heart, Lung and Blood Institute* (NHLBI, 2014). Essa ferramenta é constituída de quatorze itens, os quais avaliam o risco de viés dos estudos. Dois pesquisadores independentes realizaram a aplicação da ferramenta e, ao final, todos os estudos da revisão foram classificados em: baixo risco de viés; algumas preocupações; e alto risco de viés. Em casos de discordâncias, um terceiro pesquisador foi consultado.

3.1.2. Análise estatística

3.1.2.1. Seleção dos estudos

Considerando a heterogeneidade na apresentação dos dados a respeito de cronotipo e consumo de álcool, optou-se por incluir na metanálise apenas os estudos os quais forneciam dados que permitiam a dicotomização dessas variáveis. Para cronotipo, estabeleceu-se as categorias cronotipo vespertino e cronotipo não-vespertino. Para consumo de álcool, os participantes dos estudos foram classificados em consumidores de álcool e não-consumidores de álcool.

3.1.2.2.   Extração dos dados

Foram extraídos dos artigos originais dados a respeito de cronotipo dos participantes (contínuo ou classificados em categorias), bem como a respeito do consumo de bebidas alcóolicas (abstêmio ou consumidor de álcool, frequência de consumo, volume de consumo e frequência de *binge-drinking*).

3.1.2.3.   Análise estatística e síntese dos dados

Ambas as variáveis de interesse foram dicotomizadas para a condução da metanálise. Para estudos que apresentavam três categorias de cronotipo, os cronotipos intermediários e matutinos foram agrupados na categoria cronotipo não-vespertino, sendo comparada à categoria de cronotipo vespertino. Outrossim, quanto à variável do consumo de álcool, os dados reportados de forma contínua ou apresentados em mais de duas categorias para frequência, volume ou qualquer medida de consumo, os quais indicassem o consumo de álcool foram agrupados em uma única categoria (consumidor de álcool), sendo então contraposta à categoria de não-consumidores de álcool.

Modelos de efeitos aleatórios foram utilizados para estimar a *odds ratio* conjunta (OR) (com intervalo de confiança [IC] de 95%) de consumo de álcool de acordo com o cronotipo. A heterogeneidade estatística foi avaliada por meio da fórmula estatística I^2. Esse índice descreve a porcentagem da variabilidade nas estimativas de efeito que se deve à heterogeneidade, e não ao erro amostral (DEEKS; HIGGINS; ALTMAN, 2022). Ele foi classificado como: não importante (0-40%); moderado (30-60%); substancial (50-90%); e considerável (75-100%). Conforme orientação da *Cochrane Collaboration*, no caso de índice I^2 estimado dentro da sobreposição dos intervalos, considerou-se o p-valor correspondente para avaliar a heterogeneidade. O viés de publicação foi analisado por meio do gráfico em funil e os testes de Egger e Begg. Análises de sensibilidade, excluindo os estudos, um a um, do cálculo, também foram conduzidas, para verificar a influência de cada estudo. As análises foram conduzidas no *Stata 15* (*StataCorp, College Station, TX, USA*).

3.2.   ARTIGO 2

3.2.1.   Desenho do Estudo e Participantes

O estudo foi realizado com base em três bancos de dados independentes, de pesquisas conduzidas em momentos diferentes. Analisou-se dados a respeito do consumo de álcool e sono de estudantes de graduação do primeiro ano de universidades do Brasil,

do Chile e da Espanha.

3.2.1.1. Brasil

Os dados dos estudantes brasileiros são provenientes do projeto "GraduaUEL: Análise da Saúde e Hábitos de Vida dos Estudantes de Graduação da Universidade Estadual de Londrina", de delineamento transversal, o qual teve como objetivo analisar a saúde física e mental dos estudantes de graduação da Universidade Estadual de Londrina (UEL), bem como seus hábitos de vida.

Foi realizada uma ampla atividade de divulgação, com visitas presenciais a todas as 259 salas de aula, concomitantemente ao processo de coleta. Foram considerados como critérios de inclusão ter idade maior ou igual a 18 anos e apresentar matrícula ativa em um curso presencial no primeiro semestre de 2019. Dos 12.536 estudantes elegíveis para participar do estudo, 3.238 responderam ao questionário *online*. Desses, 720 estudantes estavam no primeiro ano da graduação, e 571 responderam na íntegra às perguntas referentes às variáveis de interesse desse estudo, sendo incluídos na análise.

3.2.1.2. Chile

Em 2021, foi realizado o "*Diagnóstico de Inserción a la Vida Universitaria*" com os alunos do primeiro ano de graduação da *Universidad de La Frontera*. O questionário incluiu questões a respeito de saúde mental, consumo de substâncias e hábitos de vida. Todos os estudantes do primeiro ano foram convidados a participar e, dos 1.942 graduandos elegíveis, 1.243 responderam ao questionário *online*. Por fim, desses, 772 responderam na íntegra às perguntas referentes às variáveis de interesse desse estudo, sendo incluídos na análise.

3.2.1.3. Espanha

Os dados dos estudantes espanhóis são provenientes de um estudo transversal realizado no ano acadêmico de 2009-2010, o qual buscou avaliar mudanças no estilo de vida, dieta e saúde cardiovascular dos estudantes da *Universidad de Castilla-La Mancha*. Todos os 770 graduandos do primeiro ano foram convidados a participar, e, desses, 683 realizaram as entrevistas presenciais e exames físicos. Por fim, 487 estudantes proveram as informações necessárias para as variáveis de interesse desse estudo, sendo incluídos na análise.

3.2.1.4. Aspectos éticos

Os projetos dos três estudos foram aprovados, respectivamente, pelo Comitê de Ética em Pesquisa da Universidade Estadual de Londrina, Paraná, Brasil (**ANEXO A**); pelo *Comité Ético Científico de la Universidad de La Frontera*, Temuco, Chile (**ANEXO B**); e pelo *Comité Ético de Investigación Clínica del Hospital Virgen de la Luz*, Cuenca, Espanha (**ANEXO C**). Ainda, todos os participantes inclusos nas análises preencheram termos de consentimento livres e esclarecidos.

3.2.2. Variáveis do Estudo

3.2.2.1. Consumo de álcool

No estudo do Brasil, o consumo de álcool foi avaliado por meio do *Alcohol, Smoking and Substance Involvement Screening Test* (ASSIST) (WHO ASSIST WORKING GROUP, 2002), validado em português (HENRIQUE *et al.*, 2004). Originalmente, o ASSIST trata, além do consumo de álcool, do consumo de tabaco e drogas ilícitas. Para a presente análise, considerou-se apenas as respostas a respeito do consumo de álcool. Ainda, não foram inclusas as questões de número 1 (frequência de consumo ao longo da vida) e 8 (exclusivamente a respeito do uso de drogas por injeção). Ressalta-se que essas duas questões não fazem parte do cálculo do escore proposto pela Organização Mundial da Saúde (OMS) (HUMENIUK *et al.*, 2010).

As demais questões do instrumento abordam a frequência de consumo, problemas relacionados ao consumo, preocupação a respeito do consumo por parte de pessoas próximas ao usuário, prejuízo na execução de atividades cotidianas e tentativas de cessar ou reduzir o consumo. Com base nessas questões, é realizada a soma da pontuação de cada participante, a qual pode variar de 0 a 39 pontos, com ponto de corte de 27 ou mais pontos para alto risco (HUMENIUK *et al.*, 2010).

Na estudo da Espanha, a ferramenta utilizada foi o *Alcohol Use Disorder Identification Test* (AUDIT) (SAUNDERS *et al.*, 1993), validado em espanhol (CARRETERO *et al.*, 2016). O teste é composto de dez questões, divididas em três domínios (padrão do consumo de álcool, sintomas de dependência e consumo nocivo de álcool) e tem como objetivo diferenciar consumidores de álcool de baixo risco e indivíduos que consomem de maneira nociva. O instrumento também pode ser utilizado para a identificação precoce de alcoolismo. A pontuação do AUDIT varia de 0 a 40 pontos (WHO, 2001), com um ponto de corte de 13 ou mais pontos para problemas físicos e psicológicos e provável dependência de álcool (CARRETERO *et al.*, 2016)

No estudo do Chile, a informação a respeito da frequência da prática de *binge-drinking* foi obtida por meio da questão: "Nos últimos 30 dias, com que frequência você consumiu cinco ou mais doses de bebidas contendo qualquer tipo de álcool, dentro de um prazo de 2 horas?". As respostas poderiam variar entre: nunca; uma a três vezes no último mês; quatro ou mais vezes no último mês (GOBIERNO DE CHILE, 2013).

As três variáveis consideram o volume de álcool consumido e o padrão de consumo dos respondentes, ou seja, avaliam dimensões individuais da prática de consumo de álcool que aumentam o risco de consequências negativas, tanto para o indivíduo quanto para outras pessoas em seu entorno (REHM, 2011; REHM *et al.*, 2010; WHITE; HINGSON, 2013). Ainda, padrões nocivos ou excessivos de consumo de álcool podem ser medidos de formas diversas. Com isso em mente, a fim de facilitar a interpretação dos resultados da presente análise, criou-se uma variável em comum entre os três países, com base nos dados das três variáveis originais, denominada "*risk of alcohol-related problems*" (RARP).

A classificação utilizada para a nova variável RARP se baseou nos pontos de corte originalmente utilizados para o ASSIST e para o AUDIT. Para a questão empregada no estudo do Chile, seguiu-se os critérios dispostos no **Quadro 2**.

Quadro 2. Critérios para classificação dos estudantes na variável *risk of alcohol-related problems* (RARP).

País	Instrumento	RARP		
		Baixo	**Moderado**	**Alto**
Brasil	Pontuação do ASSIST	0-10	11-26	≥ 27
Chile	Frequência de prática de *binge-drinking*	Não praticou *binge-drinking* no último mês	Uma a três vezes no último mês	Quatro vezes ou mais no último mês
Espanha	Pontuação do AUDIT	**Homens**		
		0-7	8-12	≥ 13
		Mulheres		
		0-5	6-12	≥ 13

RARP: risk of alcohol-related problems; **ASSIST**: Alcohol, Smoking and Substance Involvement Screening Test; **AUDIT**: Alcohol Use Disorder Identification Test.
Fonte: Carretero *et al.* (2016); Gobierno de Chile (2013); Humeniuk *et al.* (2010).

3.2.2.2.   Qualidade do sono

A variável de qualidade do sono foi avaliada, nos três países, por meio da mesma questão, a qual faz parte do *Pittsburgh Sleep Quality Index* (PSQI) (BUYSSE *et al.*, 1989): "Durante o último mês, como você classificaria a qualidade do seu sono, de uma maneira geral?". Com a finalidade de dicotomizar a variável, as respostas "muito boa" e "boa" foram definidas como "ótima qualidade do sono", e as respostas "ruim" e "muito ruim" como "qualidade do sono subótima".

3.2.2.3.   Duração do sono

Os estudos do Brasil e da Espanha avaliaram a duração do sono por meio da mesma questão, também inclusa no PSQI (BUYSSE *et al.*, 1989): "Durante o último mês, quantas horas de sono você teve por noite?". O estudo do Chile utilizou a seguinte pergunta para avaliação da duração do sono: "Aproximadamente qual é a duração do seu sono durante a noite?". Para os estudantes dos três países, foi considerada como curta duração do sono o valor inferior a sete horas por dia. Ainda, foi considerada como longa duração do sono o valor superior a oito horas por dia.

Optou-se por avaliar os dois extremos separadamente, visto que a literatura aponta que a associação da duração do sono com desfechos negativos de saúde (como mortalidade e eventos cardiovasculares) está concentrada nas categorias mais extremas (curta e longa duração), seguindo uma distribuição em forma de U (YIN *et al.*, 2017).

3.2.2.4.   Variáveis de ajuste

As seguintes variáveis foram utilizadas nas análises de ajustes: idade; sexo; nível de escolaridade dos pais; índice de massa corporal (IMC); consumo de tabaco; prática de atividade física no tempo livre; nível de escolaridade dos pais (disponível apenas para a população de estudo do Brasil e parcialmente para a população de estudo do Chile) e qualidade de saúde subjetiva .

3.2.3. Análise Estatística

As seguintes análises foram conduzidas de forma independente, no banco de dados de cada país.

3.2.3.1.   Análise descritiva

Realizou-se a análise descritiva da seguinte forma, para os três países: média e desvio padrão de variáveis contínuas (idade, IMC, duração do sono); frequências

absolutas e relativas de variáveis categóricas (sexo, frequência de consumo de álcool e qualidade do sono).

3.2.3.2.   Análise de associação

Modelos de regressão logística foram elaborados para analisar a associação entre RARP ou frequência de consumo de álcool (variáveis independentes) e qualidade ou duração do sono (variáveis dependentes). Estimou-se a *odds ratio* (OR) com intervalo de confiança de 95% (IC95%) para cada associação. Os modelos foram ajustados por idade (em anos, contínua), sexo (feminino, masculino), IMC (kg/m^2, contínua), consumo de tabaco (sim, não), prática de atividade física no tempo livre (nível baixo, nível alto), nível de escolaridade dos pais (abaixo do nível superior; nível superior) e qualidade de saúde subjetiva (ótima, subótima). Análises adicionais foram conduzidas nos bancos de dados do Brasil e do Chile para incluir ajustes por nível de escolaridade dos pais.

3.2.3.3.   Análise conjunta

Com base nos resultados dos modelos ajustados de cada país, os valores de cada OR e seus respectivos IC95% foram transformados em escala logarítmica, para possibilitar o cálculo da OR conjunta (p-OR) e IC95%. Utilizou-se o índice I^2 para análise de heterogeneidade. Por fim, foram elaborados *forest plots* para facilitar a visualização dos resultados (DEEKS; HIGGINS; ALTMAN, 2022). As análises foram conduzidas no *Stata 15* (*StataCorp, College Station, TX, USA*).

4. RESULTADOS

4.1. ARTIGO 1 - IS EVENING CHRONOTYPE ASSOCIATED WITH HIGHER ALCOHOL CONSUMPTION? A SYSTEMATIC REVIEW AND META-ANALYSIS[1]

4.1.1. Abstract

Background: A broader understanding of whether and to what extent chronotype should be considered a risk factor for alcohol consumption is needed. **Objective**: The aim of this systematic review was to summarize the evidence on the association between evening chronotype and alcohol consumption. **Methods**: A systematic search of observational studies on this association was conducted in the PubMed, Scopus, Web of Science, Cochrane Library and PsycINFO databases up to April 30th, 2023. Random-effect models estimated the pooled odds ratio (OR) of alcohol consumption according to chronotype. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and Quality Assessment tool for Observational Cohorts and Cross-sectional Studies from the National Heart, Lung and Blood Institute were followed. **Results**: A total of 33 studies involving 28 207 individuals (age range: 18–93 years) were included in this review. Overall, most studies indicated a higher volume and frequency of alcohol consumption in evening-type individuals than in individuals with different chronotypes. Additionally, a meta-analysis including 13 studies showed that evening-type individuals were 41% more likely to consume alcohol than those with other chronotypes (OR = 1.41, 95% confidence interval: 1.16–1.66; I2 = 38.0%). Limitations of the present findings are the predominance of cross-sectional studies and varied definitions of alcohol consumption. **Conclusion**: The available evidence supports an association between the evening chronotype and alcohol consumption. The evening-type population, especially young adults, is a specific target for educational interventions for preventing or reducing alcohol consumption.

PROSPERO number: CRD42022343778.

Keywords: Alcohol Drinking; Chronotype; Morningness-eveningness; Sleep timing; Systematic Review.

