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Non-pharmacotherapeutic Management of Alcohol Use Disorder in the Alaska Native Population: A Narrative Review

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Abstract

Alcohol use disorder (AUD) is a leading preventable cause of death in the United States and has had a greater health impact on Alaska Natives than on any other racial group. To date, AUD in these communities has had wide-reaching negative impacts contributing to high rates of suicide, homicide, and accidents. A variety of genetic, experiential, social, and cultural factors have been associated with this trend. For decades, the Alaska Native subgroup has received inadequate treatment. The purpose of this review is to evaluate current trends in effective interventions and to help answer the question: What may comprise a successful non-pharmacotherapeutic interventional strategy to treat and prevent AUD in Alaska Natives? A database literature search was performed in September 2022 using the PubMed library. Search terms included (alcohol use disorder) AND ((Alaska OR Alaskan) Native). Inclusion criteria included full-text articles, a focus on specific non-pharmacotherapeutic treatment strategies, and a publication date after 2005. Studies that did not evaluate non-pharmacotherapeutic interventions, evaluated a population other than Alaska Natives, evaluated a disorder other than AUD, were written in a language other than English, or were editorials or opinion pieces were excluded. The selected studies were assessed for bias utilizing the Newcastle-Ottawa Scale (NOS). Twelve studies were included in this review. This review found that early social network intervention, incentive-driven programs, culturally-driven programs, and motivational interviewing are promising non-pharmacotherapeutic interventions in the treatment of AUD in Alaska Native communities. Evidence suggests that a shift in focus to the accentuation of protective factors and the mitigation of isolation as a risk factor, rather than on the reduction of more intractable risk factors, may be associated with improved outcomes in treating AUD. The literature also suggests that successful prevention strategies should be driven by indigenous knowledge and grounded in community and culture. This study has its limitations. These include a lack of direct comparisons between studies, a lack of pooled statistical analysis or synthesis, and a lack of quantitative analysis. Instead, the majority of data is gathered from more biasprone cross-sectional studies and, thus, should be used to provide insight into potential risk factors and non-pharmacologic therapies effective in this population rather than as strong evidence in favor of one therapeutic regimen over another. For this, there is a need for more clinical trials evaluating treatments for AUD in this population. This review received support from the University of South Florida Department of Psychiatry. There were no sources of funding for this work from any institution. There are no competing financial or non-financial interests that may be interested in this work. This review is not registered. This review does not have a prepared protocol.

Categories: Psychiatry, Public Health, Substance Use and Addiction

Keywords: substance use disorder (sud), native american, addiction disorder, alaska native, alcohol use disorder

Introduction And Background

Alaska Natives comprise a diverse community. Today, Alaska Natives make up 16% of the state's population [1]. Despite this, Alaska Natives account for a majority of alcohol-related hospital admissions in the state when compared to all other races [2]. These tribes primarily belong to five distinct native groups. Southeast Alaska, with its mild coastal climate, is home to the Tlingit, Haida, and Tshimshian groups, while the state's much harsher interior is home to the Athabascan groups. The northern and northwestern coastal region was primarily settled by the Inupiaqs, while the Yupiks settled within southwest Alaska. The smallest group of Alaska natives, the Aleuts, is native to the Aleutian islands straddling the westernmost fringes of the state [1].

It is well known that chronic alcohol use has myriad systemic manifestations, most commonly affecting the liver but also every organ system in the body [3]. Notably, the range and severity of these adverse effects have a sizable genetic component [4]. As such, genetic predisposition is a risk factor in the development of alcohol use disorder (AUD), and natural variants in genotypes encode a range of activities of the alcohol dehydrogenase and aldehyde dehydrogenase enzymes, which are responsible for alcohol metabolism [4]. Studies of allelic frequency among five distinct Native Alaskan groups - Yupik, Inupiaq, Athabascan, Tlingit, and Aleut - revealed that there are no generalizable differences between Alaska Natives with alcohol dependence and those in the general population [5]. Non-genetic risk factors for AUD include the amount of

alcohol consumed, age when drinking first began, family history of alcoholism, level of education, gender, and prenatal exposure [6].

AUD remains undertreated, contributing to significant psychosocial and public health consequences [7]. Using the DSM-5 diagnostic criteria and according to the American Psychiatric Association, current treatment guidelines state initial treatment should include goal setting for alcohol reduction and harm management in addition to exploring pharmacotherapy options [7]. For example, naltrexone, disulfiram, or acamprosate may be offered as a first-line treatment to reduce cravings [7]. Non-responders to this therapy can be prescribed second-line agents such as topiramate or gabapentin. The non-pharmacotherapeutic standard of care is cognitive-behavioral therapy, twelve-step therapy, and motivational interviewing [7]. Within the Alaska Native community, this issue is of particular urgency.

Over the course of history, the classification and diagnosis of AUD have changed, and it begs the question, did this impact reporting, and how [8]? The DSM-III and its revision loosely referred to addiction but primarily focused on dependence. The DSM-IV was able to expand on the addiction process outside of dependence. Currently, the DSM-5 notably contains the addition of cravings, removal of the criteria of legal problems, and the consolidation of the diagnoses from abuse and dependence [9].

Review

Methods

Article Search and Selection

A literature search of the PubMed database was conducted in September 2022 following PRISMA guidelines [10] using the search term (alcohol use disorder) AND ((Alaska OR Alaskan) Native) to evaluate the non-pharmacologic management of AUD in Alaska Natives. Inclusion criteria included full-text articles, a focus on specific non-pharmacotherapeutic treatment strategies, and a publication date after 2005. Studies that did not evaluate non-pharmacotherapeutic interventions, evaluated a population other than Alaska Natives, evaluated a disorder other than AUD, were written in a language other than English, or were editorials or opinion pieces were excluded. Articles were classified independently by two reviewers (NG and UD), and any discrepancies were resolved by a third reviewer (EL).