4.1.2. Introduction

Human adaptation to the environment depends largely on the physiological regulation of the rhythmicity of biological parameters such as body temperature, blood pressure, temperature, and sleep (Aschoff et al. 1967). In addition, chronotype, known as individual variability regarding circadian preference for mornings or evenings, also plays a role in certain aspects of this adaptation (Kerkhof 1985; Roenneberg et al. 2003). While morning-type individuals feel more alert in the morning and go to sleep earlier, evening-type individuals feel at their best in the late afternoon or evening and go to bed relatively late (Kerkhof 1985). This disposition is a continuum between two extremes, and the majority of the population presents an intermediate typology (Natale and Cicogna 2002). Chronotype is partially genetically determined (Koskenvuo et al. 2007), although it can also be influenced by sex, age (Fischer et al. 2017), and lifestyle aspects, such as diet (Oosterman et al. 2014), social relationships (Aledavood et al. 2018), and work or study schedule (Kervezee et al. 2018).

The evening chronotype has been associated with poorer cardiovascular health (Makarem et al. 2020), depressive symptoms (Au and Reece 2017), metabolic disorders (Yu et al. 2015), and a higher frequency of asthma (Merikanto et al. 2014) and neurological and gastrointestinal disorders (Knutson and von Schantz 2018). This could be explained because evening-type individuals are more likely to adopt unhealthy behaviors, such as being less physically active (Nauha et al. 2020), more sedentary and using tobacco (Patterson et al. 2016) or psychostimulant drugs (Adan 1994), than those with different chronotypes. In this context, more frequent consumption of alcoholic beverages has been found in the evening chronotype than in the morning chronotype (Van den Berg et al. 2018; Zhang et al. 2018). However, the evidence on this matter is still inconclusive (Yang and Tucker 2022).

The rationale for the association between chronotype and alcohol consumption is based on the fact that evening-type individuals have a greater propensity for impulsivity (Evans and Norbury 2021), risk-taking (Wang and Chartrand 2015) and novelty seeking (Caci et al. 2004), and these personality traits might play an important role in the relationship between chronotype and substance use (Evans and Norbury 2021; Foulds et al. 2017). Furthermore, alcohol craving reaches its peak at night (Hisler et al. 2021), and going to bed later extends the temporal window for alcohol consumption (Wittmann et al. 2010). Although this could explain a higher alcohol consumption in individuals with an evening chronotype (Van den Berg et al. 2018; Zhang et al. 2018), this association could

be confounded by well-known predictors of alcohol consumption such as age (Global Burden of Disease (GBD), 2022), sex (Peltier et al. 2019), and socioeconomic status, among others (Beard et al. 2019).

Considering the importance of alcohol intake in the pathophysiology of several chronic diseases (i.e., mental (Churchill and Farrell 2017), cardiovascular (Minzer et al. 2020), and metabolic disorders (Suliga et al. 2019)) and its potential public health impact (Rehm and Shield 2019), a broader understanding of whether and to what extent chronotype should be considered a risk factor for alcohol consumption is needed. Therefore, the aim of this study was to systematically summarize the evidence on the association between chronotype and alcohol consumption.

4.1.3. Methods

This systematic review was developed in accordance with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) (Stroup et al. 2000) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al. 2021). No ethics approval was required given the nature of the study. The review protocol was registered at the International Prospective Register of Systematic Reviews (CRD42022343778).

4.1.3.1. Search strategy

Two independent reviewers (RS and AEM) carried out the searches in the PubMed, Scopus, Web of Science, Cochrane Library and PsycINFO databases, with no language limit. The search was focused on peer-reviewed observational studies reporting data on the participants' chronotype and alcohol consumption published from inception up to April 30th, 2023.

The search strategy was composed using "and" or "or" Boolean operators and included the following terms: "alcohol", "binge drinking", "heavy drinking", "chronotype", "morningness", "eveningness", "Munich Chronotype Questionnaire", and "Horne Östberg Questionnaire". The full search strategy is presented in the Supplementary material (**APÊNDICE A**).

4.1.3.2. Study selection

All articles identified in the search were organized in a Mendeley library for the removal of duplicates. After removing duplicates, the titles and abstracts were screened for eligibility. Subsequently, the same process was applied to the studies selected for full-

text screening. The entire selection of the studies and extraction process were conducted by two independent reviewers (RS and GDGM). Disagreements were resolved by consensus or through the consultation of a third reviewer when necessary (RR).

The inclusion criteria were as follows: (i) participants: adults (age ≥18 years); (ii) design: observational studies (i.e., cross-sectional, case-control, and cohort studies); (iii) exposure variable: eveningness or predominantly evening chronotype; (iv) comparison: noneveningness (morningness, intermediate, or neither chronotype); and (v) outcome: consumption of alcoholic beverages, regardless of the frequency, quantity and type.

Moreover, the criteria for exclusion of studies were as follows: (i) ineligible publication types, such as case series, preprints, editorials and letters to the editor; (ii) reviews; (iii) studies with participants diagnosed with conditions that might affect the results (i.e., substance use disorder, bipolar disorder, diabetes diagnosis); (iv) indirect chronotype data (i.e., genetic variants used to represent morning daytime preference, mid-sleep time or wake-up time as a proxy of chronotype); and (v) lack of data on the association between chronotype and alcohol consumption.

4.1.3.3. Data extraction

To extract and organize the data, a Microsoft Excel spreadsheet was used. The following data were extracted from the original articles: (i) the authors' surnames and year of publication; (ii) country; (iii) sample size; (iv) mean age, standard deviation, and age range of participants; (v) study population and proportion of women; (vi) chronotype assessment method; (vii) alcohol consumption assessment method; (viii) adjustment variables; and (ix) main results related to the relationship between chronotype and alcohol consumption. In addition, we extracted information on chronotype (continuous or recoded into categories) and consumption of alcoholic beverages (abstemious or alcohol consumer, binge-drinking, frequency of consumption, and volume or quantity of consumption of any alcoholic beverage or specific beverages, such as beer, wine or spirits).

4.1.3.4. Risk of bias assessment

The risk of bias and quality of the included studies were evaluated based on the Quality Assessment tool for Observational Cohorts and Cross-sectional Studies from the National Heart, Lung and Blood Institute (NHLBI, 2014).

4.1.3.5.   Statistical analyses and data synthesis

Given that the presentation format of the chronotype and alcohol consumption variables varied, the decision was made to conduct meta-analysis only if the data provided by the authors allowed for the dichotomization of both variables into evening chronotype or non-evening chronotype, and alcohol consumer or non-alcohol consumer. Hence, in studies that included three categories for chronotype (Arosemena et al., 2022; Garbazza et al., 2022; Hasler et al., 2017; Lee et al., 2022; Mule et al., 2022a; Pereira-Morales et al., 2019; Jessica Rosenberg et al., 2014; Sansom et al., 2022), the neither-types and morning-types were combined and classified as non-evening types. Similarly, when alcohol consumption was reported as a continuous variable or presented in more than two categories for frequency, quantity, or type, any levels of consumption (in the case of continuous alcohol variable) (Ishihara et al., 1985) or all categories indicating alcohol consumption (if different levels of consumption were presented as categories) (Lee et al., 2022; Sansom et al., 2022; Siudej and Malinowska-Borowska, 2021) were merged into a single category representing alcohol consumption, which was then compared to non-consumption (abstemious individuals).

Based on the studies finally included in the meta-analysis, random-effect models were used to estimate the pooled odds ratio (p-OR) (with 95% confidence intervals [CIs]) of alcohol consumption according to chronotype. Study heterogeneity was assessed using the I^2 statistic and classified as not important (0%–40%), moderate (30–60%), substantial (50–90%), and considerable (75–100%) (Higgins and Thompson, 2002). As recommended by the Cochrane Collaboration, when the I^2 was estimated in the overlapping intervals, the corresponding p-value was considered to finally evaluate the heterogeneity (Deeks et al., 2022). Publication bias was assessed through the funnel plot and Egger's and Begg's tests. Sensitivity analyses were also conducted to examine the influence of each study by excluding one by one from the calculation of the overall estimator.

STATA SE 15 software (StataCorp, College Station, TX, USA) was used for the statistical procedures.

4.1.4. Results

4.1.4.1.   Study selection

Among a total of 634 studies identified through database searching, 350 studies remained after removing duplicates. Of these, 118 studies were selected for a detailed

full-text evaluation. After excluding 85 studies due to the reasons detailed in **Figura 1** (and **APÊNDICE B**, Supplementary material), 33 studies were finally included in this systematic review.

Figura 1. Flow diagram of the study selection process.
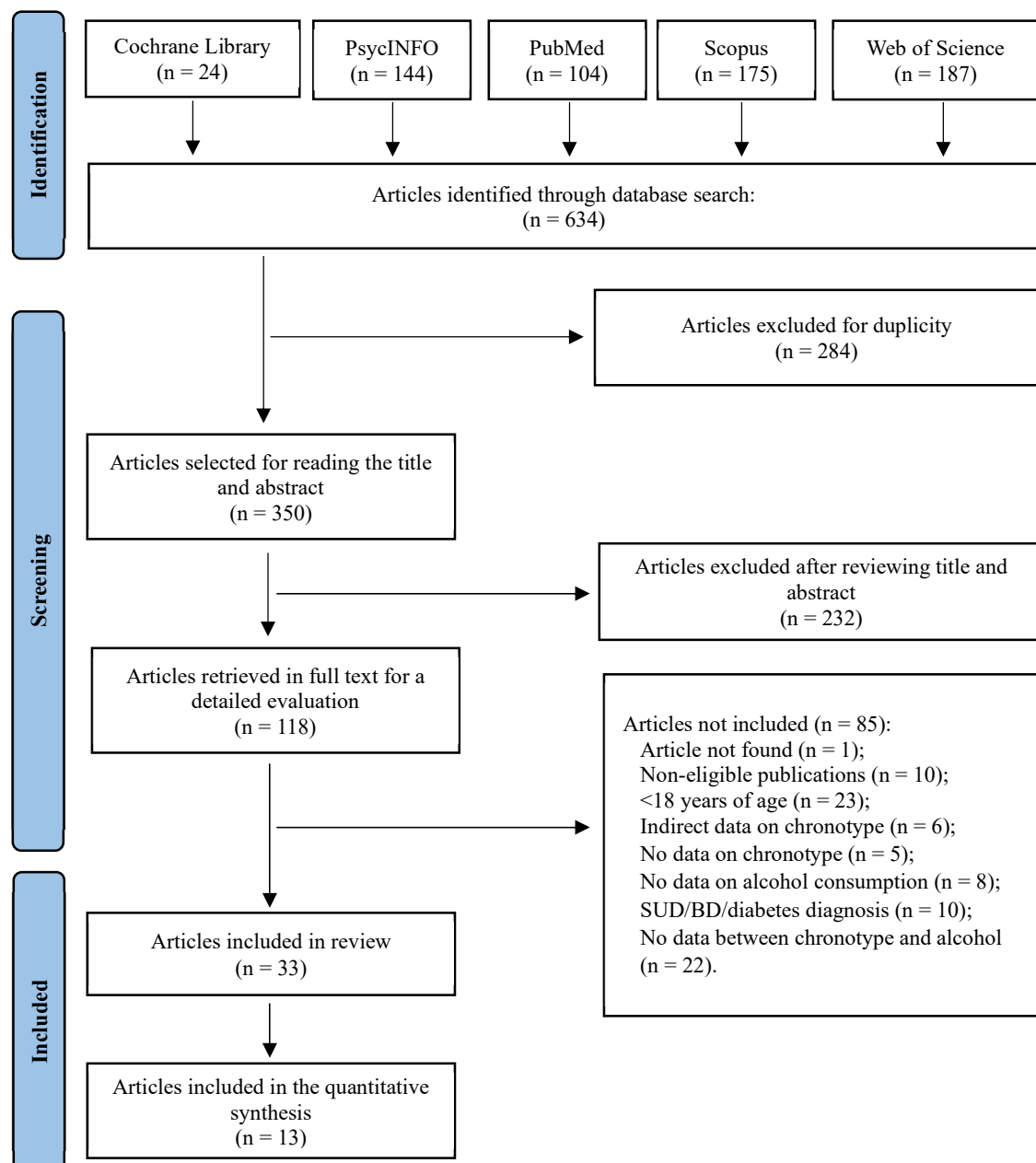
SUD: substance use disorder; BD: bipolar disorder.

4.1.4.2.   Study characteristics

The included studies were carried out in 19 different countries, and all studies used cross-sectional data, except for Hasler et al (Hasler et al. 2017). The main characteristics of the included studies are summarized in **Quadro 3** and **Quadro 4**. The mean age ranged from 19.0 to 56.6 (age range: 18–93) years, and the sample sizes ranged from 59 to 4493,

totaling 28.207 participants. Eleven studies (33.3%) exclusively examined university students (6.918 participants − 24,5%) (Esposito et al. 2002; Evans and Norbury 2021; Goodhines et al. 2019; Ishihara et al. 1985; Mule et al. 2022b; Nakade et al. 2009; Rusnac et al. 2016; Taylor et al. 2020; Van den Berg et al. 2018; Whittier et al. 2014; Zhang et al. 2018), and five studies (15.2%) included only women (Arosemena et al. 2022; Garbazza et al. 2022; Haraszti et al. 2014; Hug et al. 2019; Nakade et al. 2009). All studies assessed chronotype with self-report questionnaires. The Morningness-Eveningness Questionnaire (MEQ) (Horne and Ostberg 1976) or its reduced version (Adan and Almirall 1991) were used by almost two-thirds of the studies (n = 20; 60.6%) (Adan 1994; Barclay et al. 2013; Bruno et al. 2022; Esposito et al. 2002; Evans and Norbury 2021; Garbazza et al. 2022; Goodhines et al. 2019; Ishihara et al. 1985; Kanerva et al. 2012; Kerckhove et al. 2022; Millar et al. 2019; Mule et al. 2022b; Rusnac et al. 2016; Sansom et al. 2022; Siudej and Malinowska-Borowska 2021; Sun et al. 2020; Van den Berg et al. 2018; Vera et al. 2018; Watson et al. 2013; Whittier et al. 2014). Regarding alcohol consumption, nine studies (27.3%) reported data on the frequency (Arosemena et al. 2022; Arrona-Palacios et al. 2020; Esposito et al. 2002; Goodhines et al. 2019; Ishihara et al. 1985; Nakade et al. 2009; Rusnac et al. 2016; Siudej and Malinowska-Borowska 2021; Watson et al. 2013), eleven studies (33.3%) reported the volume of alcohol consumption (Adan 1994; Barclay et al. 2013; Evans and Norbury 2021; Goodhines et al. 2019; Hug et al. 2019; Nakade et al. 2009; Rusnac et al. 2016; Siudej and Malinowska-Borowska 2021; Van den Berg et al. 2018; Watson et al. 2013; Whittier et al. 2014), and two studies (6.1%) reported the frequency of binge drinking (Goodhines et al. 2019; Watson et al. 2013) (**Quadro 3**).

4.1.4.3.   Risk of bias assessment

The overall risk of bias was classified as some concerns in most of the studies (**Quadro 4)** The limitations of most studies were related to the cross-sectional design, the possible memory bias resulting from the self-reported data, and the lack of information about the sampling process. A detailed description of the risk of bias assessment can be found in **APÊNDICE C** (Supplementary material). However, the PRISMA checklist of items to include when reporting a systematic review or meta-analysis can be found in **APÊNDICE D** (Supplementary material).

Quadro 3. Descriptive characteristics of the included studies.

Authors, Year	Country	Sample (n)	Age $\bar{X} \pm SD$ (min–max)	Study population	♀%	Chronotype assessment	Alcohol consumption assessment
Adan, 1994	Spain	537	25.3 ± 2.9 (21-30 years)	Students and workers (doctors and nurses)	52.1%	rMEQ	Average daily consumption (cc)
Arosemena et al., 2022	United States	81	56.5 ± 7.0 (18-65 years)	Women with clinical hypothyroidism on levothyroxine treatment	100.0%	MCTQ	Alcohol use (yes if >1 drink weekly; no)
Arrona-Palacios et al., 2020	Mexico	510	27.8 ± 10.2 (18-77 years)	Adults	44.7%	MESSi	Frequency of weekly consumption
Barclay et al., 2013	United Kingdom	378	19.8 ± 1.3 (18-22 years)	Monozygotic twin pairs	66.1%	MEQ	Alcohol consumption and quantity typically consumed when drinking
Bruno et al., 2022	Italy	1297	39.2 (± 15.0) (NR-NR)	Adults	61.9%	rMEQ	Current level of consumption in relation to pre-lockdown level of consumption
Esposito, Martoni and Natale, 2002	Italy	205	23.6 ± 3.6 (18-30 years)	University students	69.8%	rMEQ	Frequency and moment of the day in which the subject usually consumed alcoholic beverages
Evans and Norbury 2021	United Kingdom	191	19.6 ± 1.4 (18-25 years)	University students	88.5%	rMEQ	Average units of alcohol per week

Garbazza et al., 2022	Italy and Switzerland	299	34.1 ± 4.3 (NR-NR)	Women in first trimester of pregnancy	100,0%	MEQ	Alcohol intake (yes; no)
Goodhines et al., 2019	United States	171	19 ± 1.1 (18-23 years)	University students	70.0%	MEQ	Frequency and quantity of alcohol consumption, as well as binge-drinking frequency
Haraszti et al., 2014	Hungary	202	37.5 ± 10.7 (21-65 years)	University workers	100.0%	CSM	Alcohol consumption (yes; no)
Hasler et al., 2017	United States	89	20.0 ± 0.6 (20 years at baseline)	Low income yong adults	0.0%	CSM	LDH
Hug et al., 2019	Switzerland	146	21.7 ± 1.7 (18-25 years)	Adults	100.0%	MCTQ	Average units of alcohol per day
Ishihara et al., 1985	Japan	449	19.5[a] ± NR (NR-NR)	University students	27.3%[a]	MEQ	Frequency of alcohol consumption
Kanerva et al., 2012	Finland	4493	51.9 ± 0.2 (25-74 years)	Adults	55.4%[b]	MEQ	FFQ
Lee et al., 2022	Korea	493	26.2 ± 3.2 (NR-NR)	Nurses	94.7%	CSM	Level of alcohol consumption
Millar et al., 2019	United States	2814	37.7 ± 13.3 (NR-NR)	Gay and bisexual men	0.0%	rMEQ	AUDIT-C
Mulè et al., 2022	Italy	533	21.5 ± 0.2 (NR-NR)	University students	62.9%	rMEQ	Alcohol use

							(yes; no)
Nakade et al., 2009	Japan	800	NR ± NR (18-29 years)	University students	100.0%	DTS	Frequency and quantity of alcohol consumption
Pereira-Morales et al., 2019	Colombia	942	21.8 ± 5.0 (18-49 years)	University students and workers	63.7%	CSM	Alcohol consumption (yes; no)
Rosenberg et al., 2014	Germany	59	NR ± NR (18-35 years)	Adults	0.0%	MCTQ	Alcohol use (yes; no)
Rusnac, Spitzenstetter and Tassi, 2016	France	188	22.4 ± 1.5 (19-25 years)	University students	50.5%	MEQ	Frequency and quantity of alcohol consumption
Sansom et al., 2022	Australia	811	56.6 ± 5,5 (42-76 years)	Mothers and fathers of a birth cohort	59.2%	MEQ	DQES
Siudej and Malinowska-Borowska, 2021	Poland	128	NR ± NR (18-70 years)	Adults	76.6%	MEQ	Frequency and quantity of alcohol consumption
Sun et al., 2020	United States	1180	48.2 ± 5.3 (NR-NR)	Middle-aged black and white adults	58.1%	rMEQ	Alcohol consumption (yes; no)
Taylor et al., 2020	United States	81	19.6 ± 1,2 (18-25 years)	University students	67.9%	CSM	AUDIT
Van den Berg, Kivelä and Antypa, 2018	Netherlands	742	21.4 ± 2.9 (18-56 years)	University students	74.5%	MEQ	Average quantity of drinks per week

Vedaa et al., 2013	Norway	1144	35.5 ± 8.3 (NR-NR)	Nurses	91.0%	DTS	AUDIT-C
Vera et al., 2018	Spain	2126	40.0 ± 13.0 (NR-NR)	Overweight and obese adults	81.0%	MEQ	Alcohol consumption (yes; no)
Watson, Buchwald and Harden, 2013	United States	2945	36.4 ± 15.7 (19-93 years)	Twins	64.2%	rMEQ	Frequency and quantity of alcohol consumption, as well as binge-drinking frequency
Whittier et al., 2014	Peru	2581	21.1 ± 2.7 (NR-NR)	University students	61.2%	MEQ	Quantity of alcohol consumption
Yang and Tucker, 2022	United States	100	NR ± NR (19-55 years)	Adults	63.0%	MEQ	AUDIT-C
Yun et al., 2015	Korea	515	M: 42.0 ± 8.5 N: 37.6 ± 7.6 E: 35.2 ± 5.9	Firefighters	7.1%[b]	CSM	AUDIT
Zhang et al., 2018	China	977	20.1 ± 1.3 (NR-NR)	University students	57.7%	MCTQ	Level of alcohol consumption

AUDIT: Alcohol Use Disorders Identification Test; AUDIT-C: The alcohol use disorders identification test — consumption; CSM: Composite Scale of Morningness; DQES: Dietary Questionnaire for Epidemiological Studies; DTS: Diurnal Type Scale (DTS) by Torsvall and Åkerstedt; FFQ: Food Frequency Questionnaire; LDH: Lifetime Drinking History; MCTQ: Munich Chronotype Questionnaire; MEQ: Morningness-Eveningness Questionnaire; MESSi: The Morningness-Eveningness-Stability-Scale improved; NR: Not reported; rMEQ: Reduced Morningness-Eveningness Questionnaire.

[a]Data referring to a broader sample (evening-types, neither-types and morning-types). Only evening-types and morning-types were included in the analyses.

[b]Mean proportion of women.

Quadro 4. Included studies on the relationship between chronotype and alcohol consumption.

Authors, Year	Adjustment variables	Main Results	Risk of bias
Adan, 1994	NA	Consumption of alcohol was greater in Evening-types, while Morning-types consumed the least. Neither-types' consumption was similar to Morning-types.	High risk of bias
Arosemena et al., 2022	Body mass index	Neither-/Evening-types reported a higher frequency of alcohol use	High risk of bias
Arrona-Palacios et al., 2020	NA	Evening-types consumed more alcohol.	High risk of bias
Barclay et al., 2013	Age, sex and sleep quality	There were significant associations between a preference for eveningness and alcohol consumption, and number of alcoholic drinks typically consumed when drinking. The results for number of alcoholic drinks lost significance when controlled for the influence of both genetic and shared environmental effects.	Low risk of bias
Bruno et al., 2022	NA	Chronotype was significantly associated with a change in alcohol consumption.	Some concerns
Esposito, Martoni and Natale, 2002	NA	Evening-types reported higher frequency of alcohol consumption, while Morning-types more frequently reported never consuming alcohol.	High risk of bias
Evans and Norbury 2021	Age and gender	Eveningness was associated with higher consumption of alcohol, and this association was found to be completely mediated by self-reported impulsivity.	Some concerns
Garbazza et al., 2022	NA	No association was found between chronotype and alcohol intake	Some concerns
Goodhines et al., 2019	NA	Morning preference was associated with lower frequency and quantity of alcohol consumption, as well as lower frequency of binge drinking.	Some concerns
Haraszti et al., 2014	Age, education, sleep quality and having children	No associations were found between morningness–eveningness score or chronotypes and alcohol consumption.	Some concerns
Hasler et al., 2017	NA	Correlations between greater eveningness and more frequent use of alcohol. Eveningness was associated with alcohol use, after 2 years of follow-up, mediated by win response in the medial prefrontal cortex.	Low risk of bias
Hug et al., 2019	Smoking	Evening chronotype was associated with higher alcohol consumption in a sample of healthy, young women, and there was an influence of smoking on this relationship.	High risk of bias

Ishihara et al., 1985	NA	The evening type consumed alcohol more frequently than the morning type.	High risk of bias
Kanerva et al., 2012	Age, sex, education, leisure physical activity, smoking and energy intake	Morning-Eveningness (ME) score was negatively associated with alcohol intake. When stratified by sex, the inverse association of the ME score and beer consumption was only significant in men.	Low risk of bias
Lee et al., 2022	NA	No association was found between chronotype and level of alcohol consumption	Some concerns
Millar et al., 2019	Age, race and ethnicity, recruitment source, relationship status and education	Alcohol consumption most often occurred from 9pm onward, especially among younger men and evening types. Additionally, feeling tired was a motivator of alcohol consumption, especially among younger men.	Some concerns
Mulè et al., 2022	NA	Evening-types were more frequent amongst beer, wine and alcohol drinkers than morning and neither-types	Some concerns
Nakade et al., 2009	NA	Students who habitually consumed alcohol showed significantly lower ME scores (more evening-typed).	Low risk of bias
Pereira-Morales et al., 2019	Perceived family chronotype, sex, age, caffeine consumption, smoking, diurnal subjective somnolence, working, hours of nocturnal sleep	Neither- and evening-types reported a higher alcohol consumption than morning-types. Alcohol consumption correlated significantly with individual chronotype.	Some concerns
Rosenberg et al., 2014	NA	Evening-types reported drinking significantly more alcoholic beverages than morning-type	Some concerns
Rusnac, Spitzenstetter and Tassi, 2016	NA	Analyses reveal significant negative correlations between the morningness-eveningness score and self-reported alcohol consumption in terms of both frequency and quantity.	High risk of bias
Sansom et al., 2022	NA	No associations were found between chronotypes and alcohol consumption.	Some concerns
Siudej and Malinowska-Borowska, 2021	NA	Evening-types more often used alcohol, and were also characterized by a higher unit alcohol consumption.	High risk of bias
Sun et al., 2020	NA	Current alcohol consumption was slightly higher in morning-types than neither- and evening-types, but no statistically significant differences were found.	High risk of bias
Taylor et al., 2020	NA	Evening-types present a higher score on the Alcohol Use Disorder Identification test (AUDIT) than non-evening types	Some concerns

Van den Berg, Kivelä and Antypa, 2018	Age and gender	Eveningness was associated with more alcohol consumption.	Low risk of bias
Vedaa et al., 2013	Gender, percentage of full-time equivalent, night shifts, caffeine consumption, anxiety and depression	Higher alcohol consumption predicted a lower score on the morningness scale.	Low risk of bias
Vera et al., 2018	Sex, age, Body Mass Index (BMI), study number and clinic center	It was demonstrated that evening chronotypes had higher odds of drinking alcohol, compared to morning chronotypes.	Some concerns
Watson, Buchwald and Harden, 2013	NA	Morning and evening types did not significantly differ in alcohol consumption frequency, but evening types consumed larger quantities and were more likely to report binge drinking.	High risk of bias
Whittier et al., 2014	NA	Alcohol consumption was significantly associated with an evening chronotype.	High risk of bias
Yang and Tucker, 2022	Race, age, body mass index, and sleep quality.	The study did not find differences in alcohol intake (amount) and alcohol misuse (AUDIT-C) among chronotypes.	Some concerns
Yun et al., 2015	Age	Even though evening-types reported more alcohol consumption than neither- and morning-types, no significant group differences were found.	Some concerns
Zhang et al., 2018	Age, sex, race, grade, the type of university, mother's and father's educations, outdoor activities, average sleep duration and social jetlag	Late chronotype was positively associated with more alcohol consumption.	Low risk of bias

NA: Not applicable.

4.1.4.4.   Data synthesis

4.1.4.4.1. *Systematic review*

Out of the 33 studies included in the systematic review, most (n=27) identified that evening-type individuals either report a higher frequency of alcohol consumption or consume greater amounts of alcohol, or both. One study found that evening types are more likely to report binge drinking (Watson et al., 2013). The only study with a

longitudinal analysis found an association between evening-type and alcohol use after 2 years of follow-up (Hasler et al., 2017). The results were consistent across different countries, age groups, and research methods.

Six studies did not find significant differences between different types of chronotypes in relation to alcohol consumption (Garbazza et al., 2022; Haraszti et al., 2014; Lee et al., 2022; Sansom et al., 2022; Yang and Tucker, 2022; Yun et al., 2015). These studies varied in study population, sample size, and the instruments used to assess the variables of interest. Furthermore, two studies adjusted the analyses for sleep quality (Haraszti et al., 2014; Yang and Tucker, 2022).

4.1.4.4.2. Meta-analysis

Meta-analytic procedures were possible for the association between chronotype and the dichotomous outcome of consuming or not consuming alcoholic beverages, for which data were provided in analysis categories only for thirteen studies (Arosemena et al., 2022; Esposito et al., 2002; Garbazza et al., 2022; Ishihara et al., 1985; Lee et al., 2022; Mule et al., 2022; Pereira-Morales et al., 2019; Rosenberg et al., 2014; Sansom et al., 2022; Siudej and Malinowska-Borowska, 2021; Vera et al., 2018; Zhang et al., 2018). While all manuscripts included in the meta-analysis assessed the chronotype using validated instruments, the consumption of alcohol was carried out through self-report of the participants, and the period of the questions varied from the recall of the last 24 hours (Vera et al., 2018), 3 weeks (Zhang et al., 2018) or 3 months (Lee et al., 2022), with most studies performing the questioning in general (current/present/regular consumption) (Arosemena et al., 2022; Garbazza et al., 2022; Pereira-Morales et al., 2019) or not specifying how it was questioned (Esposito et al., 2002; Haraszti et al., 2014; Ishihara et al., 1985; Mule et al., 2022b; J Rosenberg et al., 2014; Sansom et al., 2022; Siudej and Malinowska-Borowska, 2021; Yang et al., 2019).

The pooled OR of alcohol consumption for evening-type individuals compared to other chronotypes was 1.41 (95% CI: 1.16, 1.66; I2 = 38.0%), as depicted in **Figura 2**. The results of two of the included studies were adjusted by sociodemographic, academic, and sleep-related variables (Vera et al. 2018; Zhang et al. 2018) and one by body mass index (Arosemena et al. 2022). The other ten studies presented unadjusted results.

The funnel plot for studies related to chronotype and alcohol consumption indicated the absence of publication bias (**APÊNDICE E**), as did the Egger test (p = 0.107) and the Begg test (p = 0.714). In the sensitivity analyses, the association between

eveningness and alcohol consumption remained consistent regardless of the exclusion of each of the included studies (Supplementary material, **APÊNDICE F**).

Figura 2. Forest plot of the odds ratios and 95% confidence intervals of alcohol consumption in evening-type individuals.

Study	Year		OR (95% CI)	% Weight
Ishihara et al.	1985		2.12 (1.26, 3.57)	4.04
Esposito, Martoni & Natale	2002		1.98 (1.03, 3.80)	2.93
Rosenberg et al.	2013		1.89 (0.45, 9.74)	0.29
Haraszti et al.	2014		2.91 (0.37, 22.74)	0.05
Zhang et al.	2017		1.26 (1.05, 1.52)	23.28
Vera et al.	2018		1.52 (1.25, 1.86)	20.41
Pereira-Morales et al.	2019		1.74 (1.31, 2.32)	13.35
Siudej & Malinowska-Borowska	2021		2.47 (1.19, 5.13)	1.53
Lee et al.	2022		0.97 (0.56, 1.71)	11.50
Garbazza et al.	2022		2.55 (0.53, 12.30)	0.18
Sansom et al.	2022		0.90 (0.62, 1.34)	18.23
Mulè et al.	2022		2.43 (1.55, 3.82)	4.17
Arosemena et al.	2022		3.88 (0.58, 25.93)	0.04
Overall, DL ($I^2 = 38.0\%$, p = 0.081)			1.41 (1.16, 1.66)	100.00

NOTE: Weights are from random-effects model

OR: odds-ratio; CI: confidence interval. I^2: Heterogeneity.

4.1.5. Discussion

In the present systematic review, the available evidence suggests an association between eveningness and both a higher frequency and volume of alcohol consumption. Almost half of the studies included in this systematic review reported a greater quantity of alcohol consumption in evening-type individuals than in morning- or neither-type individuals. Moreover, the findings from a meta-analysis based on 13 studies involving 7,305 participants revealed that evening-type individuals are 41% more likely to consume alcohol than individuals with other chronotypes.

Most studies included in the quantitative synthesis used the complete Horne and Östberg's MEQ (Horne and Ostberg, 1976) or its reduced version (Adan & Almirall, 1991). These tools are widely used to assess chronotype and have consistently shown high levels of reliability across different countries (Kim and Kim, 2020). In addition, only two

of the included studies adjusted for sociodemographic variables, average sleep duration, and social jetlag, all of which were previously associated with both chronotype and alcohol consumption (Fischer et al., 2017; Global Burden of Disease (GBD), 2022; Haynie et al., 2018; Kivelä et al., 2018; Taillard et al., 2021; Zheng et al., 2021). While the use of reliable tools to assess chronotype can be considered a strength among the studies, the predominance of unadjusted analyses suggests that their results are susceptible to bias, as was also observed in the quality assessment.

Many studies (n=11) were focused on university students, and consequently, a substantial percentage of participants (24.5%) were young adults. Prior evidence showed a different relationship between chronotype and age, with a progressively later midpoint of sleep on weekends during childhood and adolescence, reaching its peak during early adulthood (18.4 years) (Fischer et al., 2017). Changes in chronotype during adolescence seem to be partially driven by gonadal hormones (Hagenauer and Lee, 2012). Similarly, young people are also more exposed to new social situations and new social roles, including starting university and/or working (Umberson et al., 2010). These new environments often result in changes in lifestyle (Assaf et al., 2019), such as the adoption of a later bedtime (Li et al., 2017) or increased consumption of psychoactive substances (Gambles et al., 2022; Henneberger et al., 2021). Along with a higher prevalence of sleep deprivation (Chowdhury et al., 2020), all the abovementioned behaviors have been associated with the evening chronotype (Evans and Norbury, 2021; Taillard et al., 2021).

Some mechanisms could explain the association between eveningness and alcohol consumption. From a biological perspective, an individual's chronotype can be determined by intrinsic characteristics, such as genetics and hormonal regulation (Koskenvuo et al., 2007; Montaruli et al., 2021). Polymorphisms in the NPAS2 gene, which play an important role in maintaining the effective synchrony of the circadian rhythm (Basu et al., 2022), have been associated with alcohol consumption (Gamble et al., 2011). Moreover, cortisol secretion levels are overall lower in evening-type individuals (Bailey and Heitkemper, 2001; Kudielka et al., 2006), and young alcohol binge drinkers have also shown decreased cortisol levels (Orio et al., 2018). Therefore, the interaction between these biological aspects in evening-type individuals can help explain their higher alcohol intake when compared with their morning-type counterparts.

From a behavioral standpoint, the misalignment between the preferred sleep timing and societal demands (e.g., work schedule, family obligations, and others) of evening-type individuals typically leads to sleep deficiency. Sleep-related cognitive

impairment may alter the individual's ability to make safe decisions, resulting in impulsive behaviors and increased risk-taking (Kenney et al., 2012; Salfi et al., 2020). Supporting this notion, Fucito et al. (2018) also found that young adults consumed more drinks after sleeping for shorter durations or waking earlier than usual. Indeed, there is a potential mediating role of impulsivity in the relationship between eveningness and alcohol consumption (Evans and Norbury, 2021). The hypothesis that sleep problems may play a role in unhealthy choices would also help to explain why, in studies that adjusted their analyses for sleep quality, the association between chronotype and alcohol consumption did not remain statistically significant (Haraszti et al., 2014; Yang and Tucker, 2022). Likewise, sleep quality seems to mediate the relationship between chronotype and substance use (Bakotic et al., 2017).

Another factor that may have a contributing role in this association is the so-called "pub hypothesis" (Wittmann et al., 2010). According to it, drinking is an "evening habit"; consequently, evening-type individuals simply have more time to consume alcohol than morning-type individuals due to their later bedtimes. Based on this idea, it could be argued that the relationship between chronotype and alcohol consists of a vicious cycle. While evening chronotype predicts sleep deprivation (Roenneberg et al., 2003) and the subsequent impulsive decision to drink (Evans and Norbury, 2021), alcohol consumption has been linked with abnormalities of the circadian rhythm (He et al., 2019). For instance, a decrease in the amplitude of the circadian temperature rhythm (Danel et al., 2001) and suppression of salivary melatonin (Rupp et al., 2007) may exert a harmful impact on both sleep duration and quality. Furthermore, Haynie et al. (2018) showed a bidirectional association, with sleep timing predicting subsequent alcohol consumption and greater alcohol consumption predicting later chronotype. Because of the aforementioned effects of alcohol on circadian rhythmicity, it has been suggested that this inverse outcome could be explained by a desynchronization of the biological clock as a consequence of greater alcohol consumption (Danel and Touitou, 2004).

Some limitations must be acknowledged when interpreting the results of this review. First, most of the included studies had a cross-sectional design; therefore, causality cannot be determined. Second, due to the varied methods used to assess alcohol consumption, especially concerning the volume and types of alcoholic drinks, we were not able to examine a dose-response effect. In addition, the assessment of alcohol consumption could introduce recall and social desirability biases. Third, only two of the twelve studies included in this meta-analysis presented adjusted ORs. Fourth, alcohol

consumption was self-reported in all studies included in the meta-analysis, with differences in the period used in the recall of each study. Consequently, the results are subject to confounding bias. Furthermore, considering that the quality assessment indicated concerns regarding the risk of bias, it is important that future studies follow guidelines for reporting observational studies. Last, caution should be exercised when interpreting the findings of the meta-analysis due to the utilization of a dichotomous variable for alcohol consumption. This binary variable does not fully capture the complexity involved in alcohol consumption, including varying frequencies, quantities, and types of beverages. Therefore, further studies are needed to investigate whether evening chronotype is also associated with more frequent consumption, higher quantities, or problematic alcohol use, such as binge drinking.

4.1.6. Conclusion

In conclusion, the available evidence supports an association between the evening chronotype and higher alcohol consumption. Although these results should be considered cautiously and do not allow causality inferences, our findings reinforce the importance of focusing on educational interventions for preventing or reducing alcohol consumption within the evening-type population, especially among young adults. This systematic research also highlights the need for longitudinal evidence on this association, as well as consistent alcohol consumption data.

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4.2. Artigo 2 - The Association Between Alcohol-Related Problems and Sleep Quality and Duration Among College Students: a Multicountry Pooled Analysis[2]

4.2.1. Abstract

Alcohol consumption and sleep disorders are both prevalent and relevant problems among college students, but the relationship between these conditions is unclear. This study aimed to analyze the association between alcohol-related problems and sleep in first-year college students from Brazil, Chile, and Spain. Cross-sectional analyses were performed with data from three independent studies with first-year college students from each country. The risk of alcohol-related problems (RARP) and sleep quality and duration were self-reported using mixed methods. Pooled odds ratios (p-OR) and 95% confidence intervals (95% CI) of suboptimal sleep quality and of short (< 7 h) and long (> 8 h) sleep duration were estimated according to RARP adjusting for the main confounders. Of the 1830 students included (31.2% Brazilian, 42.2% Chilean, and 26.6% Spanish), 61.6% were female, and the mean age was 20.0 ± 3.6 years. Overall, 25.0% and 9.9% of the students were classified as intermediate and high RARP, respectively. In the combined results for the three countries, intermediate-to-high RARP was associated with a higher likelihood of suboptimal sleep quality (p-OR: 1.24; 95% CI: 1.00 to 1.52; I^2 heterogeneity statistics: 43.0%), regardless of sociodemographic and lifestyle covariates and of self-rated health. The frequency of alcohol consumption was not associated with sleep quality or sleep duration. In this multicountry pooled analysis, first-year college students at risk of alcohol-related problems were more likely to report worse sleep quality. The coexistence of alcohol-related problems and sleep disorders could potentiate its adverse health effects among these young adults.

Key-words: Alcohol use; Sleep; College students; International study; Epidemiology.

4.2.2. Introduction

Alcohol consumption is a widely spread practice around the world. Approximately half of the global adult population is currently drinker, especially in the Americas and Europe, where prevalence rates are 54.1% and 59.9%, respectively (WHO, 2018). Although young people's drinking reflects the drinking behavior of the adult population, the prevalence of heavy episodic drinking (HED) is higher among 20–24-year-olds than in other adult age groups (WHO, 2018). Consistently, a systematic review of studies with young adults showed that two of three college students reported hazardous alcohol consumption (Davoren et al., 2016).

The transition from adolescence to early adulthood is a life critical stage that involves leaving high school behind to get into college (and/or initiate professional activity) and leaving the parents' home to have an independent life. This period is marked by the need to adapt to different physical and social contexts (Stok et al., 2018). In regard to college students, in addition to higher academic demands, the social context favors health-risk behaviors, such as unhealthy eating habits, decreased free-time physical activity, and increased sedentary behavior and alcohol consumption (Deforche et al., 2015). Additionally, the frequency of sleep-related problems increases because of difficulties regarding regularity, quantity, and quality of sleep (Suardiaz-Muro et al., 2020). Importantly, these unhealthy behaviors, particularly sleep disorders (Etindele Sosso & Matos, 2021; Etindele Sosso et al., 2021; Papadopoulos et al., 2020) and alcohol consumption (Collins, 2016), are generally more prevalent at lower socioeconomic levels (e.g., due to the need to work in addition to studying and distance from home to university) and could be affected by changes in social support (e.g., establishing new social relationships and living in a new neighborhood).

In college students, male and white individuals are more likely to binge drink than women and nonwhite students, respectively (Romano et al., 2021). Alcohol consumption has also been associated with smoking (Htet et al., 2020), age above 19 years (Ajayi et al., 2019), poor subjective health status, and poorer family background (Yi et al., 2017). In addition to these potential risk factors, alcohol intake has been associated with several harmful health consequences, such as increasing the risk of dementia, cirrhosis, and numerous types of cancer (Gronbaek, 2009). Furthermore, unhealthy alcohol use has been associated with depression, anxiety (Khan et al., 2020), shorter sleep duration (Schoenborn & Adams, 2008), poor sleep quality (Kenney et al., 2014), and insomnia

(Zheng et al., 2020). Both alcohol consumption and sleep disorders can affect not only their quality of life and general health but also their academic performance (Lund et al., 2010; Saether et al., 2019; Seoane et al., 2020; Tembo et al., 2017). Indeed, those with higher academic grades tend to be more cautious with their drinking habits (Krieger, Young, Anthenien, & Neighbors, 2018).

A literature review on the determinants of sleep quality in college students reported that alcohol consumption did not benefit sleep, and higher drinking motives were closely associated with poor sleep quality (Wang & Biro, 2021). Studies on the relationship between alcohol use and sleep among university students have found mixed results. Some studies have reported that harmful or excessive alcohol consumption is associated with later bedtimes and rise times (Van Reen et al., 2016), poorer sleep quality (Campos Vicentini et al., 2021; Kenney et al., 2012), and insomnia (Hsieh et al., 2019). Furthermore, the use of alcohol for sleep aid by college students has been associated with negative drinking consequences and insomnia symptoms (Goodhines et al., 2019). In contrast, no significant association with sleep parameters was found in other studies in college students from different countries (Araujo et al., 2014; Mesquita et al., 2010; Navarro-Martinez et al., 2020). Last, a study found that binge drinking was associated with more insomnia symptoms in girls but not in boys (Silva-Fonseca et al., 2021), and another study found that high-risk alcohol consumption was associated with 55% lower odds of poor sleep efficiency, but no relationship was found with the other parameters of sleep duration and sleep quality (Velez et al., 2013).

It is possible that such inconsistencies are due to the characteristics of the populations analyzed with respect to cultural, economic, and social aspects (e.g., type and alcohol content of the most consumed beverages, opportunities for group consumption, such as meetings or parties, etc.), which may influence the motivation, frequency, and total amount of alcohol consumed in different countries (Balogun et al., 2014; Geusens et al., 2019; Inac et al., 2021; Kenney et al., 2014). Therefore, epidemiological studies are warranted to transcend these disparities and offer cross-cultural evidence, exploring whether an association remains despite sociocultural and economic contexts. In this sense, this study estimates the cross-sectional association between alcohol-related behavior and self-reported parameters of sleep duration and quality in first-year college students from different countries. For this purpose, we present the results of three separate cross-sectional studies based on data obtained in Brazil in 2019, in Chile in 2021, and in Spain in 2009. In addition to presenting separate results for each study, a pooled analysis

was performed to assess the association between alcohol and sleep by combining their results and estimating the heterogeneity between them.

4.2.3. Methods

4.2.3.1. Study design and participants

The present study is based on data on alcohol consumption and sleep obtained in three independent databases of first-year college students conducted at different time points in Brazil, Chile, and Spain. The main aspects of the methodology of each study are described below, as well as the similarities and differences that should be considered for the interpretation of the presented findings.

Brazilian data were obtained throughout a cross-sectional study aimed at assessing the mental and physical health of college students at a public university in Londrina, a large city in southern Brazil. A broad dissemination process was conducted concurrently with the collection period, with the aim of clarifying the importance of the study, inviting all students to participate (on-site visits at all 259 classrooms of the university), resolving doubts, and increasing the response rate. Students were also invited to participate by messages recorded in the university communication channels (radio and television), explanatory banners and flyers distributed throughout the campus, and through social media and email. Of the 12,536 students from all academic areas enrolled in the university invited to participate, 3.238 (25.8%) answered an online questionnaire during the first semester of 2019. Of the studied sample, 720 were first-year students, among whom 571 provided complete answers and were included in the present analysis. The participants included in the final analysis did not differ in sex, age, or parental socioeconomic status from the whole study sample.

In Chile, cross-sectional data collection occurs annually with first-year college students for both administrative and scientific purposes at a public university in Temuco, a medium-sized city in the southern region of the country. According to the 2021 college enrollment records, all first-year college students were invited to voluntarily participate in an online health survey. In addition, they were informed that the data would be analyzed globally for use in institutional reports and for research purposes. Of the 1,942 eligible students invited to participate, 1243 (63.5%) agreed to answer an online questionnaire, of whom 772 students provided complete data for the main variables of interest in this study. The participants included in the final analysis did not differ in sex and age from the whole sample.

In Spain, data came from a cross-sectional study aimed at assessing the changes in lifestyle, diet, and cardiovascular health that occurred during attendance to the 2009–2010 academic year in a public university in Cuenca, a small city in central-eastern Spain. According to university enrollment records, all first-year university students of the Universidad de Castilla-La Mancha, Spain, were invited to participate. Of the 770 invited students, 683 (88.7%) agreed to participate in a face-to-face interview and physical exam (Garrido-Miguel et al. 2019). In this analysis, data were obtained from a subsample of 487 students, among which all variables of interest were assessed. The Spanish students included in the present analysis did not differ in sex, age, or parental socioeconomic status from the whole sample participating in the study.

The study protocols of the three studies were approved by the Research Ethics Committee of the Universidade Estadual de Londrina, Parana, Brazil; by the Ethics Committee of the Universidad de la Frontera, Temuco, Chile; and by the Clinical Research Ethics Committee of the Hospital Virgen de la Luz Hospital, Cuenca, Spain. All students included in the present analyses fulfilled an informed consent form before participating in the corresponding study.

4.2.3.2.   Study Variables

The main characteristics of variables regarding alcohol consumption (independent variable), sleep parameters (dependent variable), and covariates obtained in each study are described in sequence.

Alcohol consumption was assessed with the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (WHO ASSIST Working Group, 2002), validated in Portuguese (WHO, 2010), in Brazil, and with the Alcohol Use Disorder Identification Test (AUDIT) (Saunders et al., 1993), validated in Spanish (Garcia Carretero, Novalbos Ruiz, Martinez Delgado, & O'Ferrall Gonzalez, 2016), in Spain. In Chile, information was obtained on the frequency of alcohol consumption and on binge drinking in the last month with the question "During the last month, how often did you have 5 or more drinks containing any kind of alcohol within a two-hour period?" (Gobierno de Chile, 2013). These three alcohol-related variables (i.e., measured with ASSIST, AUDIT, and binge drinking in the abovementioned corresponding country) consider both the overall volume of alcohol consumption and the pattern of drinking, i.e., the dimensions of individual-level drinking that increase the risk of adverse consequences for both the drinker (e.g., alcohol-induced diseases, dependent syndrome, and changes in brain function) and others

(e.g., family disruption, problems at the workplace, injuries, and sexual assaults) (Rehm, 2011; Rehm et al., 2010; White & Hingson, 2013). Therefore, taking into account that "excessive or harmful patterns of alcohol drinking" can be measured with different approaches, to facilitate the interpretation of the results, from this point on, this construct will be referred to as "risk of alcohol-related problems" (RARP). RARP was defined on the basis of the alcohol-related variables available in each country and classified into three risk levels (low, moderate, and high) as follows: Brazil, ASSIST score 0–10 (low), 11–26 (moderate), and ≥ 27 (high) (WHO, 2010); Chile, did not consume 5 or more drinks of alcohol on one occasion (low), consumed 5 or more drinks of alcohol on one occasion 1–3 times a month (moderate), and consumed 5 or more drinks of alcohol on one occasion 4 or more times during the month (high) (Gobierno de Chile, 2013); and Spain, AUDIT score 0–7 in men and 0–5 in women (low), 8–12 in men and 6–12 in women (moderate), and ≥ 13 in both sexes (high) (Garcia Carretero et al., 2016).

Sleep quality was determined in all countries using the following question from the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989): "During the past month, how would you rate your sleep quality overall?" Responses "very good/fairly good" were defined as "optimal sleep quality," and "fairly bad/very bad" were defined as "suboptimal sleep quality." This question is frequently used in epidemiological studies to characterize self-reported overall sleep quality, either individually or as a PSQI item (Araujo et al., 2014; Mesquita et al., 2010; Velez et al., 2013). For self-reported sleep duration, Brazil and Spain used the question "In the past 30 days, approximately how long did you sleep each night?", while in Chile, the students were asked, "Approximately how long do you usually sleep at night?". In the three countries, sleep duration was defined as short when the answer was < 7 h/day (versus ≥ 7 h/day) and long when it was > 8 h/day (versus ≤ 8 h/day). The rationale to study the two extreme sleep durations separately is because sleep duration follows a U-shaped association (increased risk at the two extreme durations and reduced risk at intermediate durations) with negative health outcomes, such as cardiovascular events and mortality (Yin et al., 2017). On the one hand, sleep duration may be short due to problems in initiating or maintaining sleep (Mesas et al., 2011), leading to sleep deprivation effects such as attention deficit (Lee, Kim, & Lee, 2019) and aggression (Krizan & Hisler, 2019). On the other hand, long sleep may be related to sleep inertia leading to excessive daytime sleepiness (Mesas et al., 2011) and lower quality of life (Rezaei et al., 2017).

Information was also obtained in each country for the following covariates, which could confound the study association because of their potential association with both alcohol consumption and sleep quality: age (Ajayi et al., 2019; Van Reen et al., 2016), sex (Ajayi et al., 2019; Van Reen et al., 2013), parental education (an indicator of socioeconomic status only available in Brazil (for total sample) and in Chile (for 640 of the 772 students)) (Busto Miramontes et al., 2021; Etindele Sosso et al., 2021), body mass index (Araujo et al., 2014; Duran et al., 2017), tobacco consumption (Vera et al., 2021), free-time physical activity (Memon et al., 2021; Yi et al., 2017), and self-rated health (Freire et al., 2014; Yi et al., 2017).

4.2.3.3. Statistical analysis

The following statistical analyses were performed separately in each country's database. Considering the differences between the study variables used in each country, no single database mixing data from the studies was created or analyzed.

After selecting students with complete data for the variables of interest, a descriptive analysis was conducted to calculate the mean ± standard deviation (SD) for continuous variables (i.e., age, body mass index (BMI), and sleep duration) and the absolute and relative frequency (%) of the categories for categorical variables (e.g., sex, frequency of alcohol consumption, and sleep quality).

In the analyses of the association between the risk of alcohol-related problems (RARP) or the frequency of alcohol consumption (independent variables) and the quality and duration of sleep (dependent variables), logistic regression models were built to estimate the odds ratio (OR) and the respective 95% confidence interval (CI) for each association. To control for the confounding effect of covariates selected based on the available evidence, the models adjusted for age (years, continuous), sex (female, male), body mass index (kg/m2, continuous), tobacco consumption (yes, no), free-time physical activity (lower, higher level), and self-rated health (optimal, suboptimal). Because the variable parental education was available only for Brazil and Chile (partially), additional analyses were carried out with the datasets of these two countries with the inclusion of parental education in the adjustment.

Based on the results of the fully adjusted model obtained for each country, the values of each OR and the lower and upper limits of the CI were transformed into a logarithmic scale for calculating the pooled OR (p-OR) and its 95% CI. This meta-analytic procedure was performed with DerSimonian and Laird random-effect models

(DerSimonian & Laird, 1986). Forest plots were generated to facilitate the visualization of these pooled results. The I^2 statistic was used to assess heterogeneity (Higgins et al., 2021).

All statistical analyses were performed using StataSE, version 15 (StataCorp, College Station, TX).

4.2.4. Results

The population included in this analysis was similar to age across the countries, with a mean ± SD of 20.5 ± 4.3 years in Brazil, 19.4 ± 2.2 years in Chile, and 20.3 ± 4.5 years in Spain. Regarding sex, the proportion of females was 65.1% in Brazil, 49.9% in Chile, and 76.0% in Spain. The mean values for body mass index ranged from 22.6 in Spain to 24.5 kg/m2 in Chile. More than half of the included participants were classified as having a lower level of free-time physical activity (range from 64.3 in Chile to 69.4% in Brazil). When considering self-rated health, most Brazilian students (76.4%), almost half of Chilean students (55.6%), and one of ten Spanish students (10.3%) reported suboptimal health. Tobacco consumption did not reach one-third of the population, with similar values across the countries: 29.8% for Brazil, 23.6% for Chile, and 29.2% for Spain (**Tabela 1**).

Regarding alcohol consumption, the proportion of students who reported this behavior was 77.8% in Brazil, 69.4% in Chile, and 91.4% in Spain. Brazilian students had the lowest proportion of individuals classified as at RARP (1.9%), followed by those from Chile (13.5%) and Spain (13.6%). According to the self-reported sleep duration, Brazilian participants had the lowest sleep duration (7.0 ± 1.2 h), followed by Spanish participants (7.2 ± 1.1 h) and Chilean participants (7.4 ± 1.2 h). When considering sleep quality, suboptimal sleep quality was reported by 43.4% of the students in Brazil, 41.6% in Chile, and 22.4% in Spain. More details of the characteristics of the study sample by country are available in **Tabela 1**.

Tabela 1. Characteristics of the study participants by country.

Characteristic	Brazil	Chile	Spain
Total	571 (100.0)	772 (100.0)	487 (100.0)
Age (years)			
Mean ± SD	20.5 ± 4.3	19.4 ± 2.2	20.3 ± 4.5
Sex			
Female	372 (65.1)	385 (49.9)	370 (76.0)
Male	199 (34.9)	387 (50.1)	117 (24.0)
Parental highest level of education[b]			
Lower than university studies	304 (53.2)	442 (69.0)	NA
University studies	267 (46.8)	198 (31.0)	NA
Body Mass Index (Kg/m^2)			
≤24.9	345 (60.4)	482 (62.4)	394 (80.9)
≥25.0	226 (39.6)	290 (37.6)	93 (19.1)
Mean ± SD	23.7 ± 4.6	24.5 ± 4.6	22.6 ± 3.6
Free-time physical activity			
Lower level	396 (69.4)	496 (64.3)	320 (65.7)
Higher level	175 (30.6)	276 (35.8)	167 (34.3)
Tobacco consumption			
Yes	170 (29.8)	182 (23.6)	142 (29.2)
No	401 (70.2)	590 (76.4)	345 (70.8)
Alcohol consumption			
Yes	444 (77.8)	536 (69.4)	445 (91.4)
No	127 (22.2)	236 (30.6)	42 (8.6)
Frequency of alcohol consumption			
Yes, frequently	202 (35.4)	61 (7.9)	117 (24.0)
Yes, occasionally	111 (19.4)	475 (61.5)	196 (40.2)
Abstemious or almost never	258 (45.2)	236 (30.6)	174 (35.7)
Risk of alcohol-related problems			
High	11 (1.9)	104 (13.5)	66 (13.6)
Intermediate	133 (23.3)	207 (26.8)	120 (24.6)
Low	427 (74.8)	461 (59.7)	301 (61.8)
Self-rated health			
Optimal	135 (23.6)	429 (55.6)	437 (89.7)
Suboptimal	436 (76.4)	343 (44.4)	50 (10.3)
Sleep duration (hours)			
<7	287 (50.3)	144 (18.7)	124 (25.5)
7-8	257 (45.0)	522 (67.6)	314 (64.5)
>8	27 (4.7)	106 (13.7)	49 (10.1)

Mean ± SD	7.0 ± 1.2	7.4 ± 1.2	7.2 ± 1.1
Sleep Quality			
Optimal	323 (56.6)	451 (58.4)	378 (77.6)
Suboptimal	248 (43.4)	321 (41.6)	109 (22.4)

SD: Standard deviation.
[a]Values are the number and % of individuals in each category, except when indicated mean ± standard deviation (SD).
[b]Data available for 640 (82.9%) students in Chile

The results of the pooled analysis presented in **Figura 3** show that the presence of intermediate-to-high RARP was associated with a higher likelihood of reporting suboptimal sleep quality (p-OR = 1.24; 95% CI: 1.00 to 1.52), regardless of all potential confounding covariates. Moderate nonsignificant heterogeneity between countries (I2: 43.0%; p = 0.119) was identified in the association between RARP and sleep quality. On the other hand, no association with the risk of alcohol-related problems was found when the pooled ORs estimated the likelihood of reporting short (< 7 h) (**Figura 4**) and long (> 8 h) (**Figura 5**) sleep durations.

As presented in the supplementary material (**APÊNDICE G**), the results of additional analyses adjusted for parental education remained similar to the main analyses, although with larger confidence intervals for Chile because of the lower sample size.

4.2.5. Discussion

In this cross-sectional study performed with data from first-year college students from three different countries, the risk of alcohol-related problems was associated with worse subjective sleep quality. The frequency of alcohol consumption was not associated with sleep quality or sleep duration. Although more studies are needed to further explore the temporal relationship and the potential mediators of this association, our results indicate that alcohol consumption and sleep problems are prevalent public health issues among college students that may coexist, despite the different socioeconomic and cultural backgrounds of the included countries.

Specifically, we found that intermediate-to-high RARP was associated with a higher likelihood of reporting suboptimal sleep quality, but no association between the frequency of alcohol consumption and sleep was found. Because RARP is more closely related to the amount than to the frequency of alcoholic beverages consumed, this reinforces the idea that the dose could be more relevant than the frequency of consumption with respect to the harmful consequences of alcohol to health. Alternatively, to have a more comprehensive understanding of its effects on health, other authors have proposed the inclusion of multidimensional aspects of the alcohol intake pattern, such as

the type of beverage (i.e., distilled or fermented) and whether the alcohol consumption was with meals or binge-eating episodes (Gea et al., 2014; Jani et al., 2021; Morales et al., 2021). Therefore, future studies based on a more detailed description of the patterns of alcohol consumption and context in which alcohol consumption took place are warranted for a deeper understanding of its potential deleterious effects on sleep.

Figura 3. Pooled odds ratio (OR) and 95% confidence interval (CI) of suboptimal sleep quality according to the risk of alcohol-related problems. The OR and the 95% CI of each country were obtained through logistic regression models adjusted by age (years, continuous), sex (female, male), body mass index (Kg/m^2, continuous), tobacco consumption (yes, no), free-time physical activity (lower, higher level) and self-rated health (optimal, suboptimal).

Risk of alcohol-related problems and suboptimal sleep quality

Country	Sample size	Odds ratio (95%CI)	% Weight
Intermediate risk			
Brazil	571	1.74 (1.12, 2.69)	22.40
Chile	772	1.01 (0.70, 1.47)	31.25
Spain	487	1.02 (0.59, 1.77)	14.25
Subgroup, IV (I² = 49.0%, p = 0.141)		1.21 (0.94, 1.56)	67.90
High risk			
Brazil	571	1.40 (0.40, 4.91)	2.74
Chile	772	0.91 (0.56, 1.49)	17.96
Spain	487	2.18 (1.18, 4.03)	11.40
Subgroup, IV (I² = 58.1%, p = 0.092)		1.29 (0.89, 1.86)	32.10
Heterogeneity between groups: p = 0.787			
Overall, IV (I² = 43.0%, p = 0.119)		1.24 (1.00, 1.52)	100.00

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The colored diamonds indicate the odds ratios for each study, and their respective 95% CIs are indicated by adjacent horizontal lines (Brazil, green; Chile, blue; Spain, red). The transparent diamonds indicate the pooled OR (center of the diamonds) and the 95% CI (width of the diamonds) calculated for the association between the intermediate risk and the high risk subgroup categories of alcohol consumption, as well as for the set of both categories (overall) and suboptimal sleep quality. The vertical black line indicates OR = 1, that is, the value at which the relationship between alcohol and sleep would be zero. When the 95% CI crosses this line, the association tested is not statistically significant (p > 0.05). The weight column indicates the proportion of each study and category considered for the calculation of the overall polled OR and is determined according to the number of participants and cases with long sleep duration analyzed in each country.

Figura 4. Pooled odds ratio (OR) and 95% confidence interval (CI) of short sleep duration (< 7 h) according to the risk of alcohol-related problems. The OR and the 95% CI of each country were obtained through logistic regression models adjusted by age (years, continuous), sex (female, male), body mass index (Kg/m^2, continuous), tobacco consumption (yes, no), free-time physical activity (lower, higher level), and self-rated health (optimal, suboptimal).

Risk of alcohol-related problems and short sleep duration (<7h)

Country	Sample size		Odds ratio (95%CI)	% Weight
Intermediate risk				
Brazil	571		1.53 (1.00, 2.36)	25.34
Chile	772		0.79 (0.52, 1.19)	27.26
Spain	487		0.81 (0.48, 1.37)	16.99
Subgroup, IV (I² = 64.5%, p = 0.060)			1.01 (0.78, 1.31)	69.60
High risk				
Brazil	571		1.03 (0.29, 3.60)	2.95
Chile	772		0.95 (0.55, 1.65)	15.48
Spain	487		0.73 (0.39, 1.36)	11.98
Subgroup, IV (I² = 0.0%, p = 0.791)			0.86 (0.58, 1.28)	30.40
Heterogeneity between groups: p = 0.509				
Overall, IV (I² = 23.5%, p = 0.258)			0.96 (0.78, 1.20)	100.00

The colored diamonds indicate the odds ratios for each study, and their respective 95% CIs are indicated by adjacent horizontal lines (Brazil, green; Chile, blue; Spain, red). The transparent diamonds indicate the pooled OR (center of the diamonds) and the 95% CI (width of the diamonds) calculated for the association between the intermediate risk and the high risk subgroup categories of alcohol consumption, as well as for the set of both categories (overall) and short sleep duration. The vertical black line indicates OR = 1, that is, the value at which the relationship between alcohol and sleep would be zero. When the 95% CI crosses this line, the association tested is not statistically significant (p > 0.05). The weight column indicates the proportion of each study and category considered for the calculation of the overall polled OR and is determined according to the number of participants and cases with short sleep duration analyzed in each country.

In a study with medical students in Brazil, alcohol drinkers (regardless of the frequency or dose) had poor sleep quality (PSQI > 5) more frequently than non-drinkers (80% versus 64%, respectively) (Campos Vicentini et al., 2021). Considering that our findings are based on students from different areas of knowledge, it is possible that the association found by those authors (Campos Vicentini et al., 2021) is specific to the medical course because students in that course have a full-time curricular load and are known to have a rigorous study demand, aspects related to high burnout rates in that population (Shadid et al., 2020) that could increase vulnerability to both alcohol

consumption and sleep disorders. In this regard, it is noteworthy that the prevalence rate of poor sleep quality in the three countries included in the present analyses ranged from 22.4 to 43.4%, while in those medical students, it was 73.3% (Campos Vicentini et al., 2021).

Figura 5. Pooled odds ratio (OR) and 95% confidence interval (CI) of long sleep duration (> 8 h) according to the risk of alcohol-related problems. The OR and the 95% CI of each country were obtained through logistic regression models adjusted by age (years, continuous), sex (female, male), body mass index (Kg/m^2, continuous), tobacco consumption (yes, no), free-time physical activity (lower, higher level), and self-rated health (optimal, suboptimal).

Risk of alcohol-related problems and long sleep duration (>8h)

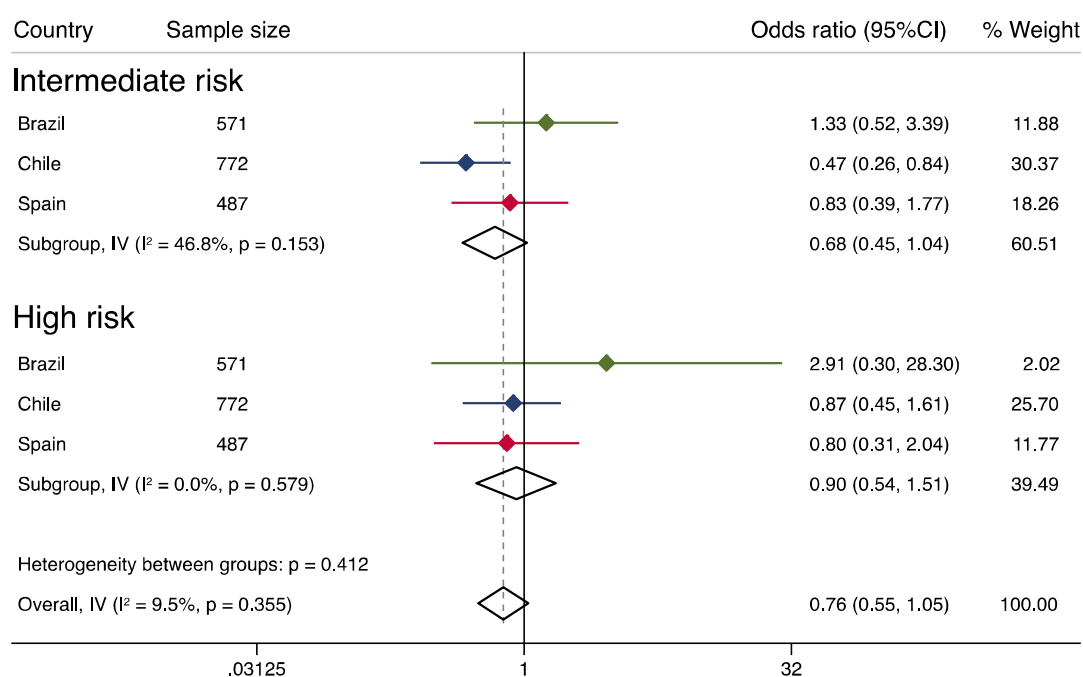| Country	Sample size	Odds ratio (95%CI)	% Weight
Intermediate risk			
Brazil	571	1.33 (0.52, 3.39)	11.88
Chile	772	0.47 (0.26, 0.84)	30.37
Spain	487	0.83 (0.39, 1.77)	18.26
Subgroup, IV (I² = 46.8%, p = 0.153)		0.68 (0.45, 1.04)	60.51
High risk			
Brazil	571	2.91 (0.30, 28.30)	2.02
Chile	772	0.87 (0.45, 1.61)	25.70
Spain	487	0.80 (0.31, 2.04)	11.77
Subgroup, IV (I² = 0.0%, p = 0.579)		0.90 (0.54, 1.51)	39.49
Heterogeneity between groups: p = 0.412			
Overall, IV (I² = 9.5%, p = 0.355)		0.76 (0.55, 1.05)	100.00

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The colored diamonds indicate the odds ratios for each study, and their respective 95% CIs are indicated by adjacent horizontal lines (Brazil, green; Chile, blue; Spain, red). The transparent diamonds indicate the pooled OR (center of the diamonds) and the 95% CI (width of the diamonds) calculated for the association between the intermediate risk and the high risk subgroup categories of alcohol consumption, as well as for the set of both categories (overall) and long sleep duration. The vertical black line indicates OR = 1, that is, the value at which the relationship between alcohol and sleep would be zero. When the 95% CI crosses this line, the association tested is not statistically significant (p > 0.05). The weight column indicates the proportion of each study and category considered for the calculation of the overall polled OR and is determined according to the number of participants and cases with long sleep duration analyzed in each country.

In the current study, we found an association between alcohol-related problems and suboptimal sleep quality but not between short and long sleep durations. In agreement with our findings, Van Reen et al. (2016) found in first-year college students that

increased alcohol consumption was associated with later bedtimes and rise times, but they did not find differences in the number of hours of sleep between drinking groups (Van Reen et al., 2016). Another recent study with Brazilian students found that binge drinkers had higher scores on the Insomnia Severity Index than non-drinkers, although this relationship was observed only in the female sex (Silva-Fonseca et al., 2021). In contrast with our findings, studies using mixed methods of alcohol consumption assessment did not find significant associations with self-rated sleep quality as measured with the PSQI (Araujo et al., 2014; Mesquita et al., 2010; Velez et al., 2013) or the Athens Insomnia Scale (Navarro-Martinez et al., 2020). One of the main factors that could help to understand these discrepancies is the variety of methodological approaches used to assess both potentially abusive alcohol consumption and impaired sleep parameters. In addition, it should also be considered that not all studies adjusted the analyses for the same confounders, so that the loss of significance in some of the studies cited may be due to adjustment for some covariates that we did not take into account. Finally, although in our study we have combined results from three countries that comprise a larger total sample than the others, it should be considered that in our case, the RARP association with poorer sleep quality was statistically significant but borderline and of only modest magnitude (OR = 1.24; 95% CI: 1.00, 1.52). This suggests that future studies on the subject in university students should include a large enough sample size to detect small differences in analyses adjusted for several confounders, especially sociodemographic and lifestyle factors.

Some mechanisms may partially explain the association between harmful alcohol intake and worse sleep quality. Unresolved emotional problems, which are particularly frequent in adolescents and younger adult age groups, have harmful consequences on sleep quality (Kahn et al., 2013). The mediating role of coping motives has already been evidenced in the relationship between alcohol and other mental health outcomes, such as depressive symptoms (Villarosa et al., 2018). Therefore, the association between alcohol-related problems and sleep disorders could be related to the emotional distress behind coping-motivated drinking (Villarosa et al., 2018). Another possible explanation is that people with sleep disorders are more likely to use alcohol as a sleeping aid (Roehrs et al., 1999). Indeed, alcohol intake causes a reduction in sleep onset latency and a more consolidated first half sleep, but an increase in sleep disruption has been reported in the second half of sleep (Ebrahim et al., 2013). Additionally, cumulative alcoholic neurotoxicity may lead to insomnia, thus leading to a cycle of poor sleep quality and

subsequent alcohol use. Thus, the chronic use of this strategy could favor deterioration in the quality of sleep. This pathway was recently confirmed in a community-based study in which a significant linear association between alcohol intake and poor overall sleep quality was observed after 6 years of follow-up (Zheng et al., 2020).

In the present study, we found that Chilean and Spain students had a higher prevalence of RARP (> 13%) than Brazilian students (< 2%). In addition to being due to the use of different instruments for risk assessment in each country, this discrepancy could be justified by the environmental and cultural context in which the data collection took place in Chile and Spain, respectively. First, Chilean data were collected in the first semester of 2021 under the influence of stressors associated with the coronavirus pandemic, such as home confinement, restrictions on movement, and social interactions. Graupensperger et al. reported a negative impact of COVID-19 pandemic on the mental health and well-being of college students, specifically in sleep health and substance use (Graupensperger et al., 2021). Additionally, Spain has a long tradition of alcohol consumption, a higher social tolerance to the damage produced by alcohol, and an easy availability of alcoholic beverages for young people (Gual, 2006).

Alcohol consumption in the early life stage causes damage to the development of the nervous system and increases the risk of harmful consequences, such as lower academic performance (Tembo et al., 2017), early and unwanted pregnancy, violence, and traffic accidents (CISA, 2019). Furthermore, the implications of alcohol consumption that occur early in life can be even more impactful throughout adulthood because the earlier the onset of alcohol consumption, the greater the risk of developing alcohol dependence (CISA, 2019). The coexistence of problems related to alcohol consumption and poor-quality sleep, as suggested by our results, could broaden the spectrum of detrimental consequences of both conditions for the health of these young people. For instance, some studies have reported an association between poor sleep quality and mental health problems (Milojevich & Lukowski, 2016; Ramsawh et al., 2009). In college students in particular, nocturnal sleep disturbances have been shown to predict depression, somatization, obsessive–compulsive behaviors, and psychological distress (Taylor et al., 2011).

Some methodological aspects must be considered for the correct interpretation of the present findings. First, we included three countries with different sociocultural settings, which enhances the external validity of our findings. Nevertheless, the present results cannot be extrapolated to the young adult population in general or to all college

students from the studied countries because the sample only included first-year students from three specific public universities. Second, different instruments were used to assess alcohol-related problems in each country. The questionnaires used in Brazil and Spain were to assess the risk of alcohol-related problems (ASSIST) and the risk of alcohol dependence (AUDIT), respectively, while in Chile, one question was used to assess binge drinking. Moreover, we used self-reported measures of sleep and alcohol consumption, which may be affected by information bias due to social desirability.

Third, the studies were conducted at different time points, and changes over time in both drinking and sleeping behaviors could have influenced the magnitude of the estimations across the studies. Specifically, the Spanish study was conducted 10 years before the Brazilian study and 12 years before the Chilean study, and this last was carried out in the context of the COVID-19 pandemic. On the one hand, although it is expected that there may be changes over so many years, in Spanish university students, the frequency of alcohol consumption remained stable at high levels throughout these years (91.4% in 2009 and 89.9% in 2017) (Cobo-Cuenca et al., 2019). On the other hand, there is evidence that during pandemic confinement, alcohol consumption increased in frequency and decreased in quantity and heavy drinking (Jackson et al., 2021), mainly driven by a reduced frequency of heavy episodic drinking events (Kilian et al., 2021). However, particularly in Chilean college students, the increase was relatively small when comparing data from alcohol drinking frequency in 2017 (65.9%) (Morales Illanes et al., 2017) with current data (69.4%), possibly because opportunities for group drinking were replaced by drinking with family due to pandemic-related health restrictions (Jackson et al., 2021). With respect to pandemic-related changes in sleep, there was an overall worsening of sleep quality and a significant delay in bedtime and wake-up time (Bruni et al., 2021; Cellini et al., 2020), although no change in bedtime was observed among university students (Cellini et al., 2020). Despite the temporal issue and of the sociocultural differences between countries related to political, economic, and cultural differences, the heterogeneity between studies was only moderate and was not statistically significant (I2: 43.0%; p = 0.119).

Fourth, the cross-sectional design limits us from stating causal associations. Finally, although the pooled analysis considered individual results adjusted for important main confounders of the study association, including physical activity and self-rated health, residual confounding due to nonincluded sociodemographic covariates (e.g., economic level (in this study, the highest parental education level was considered an

economic indicator and was available only for the analyses in Brazil and Chile), place of residence, and social support) is still possible. Therefore, future studies should collect more elaborate socioeconomic data that would make it feasible to explore in depth the potential influence of socioeconomic disparities on the relationship between alcohol and sleep and its health consequences (Papadopoulos et al., 2020).

The present study shows that college students at risk of alcohol-related problems are more likely to report poor sleep quality. Furthermore, the coexistence of alcohol-related problems and sleep disorders could have a synergistic effect and increase the harmful consequences on students' physical and mental health. In addition to the known deleterious health and social effects of inappropriate alcohol use across the lifespan, our study pointed out that this lifestyle behavior may be implicated in the early onset of sleep disorders. Although this suggested that physiopathology path requires further research based on prospective designs, our study provides preliminary evidence to support the development of strategies to prevent sleep disorders based on the control of alcohol use by college students. For this purpose, the entire university community and policy makers should be involved to discuss policies for promoting healthy lifestyle strategies focused on mental and sleep health, such as favoring the hours and quality of rest and recreation activities, in addition to campaigns to prevent the consumption of alcohol and other drugs.

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5. CONCLUSÃO

A presente tese teve como um de seus objetivos sintetizar as evidências referentes à associação entre o cronotipo vespertino e o consumo de álcool. Por meio de uma revisão sistemática com metanálise, verificou-se que o cronotipo vespertino está associado ao consumo de álcool em adultos. Adicionalmente, os dados publicados na literatura sugerem que pessoas vespertinas consomem álcool com maior frequência e em maior quantidade.

O segundo objetivo da tese consistiu em estudar a associação entre problemas relacionados ao álcool e sono em estudantes do primeiro ano de universidades do Brasil, Chile e Espanha. A análise conjunta dos dados mostrou uma associação entre baixa qualidade subjetiva do sono e RARP. Em contrapartida, não foi constatada associação com a duração do sono (curta ou longa).

Por fim, em resposta ao objetivo geral dessa tese, concluiu-se que o sono está associado ao consumo de álcool. Acredita-se que, devido ao fato de pessoas com cronotipo vespertino apresentarem uma menor quantidade e qualidade do sono, há um aumento da impulsividade e da propensão ao risco, resultando na adoção de comportamentos não saudáveis, e, dentre eles, o consumo de álcool. Em contrapartida, indivíduos com risco de problemas relacionados ao álcool também apresentam uma menor qualidade subjetiva de sono.

6. CONSIDERAÇÕES FINAIS

Os achados apresentados nessa tese contribuem para a ampliação dos conhecimentos acerca de um dos maiores problemas de saúde pública no mundo. Sabe-se que o álcool é a única substância psicoativa e capaz de produzir dependência que não é controlada por leis regulatórias a nível internacional (WORLD HEALTH ORGANIZATION, 2018). Dessa forma, apesar de não suprir a necessidade de uma regulamentação mais efetiva, a elucidação dos fatores associados a essa prática é uma alternativa importante para o direcionamento de estratégias de enfrentamento.

Nesse sentido, evidências recentes sugerem que tratamentos focados na saúde do sono reduzem a frequência de problemas relacionados ao álcool (MILLER *et al.*, 2023). Ainda, intervenções voltadas para a conscientização já se mostraram eficazes na redução do consumo de álcool e de *binge-drinking* (TEESSON *et al.*, 2020). Acredita-se que tais medidas podem ser ainda mais eficientes quando direcionadas a populações de risco, como indivíduos com má qualidade do sono e/ou de cronotipo vespertino.

Apesar de a cronobiologia se destacar principalmente no estudo dos ambientes de trabalho, particularmente trabalhos por turno, os resultados aqui expostos se somam à crescente literatura a respeito dos impactos do cronotipo sobre o estado de saúde das populações no geral (BHAR; BAGEPALLY; RAKESH, 2022; LOTTI *et al.*, 2022; SEÇIL; HAVVA, 2023; VAN DER MERWE; MÜNCH; KRUGER, 2022). Na realidade, as implicações do sono e do cronotipo na vida dos indivíduos ultrapassam até mesmo as barreiras tradicionais da pesquisa em saúde, abrangendo aspectos como segurança pública (WEAVER; BARGER, 2019), bem como participação e ideologia política (KSIAZKIEWICZ, 2019; KSIAZKIEWICZ, 2022).

De forma geral, pode-se inferir que todos esses desfechos sofrem influência do sono e do cronotipo por meio da psicologia e do processo de tomada de decisões. Conforme discutido anteriormente, a privação do sono afeta as funções cognitivas e a capacidade de julgamento (SATTERFIELD; KILLGORE, 2019). Se partirmos dessa perspectiva, são diversos os caminhos para a pesquisa no campo da cronobiologia.

Por fim, é importante salientar as limitações encontradas ao longo da construção dessa tese no que diz respeito aos dados disponíveis sobre o consumo de álcool. Além dos desafios impostos pela falta de padronização nas medidas de frequência e quantidade de consumo, a predominante ausência de informações referentes ao tipo de bebida de consumida impossibilitou uma análise mais aprofundada dessa variável. Dessa forma,

julga-se imprescindível uma maior padronização e detalhamento nos registros de consumo de álcool na literatura, possibilitando um maior esclarecimento da forma como o sono interfere no consumo dessa substância.

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APÊNDICE A – SEARCH STRATEGY USED IN EACH DATABASE.

DATABASE	SEARCH STRATEGY
Cochrane Library	(alcohol* OR "binge drinking" OR "heavy drinking") AND (chronotype OR morningness OR eveningness OR "Munich Chronotype Questionnaire" OR "Horne Östberg Questionnaire")
PsycINFO	(alcohol* OR "binge drinking" OR "heavy drinking") AND ((chronotype OR morningness OR eveningness OR "Munich Chronotype Questionnaire" OR "Horne Östberg Questionnaire"))
PubMed	(alcohol*[Title/Abstract] OR "binge drinking"[Title/Abstract] OR "heavy drinking"[Title/Abstract] OR Alcohols[MeSH Terms] OR Binge Drinking[MeSH Terms]) AND (chronotype[Title/Abstract] OR chronotype[MeSH Terms] OR morningness[Title/Abstract] OR eveningness[Title/Abstract] OR "Munich Chronotype Questionnaire"[Title/Abstract] OR "Horne Östberg Questionnaire"[Title/Abstract])
Scopus	(TITLE-ABS-KEY (alcohol* OR "binge drinking" OR "heavy drinking") AND TITLE-ABS-KEY (chronotype OR morningness OR eveningness OR "Munich Chronotype Questionnaire" OR "Horne Östberg Questionnaire"))
Web of Science	TS=(alcohol* OR "binge drinking" OR "heavy drinking") AND TS=(chronotope OR morningness OR eveningness OR "Munich chronotope Questionnaire" OR "Horne Östberg Questionnaire")

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APÊNDICE C – QUALITY ASSESSMENT OF THE INCLUDED STUDIES.

Authors, Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Adan, 1994	Y	N	NR	CD	N	N	NA	N	Y	N	N	NA	NA	NA
Arosemena et al., 2022	Y	Y	NR	Y	N	N	NA	Y	Y	N	N	NA	NA	Y
Arrona-Palacios et al., 2019	Y	Y	NR	CD	N	N	NA	Y	Y	N	N	NA	NA	NA
Barclay et al., 2013	Y	Y	Y	Y	N	N	NA	Y	Y	N	N	NA	NA	Y
Bruno et al., 2022	Y	Y	CD	Y	N	N	NA	N	Y	N	N	NA	NA	NA
Esposito, Martoni and Natale, 2002	Y	N	NR	CD	N	N	NA	N	Y	N	N	NA	NA	NA
Evans and Norbury 2021	Y	Y	NR	Y	N	N	NA	Y	Y	N	N	NA	NA	Y
Garbazza et al., 2022	Y	Y	NR	Y	N	N	NA	Y	Y	N	CD	NA	NA	N
Goodhines et al., 2019	Y	Y	NR	Y	N	N	NA	Y	Y	N	N	NA	NA	NA
Haraszti et al., 2014	Y	Y	NR	Y	N	N	NA	Y	Y	N	N	NA	NA	Y
Hasler et al., 2017	Y	Y	NR	Y	N	N	NA	Y	Y	Y	N	NA	NA	N
Hug et al., 2019	Y	Y	NR	Y	N	N	NA	N	Y	N	N	NA	NA	N
Ishihara et al., 1985	Y	Y	NR	CD	N	N	NA	N	Y	N	N	NA	NA	NA
Kanerva et al., 2012	Y	Y	Y	Y	Y	N	NA	Y	Y	N	N	NA	NA	Y
Lee et al., 2022	Y	Y	NR	Y	N	N	NA	Y	Y	N	Y	NA	NA	N
Millar et al., 2019	Y	Y	NR	Y	N	N	NA	N	Y	N	N	NA	NA	Y
Mulè et al., 2022	Y	Y	NR	Y	N	N	NA	Y	Y	N	CD	NA	NA	N
Nakade et al., 2009	Y	Y	Y	CD	N	N	NA	Y	Y	N	N	NA	NA	NA
Pereira-Morales et al., 2019	Y	Y	NR	Y	N	N	NA	N	Y	N	N	NA	NA	Y
Rosenberg et al., 2013	Y	N	NR	Y	N	N	NA	Y	Y	N	N	NA	NA	N
Rusnac, Spitzenstetter and Tassi, 2016	Y	N	NR	Y	N	N	NA	Y	Y	N	N	NA	NA	NA
Sansom et al., 2022	Y	Y	NR	Y	N	N	NA	Y	Y	N	Y	NA	NA	N
Siudej and Malinowska-Borowska, 2021	Y	N	NR	CD	N	N	NA	N	Y	N	N	NA	NA	NA

Study	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
Sun et al., 2019	Y	Y	NR	CD	N	N	NA	N	Y	N	N	NA	NA	NA
Taylor et al., 2020	Y	Y	NR	CD	N	N	NA	N	Y	N	Y	NA	NA	N
Van den Berg, Kivelä and Antypa, 2018	Y	Y	NR	Y	N	N	NA	Y	Y	N	N	NA	NA	Y
Vedaa et al., 2013	Y	Y	Y	Y	N	N	NA	Y	Y	N	N	NA	NA	N
Vera et al., 2018	Y	Y	NR	CD	N	N	NA	N	Y	N	N	NA	NA	Y
Watson, Buchwald and Harden, 2013	Y	Y	NR	CD	N	N	NA	N	Y	N	N	NA	NA	CD
Whittier et al., 2014	Y	Y	CD	Y	N	N	NA	N	Y	N	N	NA	NA	NA
Yang and Tucker, 2022	Y	Y	NR	Y	N	N	NA	N	Y	N	N	NA	NA	Y
Yun et al., 2015	Y	Y	NR	Y	N	N	NA	N	Y	N	N	NA	NA	Y
Zhang et al., 2017	Y	Y	Y	Y	Y	N	NA	N	Y	N	N	NA	NA	NA

Y: Yes; N: No; CD: Cannot determine; NA: Not applicable; NR: Not reported.
(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? Were inclusion and exclusion criteria prespecified and applied uniformly to all participants? (5) Was a sample size justification, power description, or variance and effect estimates provided? (6) For the study's analysis, 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) 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 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 clearly defined, valid, reliable, and implemented consistently across all study participants? (12) Were the outcome assessors blinded to the exposure status of the 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)?
*For this analysis, age was the only variable considered a key potential confounding variable.

APÊNDICE D – PRISMA CHECKLIST OF ITEMS TO INCLUDE WHEN REPORTING A SYSTEMATIC REVIEW OR META-ANALYSIS.

For abstract			
Section/Topic	**#**	**Checklist item**	**Reported (Yes/No)**
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesis results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes

| OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes
For main article			
Section/Topic	**#**	**Checklist item**	**Reported on page #**
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	6-7
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	7-8
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Table S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6-8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study	6-8

		investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	7-8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7-8
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	8
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	7-8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	7-8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7-8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	7-8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	8-9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	9
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	8-9

Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	9 Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Table S2
Study characteristics	17	Cite each included study and present its characteristics.	9-10 Tables 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table S3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figure 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figure 2 Table S5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	10-12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Table S5
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Figure S3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	NA
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	13-16

	23b	Discuss any limitations of the evidence included in the review.	13-16
	23c	Discuss any limitations of the review processes used.	15-16
	23d	Discuss implications of the results for practice, policy, and future research.	15-16
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	17
Competing interests	26	Declare any competing interests of review authors.	17
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NA

NA: Not applicable.

**APÊNDICE E -** FUNNEL PLOT FOR THE ASSOCIATION OF CHRONOTYPE WITH ALCOHOL CONSUMPTION.
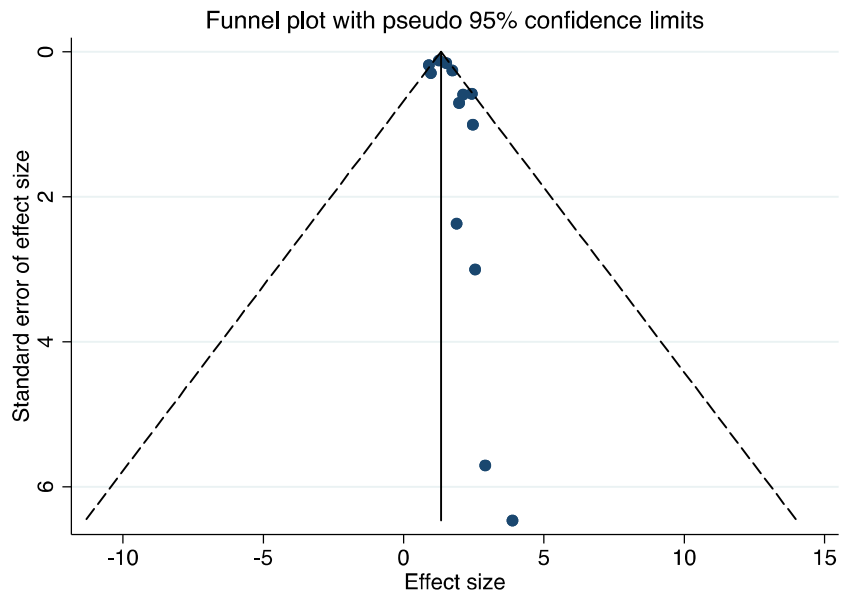
Funnel plot with pseudo 95% confidence limits

Study omitted	Estimate	95% Conf. Interval	
Ishihara et al.	1.3733075	1.1244961	1.6221187
Esposito, Martoni & Natale	1.3918918	1.1351289	1.6486547
Rosenberg et al.	1.4128450	1.1534399	1.6722503
Haraszti et al.	1.4132782	1.1544989	1.6720575
Vera et al.	1.3987119	1.0980843	1.6993394
Zhang et al.	1.4908884	1.1586922	1.8230845
Pereira-Morales et al.	1.3491371	1.0897573	1.6085167
Siudej & Malinowska-Borowska	1.3893056	1.1394520	1.6391591
Mulè et al.	1.3487011	1.1208448	1.5765574
Garbazza	1.4113147	1.1531011	1.6695284
Arosemena et al.	1.4124849	1.1544418	1.6705281
Sansom et al.	1.4654967	1.2558022	1.6751912
Lee et al.	1.4655235	1.1981230	1.7329240
Combined	1.4072397	1.1571519	1.6573275

APÊNDICE G – ASSOCIATION BETWEEN RISK OF ALCOHOL-RELATED PROBLEMS AND SLEEP PARAMETERS ADJUSTED BY AGE, SEX, BODY MASS INDEX, TOBACCO CONSUMPTION, FREE-TIME PHYSICAL ACTIVITY, SELF-RATED HEALTH AND PARENTAL EDUCATION IN BRAZIL AND CHILE.

Sleep parameter	Brazil		Chile	
	OR (CI 95%)	**p-value**	**OR (CI 95%)**	**p- value**
Suboptimal sleep quality				
Risk of alcohol-related problems				
Low	1.00		1.00	
Intermediate	1.68 (1.08, 2.61)	0.021	0.99 (0.66, 1.48)	0.962
High	1.51 (0.43, 5.33)	0.525	0.79 (0.45, 1.37)	0.395
Short Sleep				
Risk of alcohol-related problems				
Low	1.00		1.00	
Intermediate	1.47 (0.95, 2.28)	0.080	0.79 (0.49, 1.29)	0.349
High	0.97 (0.28, 3.43)	0.964	0.72 (0.38, 1.37)	0.316
Long sleep				
Risk of alcohol-related problems				
Low	1.00		1.00	
Intermediate	1.36 (0.52, 3.54)	0.524	0.46 (0.24, 0.89)	0.020
High	2.54 (0.26, 25.25)	0.427	0.69 (0.32, 1.51)	0.359

UNIVERSIDADE ESTADUAL DE LONDRINA - UEL
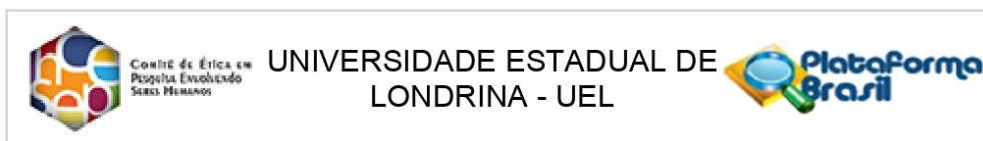
PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: GRADUAUEL - ANÁLISE DA SAÚDE E HÁBITOS DE VIDA DOS ESTUDANTES DE GRADUAÇÃO DA UEL

Pesquisador: Camilo Molino Guidoni

Área Temática:

Versão: 1

CAAE: 04456818.0.0000.5231

Instituição Proponente: CCS - Departamento de Ciências Farmacêuticas

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.097.110

Apresentação do Projeto:

O pesquisador afirma que O ingresso no ensino superior representa uma fase com diversos aspectos positivos para os jovens, como possibilidade de fazer novas amizades e adquirir novos conhecimentos, porém também envolve situações que podem torná-los vulneráveis a determinados riscos à saúde. As exigências acadêmicas e as relações entre pares e com professores podem levar a sofrimento psíquico, à adoção de comportamentos não saudáveis, comprometer a qualidade do sono e elevar o risco de problemas como síndrome de burnout, consumo abusivo de substâncias lícitas e ilícitas, medicamentos, entre outros. A exposição a violências, além do trote, também pode ocorrer, especialmente em um contexto de ampliação de acesso de um público historicamente excluído do ensino superior. Identificar a prevalência dos principais problemas de saúde, exposição a violências e hábitos de vida não saudáveis pode contribuir para o estabelecimento e políticas universitárias e ações que visem melhorar a qualidade de vida e saúde dos estudantes.

Objetivo da Pesquisa:

Objetivo Primário:

Analisar aspectos relacionados à saúde, à exposição a violências e aos hábitos de vida de estudantes universitários.

Endereço: LABESC - Sala 14		
Bairro: Campus Universitário	**CEP:** 86.057-970	
UF: PR	**Município:** LONDRINA	
Telefone: (43)3371-5455		**E-mail:** cep268@uel.br

Página 01 de 03

Continuação do Parecer: 3.097.110

Objetivos Secundários:

-Caracterizar os participantes segundo variáveis sociodemográficas e perfil acadêmico;- Descrever os hábitos de vida e as condições de saúde dos estudantes universitários;- Determinar a prevalência de sintomas depressivos, baixa qualidade do sono e síndrome de burnout entre os estudantes;Caracterizar a violência sofrida no ambiente acadêmico;- Determinar o consumo de bebidas alcoólicas e de outras substâncias ilícitas pelos

estudantes universitários;- Caracterizar o perfil de consumo de medicamentos dos universitários;- Identificar fatores associados à prevalência de sintomas depressivos, baixa qualidade do sono, síndrome de burnout, exposição a violências e consumo de medicamentos entre os estudantes.

Avaliação dos Riscos e Benefícios:

Riscos:

Destaca-se, ainda, que quanto aos riscos do desenvolvimento desta pesquisa, entende-se que estes serão mínimos, e caso ocorram, o participante será prontamente atendido e amparado pelos pesquisadores.

Benefícios:

Espera-se, com este estudo, contribuir para ampliar o conhecimento sobre saúde mental, hábitos de vida, aspectos relacionados ao sono, consumo de medicamentos e violência entre os estudantes universitários, entre outros aspectos relacionados à saúde e ao bem-estar dos estudantes. Também se espera que os resultados possam subsidiar o planejamento de ações que reduzam a ocorrência de transtornos mentais e violência nesse ambiente, bem como ações que melhorem a qualidade de vida dos estudantes. Espera-se, ainda, contribuir para a formação de recursos humanos em pesquisa, com a incorporação de alunos da graduação e da pós-graduação nas atividades desta investigação epidemiológica.

Comentários e Considerações sobre a Pesquisa:

Trata-se de pesquisa relevante que propiciará diagnósticos acadêmicos institucionais importante para direcionamento de políticas internas relativas ao tema.

Considerações sobre os Termos de apresentação obrigatória:

- folha de rosto adequada.

- autorização da co-participante.

- TCLE fundamentado da resolução CNS 466/12.

- orçamento, financiameto e cronograma adequados.

Continuação do Parecer: 3.097.110

Conclusões ou Pendências e Lista de Inadequações:

Não há.

Considerações Finais a critério do CEP:

Prezado (a) Pesquisador (a),

Este é seu parecer final de aprovação, vinculado ao Comitê de Ética em Pesquisas Envolvendo Seres Humanos da Universidade Estadual de Londrina. É sua responsabilidade imprimi-lo para apresentação aos órgãos e/ou instituições pertinentes.

Coordenação CEP/UEL.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1272279.pdf	07/12/2018 14:15:40		Aceito
Folha de Rosto	Folha_de_rosto.pdf	07/12/2018 14:00:24	Camilo Molino Guidoni	Aceito
Outros	CoParticipante.pdf	07/12/2018 12:01:02	EDMARLON GIROTTO	Aceito
Projeto Detalhado / Brochura Investigador	ProjetoGraduaUEL.pdf	06/12/2018 20:05:36	EDMARLON GIROTTO	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.pdf	06/12/2018 14:32:06	EDMARLON GIROTTO	Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

LONDRINA, 20 de Dezembro de 2018

_____

Assinado por:
Alexandrina Aparecida Maciel Cardelli
(Coordenador(a))

UNIVERSIDAD DE LA FRONTERA

COMITÉ ÉTICO CIENTÍFICO

ACTA N°026_22

ACTA DE EVALUACIÓN
PROYECTO DE INVESTIGACIÓN FOLIO N°150/21

En la ciudad de Temuco, el 23 de marzo de 2022, el Comité Ético Científico de la Universidad de La Frontera, (Resolución Exenta N°1090 de fecha 12 de marzo de 2014 y sus posteriores modificaciones contenidas en Res. Ex. N°1090 del 12.03.2014, Res. Ex. N°4183 del 17.10.2017), en sesión ordinaria N°04_22, presidido por el Dr. Nicolás Saavedra Cuevas, con asistencia de sus miembros permanentes señor(a):

NOMBRE	PROFESIÓN
Sr. Nicolás Aguilar Farías	Kinesiólogo
Sr. Pablo Betancourt Henríquez	Cirujano Dentista
Sr. Roberto Contreras Eddinger	Abogado
Sra. Paola Durán Cuevas	Ing. Agrícola
Sr. Roberto Henzi Miranda	Médico Veterinario
Srta. Verónica Iturriaga Wilder	Cirujano Dentista
Sr. Julio López Fenner	Ing. Civil Matemático
Sra. Carolina Matamala Riquelme	Socióloga
Sra. Karin Morales Manríquez	Enfermera
Sra. Daniela Nuñez Romero	Médico Veterinario
Sr. Mario Pellon Arcaya	Médico Cirujano
Sr. Lucio Rehbein Felmer	Psicólogo
Sr. Luis San Martín Villagra	Integrante Comunidad/Prof. Normalista de Enseñanza Básica

Han evaluado y sancionado el Proyecto de Investigación, inscrito en la Dirección de Investigación como Proyecto de Investigación Científica con Fondos Propios 2021, según se indica:

Título	"Conductas de riesgo y calidad de vida en estudiantes de primer año de la Universidad de La Frontera"
Investigador Responsable	DRA. GLADYS MORALES ILLANES
Tipo de Proyecto	FONDOS PROPIOS 2021
Institución	UNIVERSIDAD DE LA FRONTERA
N° Folio del Proyecto UFRO	150/21
Decisión	APROBADO

Universidad de La Frontera, Comité Ético Científico, Av. Francisco Salazar N°01145, Fono: 45/2734114, Temuco, Chile

Fecha de Presentación al Comité Ético Científico (CEC)	24.12.2021
Fecha enmiendas solicitadas por CEC a IR	07.01.2022
Fecha Respuesta Investigador Responsable a CEC	07.01.2022
Versión	N°2
Documentos Revisados CEC	• Carta de solicitud revisión de Proyecto de Investigación. • Carta Compromiso del investigador • Carta de Apoyo Director de Depto. • Carta Directora De Investigación UFRO. • Carta Director Desarrollo estudiantil. UFRO. • Versión completa y definitiva del Proyecto de Investigación. • Resumen del Proyecto. • Carta de apoyo Universidad Castilla. La Mancha. España. • Curriculum IR • Curriculum coinvestigadores.

Propósito de la Investigación: Analizar las conductas de riesgo y calidad de vida de los estudiantes universitarios que ingresan a primer año en la Universidad de La Frontera en los años 2020 y 2021.

El Comité Ético Científico de la Universidad de La Frontera, certifica que después de evaluar el Proyecto de Investigación presentado por la Dra. Morales, se determinó que cumple las siguientes consideraciones éticas en el Área de Investigación de Seres Humanos:

1. **Validez científica:** Estudio de corte transversal, con datos provenientes de base de datos anonimizada de los resultados de la Encuesta de salud UFRO 2020 y 2021, cuyo responsable es el Director de la DDE. Estos datos incluyen las siguientes variables: Antecedentes sociodemográficos, depresión, ansiedad y estrés, intento de suicidio; consumo de sustancias; actividad física; sueño, hábitos alimentarios, salud sexual y calidad de vida.
La participación por parte de los estudiantes fue voluntaria, se aplicó una encuesta on-line durante el período de matrícula en el 2020 y durante el período de inducción en el 2021.

    Analisis Estadístico: Los datos serán presentados como promedio y DS para variables continuas, y como porcentajes para variables categóricas. Se realizarán comparaciones entre los grupos a través de test Chi-cuadrado y test student. Asimismo, se estimará la magnitud de las asociaciones por ejemplo a través de regresión logística, ajustando por variables confusoras. Los análisis estadísticos se realizarán con el Software estadístico STATA 16.0.

2. **Utilidad social de la investigación (para los participantes, la sociedad o el conocimiento):** Los estudiantes universitarios se encuentran en una etapa crítica para el desarrollo de sus hábitos en estilos de vida, que afectan sus hábitos alimentarios, práctica de actividad física, consumo de sustancias, salud mental, salud sexual, entre otras. A nivel internacional existen diversos estudios que han evidenciado el deterioro de los estilos de vida en el transcurso de los años de universidad. A nivel nacional nuestro grupo de investigación ha evidenciado altas prevalencias de consumo de tabaco y alcohol en los jóvenes universitarios. Asimismo, hemos comunicado altas prevalencias de factores de riesgo cardiovasculares en universitarios chilenos. Por lo tanto, queremos continuar aportando con nueva evidencia en temáticas de interés para los tomadores de decisión a nivel de las universidades y también contribuyendo en las políticas públicas que benefician a los estudiantes de Educación Superior.

3. **Evaluación riesgo/beneficio (relación riesgo-beneficio no desfavorable y minimización de los riesgos):** No aplica

4. **Selección equitativa de la muestra:** Estudiantes de primer año matriculados el 2020 (n= 1928) en la Universidad de La Frontera, pertenecientes a cualquiera de las carreras de la Universidad que respondieron la encuesta en salud UFRO on-line. Estudiantes de primer año matriculados el 2021 (n=1234) en la Universidad de La Frontera, pertenecientes a cualquiera de las carreras de la Universidad que respondieron la encuesta en salud UFRO online.

5. **Protección a los participantes:**

    a) **Población/Grupos vulnerable:** Estudiantes de primer año, de la Universidad de La Frontera, con ingreso en los años 2020 y 2021, pertenecientes a cualquiera de las carreras de la Universidad.

    b) **Libertad para participar**: La participación por parte de los estudiantes en la Encuesta de salud UFRO 2020 y 2021 fue voluntaria, se aplicó una encuesta on-line durante el período de matrícula en el 2020 y durante el período de inducción en el 2021.

    c) **Intimidad y Confidencialidad**: La IR trabajará con una base de datos anonimizada de los resultados de la Encuesta de salud UFRO 2020 y 2021 que será entregada por el Director de la Dirección de Desarrollo Estudiantil, DDE, Dr. Alex Seguel. (Se adjunta la carta de apoyo). Por lo tanto, la IR no tendrá acceso a ningún dato confidencial de ningún estudiante que pueda identificarlo.

    d) **Cobertura de Costos del Estudio**: No aplica

    e) **Quien asume los eventuales costos ante posibles eventos adversos graves:** No aplica.

6. **Procesos de Consentimiento Informado y revisión de los documentos en que se registran**: No aplica

7. **Consentimientos Informados por representación en el caso de las personas incompetentes que participan en una investigación:** No aplica.

8. **Compensación, mediante seguros o garantías, de los eventos adversos que pudieran preverse o que sin previsión causen daño:** No aplica

9. La IR cuenta con el apoyo del Director de Desarrollo Estudiantil de la Universidad de La Frontera, quien le entregará las bases de datos anonimizada de los cohortes 2020 y 2021, para el desarrollo de las actividades comprometidas en la investigación.

10. Intervención de Investigadores Idóneos con la experiencia y la calificación profesional acorde con el nivel de complejidad de la Investigación: Los profesionales que realizan el estudio tienen suficiente competencia científica en cuanto a experiencia y entrenamiento en las técnicas que se usaran.

11. La Dra. Morales y su equipo de investigación deberá contemplar los resguardos de protección establecido por la autoridad sanitaria en contexto de pandemia por COVID-19. Considerar las restricciones de movilidad e interacción según la fase establecida por el MINSAL en el momento que realice dichas actividades del proyecto.
(https://www.gob.cl/coronavirus/?gclid=CjwKCAiA24SPBhB0EiwAjBgkhgr6EYPGRve6Od-W7m8MI0YiLD1D6FRbrW9NTSQqGZwuYrnfHXeBzBoCpIEQAvD_BwE)

Con base a los antecedentes antes expuestos, el Comité Ético Científico de la Universidad de La Frontera, **Aprueba**, el Proyecto de Investigación, **"Conductas de riesgo y calidad de vida en estudiantes de primer año de la Universidad de La Frontera"**, presentado por la Dra. Gladys Morales Illanes, inscrito en la Dirección de Investigación como Proyecto de Investigación Científica con Fondos Propios 2021.

Mediante la presente, recordamos a Usted lo siguiente:

1. Debe conservar toda la documentación en su poder por lo menos hasta tres años finalizada la investigación.

2. Debe contar con carta de autorización firmada por el Director (es) de los Establecimientos Educacionales en que se realizará la investigación.

3. Informar al Comité Ético Científico la finalización de la Investigación.

4. La validez de esta aprobación es hasta que finalice la investigación, excepto si existe algún tipo de modificación de orden metodológico, ético, presencia de eventos adversos o bioseguridad los que deben ser informados de inmediato al CEC.

Firman para constancia:

MG. KARIN MORALES MANRÍQUEZ
1° VICEPRESIDENTE – COMITÉ ÉTICO CIENTÍFICO
UNIVERSIDAD DE LA FRONTERA

DR. NICOLÁS SAAVEDRA CUEVAS
PRESIDENTE - COMITÉ ÉTICO CIENTÍFICO
UNIVERSIDAD DE LA FRONTERA

cc.
Dra. Gladys Morales Illanes, Investigador Responsable.
Archivo CEC

Universidad de La Frontera, Comité Ético Científico, Av. Francisco Salazar N°01145, Fono: 45/2734114, Temuco, Chile

UNIVERSIDAD DE LA FRONTERA

COMITÉ ÉTICO CIENTÍFICO

UNIVERSIDAD DE LA FRONTERA
Vicerrectoría de Investigación y Postgrado
Comité Ético Científico

Temuco, 09 de *diciembre* de 2021

C O N S T A N C I A

Prof. Dr. León Bravo Ramírez
Presidente Comité Ético Científico
Universidad de La Frontera
P R E S E N T E

Yo, Alex Seguel Fuentealba, RUT: 15.257.114-3, Director de Desarrollo Estudiantil de la Universidad de La Frontera, por medio de la presente autorizo a la Dra. Gladys Morales Illanes a trabajar con la datos de la encuesta de salud estudiantil 2020 y 2021, para los fines descritos en el Proyecto de Investigación con fondos propios DFP21-0029, titulado *"Conductas de riesgo y calidad de vida en estudiantes de primer año de la Universidad de La Frontera"*. La Dra. Morales es la Investigadora Responsable de este proyecto, adscrita al Departamento de Salud Pública de la Universidad de La Frontera.

Lo anterior, a contar de la certificación, otorgada por el Comité Ético Científico de la Universidad de La Frontera y de acuerdo a la normativa legal vigente, le entregaré a la Dra. Morales las bases de datos 2020 y 2021 ANONIMIZADAS, para el desarrollo de las actividades comprometidas en la investigación.

Dr. Alex Seguel Fuentealba
Director de Desarrollo Estudiantil
Universidad de La Frontera

DICTAMEN DEL COMITÉ ÉTICO DE INVESTIGACIÓN CLÍNICA
Área de Salud de Cuenca

D. Ricardo de Miguel Ibáñez, como Presidente del Comité Ético de Investigación Clínica (CEIC) del Área de Salud de Cuenca:

C E R T I F I C A

Que este Comité ha evaluado el Proyecto de Investigación: **Estilos de vida, adiposidad y función vascular de los estudiantes universitarios de Castilla La Mancha** (REG: 2016/PI1116), emitiendo un informe FAVORABLE, aunque se recomienda puntualizar los siguientes aspectos:

• Existe una incongruencia en la metodología, ya que la muestra data del 2016, sin embargo los objetivos pretenden analizar datos desde el 2009. Aunque este CEIC conoce la línea de trabajo del grupo de la investigación, sería bueno especificar en el protocolo la continuidad con proyectos previos.
• Los cuestionarios propuestos son muchos, por lo que el grupo de trabajo debe tener en cuenta el tiempo que va a llevar hacerlos por los sujetos del estudio.

Y para que así conste donde proceda firmo el presente certificado en Cuenca a trece de febrero de dos mil diecisiete.

Presidente del CEIC

Fdo.: Ricardo de Miguel Ibáñez

COD. 025844

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