Qualitative Analysis

The Newcastle-Ottawa Scale (NOS) [11] was used for risk of bias assessment. The NOS criteria allowed for a maximum of four stars in the selection, two stars in comparability, and three stars in the outcome: the total range was 0-9 for randomized control trials and cohort studies. The total range was 0-8 for cross-sectional studies. Cohort studies, randomized controlled trials, and cross-sectional studies were analyzed with respective NOS guidelines.

	,	analysis of study ris										
		Selection					Comp	arability	Outcome			
Cohort studies	3											
Author and year	Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertain of exposi	nment interest	tration that outcome of was not present at the start udy		arability of cohorts on the	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	То
Beckstead, 2015	Cohort	1	1	1	1		0		1	1	1	7
Randomized o	controlled tria	al										
		Selection					Comp	arability	Outcome			
Author and year		Is the case definition adequate	Representativeness of the cases	Selection		n of controls	contro	arability of cases and Is on the basis of the	Ascertainment of exposure	The same method of ascertainment for cases and controls	Non- response rate	То
McDonell, 2021	RCT	1	1	1	1		0		1	1	1	7
								Comparability		Outcome		
Author and Year	Study	Representa		Sample size	Non- respondents	Ascertainment of the exposure (risk factor		Comparability of cohof the design or anal		sis Assessment of outcome	Statistical test	То
Lillie, 2021	Cross- section	1		1	1	1		0		1	1	6
Philip, 2016	Cross- section	1		1	1	1		0		1	1	6
Seale, 2006	Cross- section	1		1	1	1		0		1	1	6
Hirchak, 2018	Cross- section	1		1	1	1		0		1	1	6
Dickerson, 2016	Cross- section	1 nal		1	1	1		0		1	1	6
Allen, 2014	Cross- section	1		1	1	1		0		1	1	6
Skewes, 2016	Cross- section	1		1	1	1		0		1	1	6
Mohney, 2022*	Book chapte	- r		-	-	-		-		-	-	-
Emerson, 2019*	Review	v -		-	-	-		-		-	-	-

TABLE 1: NOS qualitative analysis of study risk

NOS: Newcastle-Ottawa Scale, RCT: randomized controlled trial

Results

An initial keyword search identified 282 articles for inclusion. A filter was applied to select for publication year, English language, and full text, leaving 192 articles for screening. Of these articles, 78 were excluded according to exclusion criteria, leaving 12 articles for further assessment. These 12 included articles

included one cohort study, one randomized controlled trial, seven cross-sectional studies, two reviews, and one book chapter (Figure 1). Data collection was conducted by a single reviewer (NG). In data collection, particular focus was placed on historical elements of AUD in Alaska Natives, psychosocial risk factors for AUD in Alaska Natives, and interventions for AUD in Alaska Natives.

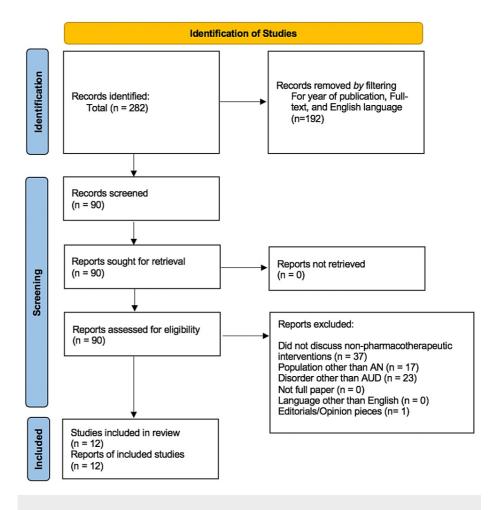


FIGURE 1: Article selection flow diagram

Qualitative assessment

The studies were assessed with appropriate guidelines to characterize their quality based on several criteria (Table 1). NOS scores of 7-9 were deemed sufficient for randomized controlled trials and cohort studies as it fell in the region of "high quality" study according to the NOS guidelines [11]. NOS scores 6-8 were deemed sufficient for cross-sectional studies. All 12 articles were within this range.

Risk factors for alcohol use in Alaska Natives

Alaska Natives experience a steadily increasing burden of alcohol use that far exceeds that of other American populations such as non-native Alaskans and Native Americans on the mainland US [12]. Research seeking to identify etiologies of alcohol use specific to Alaska Natives identified several criteria including genetics, traumatic exposure, home environment, peer interactions, and sociocultural factors [12].

Deficiencies in socialization coupled with negative-effect regulation have been implicated in the pathogenesis of AUD [8]. The introduction of alcohol into Alaska Native communities is relatively new, as these populations had no exposure to alcohol prior to contact with European colonizers [2]. Federal assimilation programs also created "lost generations" by forcibly removing children from their homes and placing them in boarding schools in which they were punished for speaking their native languages [2]. The denial of cultural customs has been attributed to impeding the successful development of native youth [2]. As such, social isolation coupled with geographic isolation may play a role in the pathophysiology of AUD within the Alaska Native subgroup.

Interventions to address alcohol use in Alaska Native communities

Today, excessive alcohol consumption is a leading preventable cause of death in the United States, disparately harming indigenous groups more severely than any other racial group [13]. Historically, many restrictive interventions have been implemented in an effort to reduce the alcohol use discrepancy faced by Alaska Natives. Alcoholic beverages have been banned by popular vote in many native villages [2]. Although proven to provide safety benefits, namely, with regard to alcohol-related violence, these local option laws remain controversial in their efficacy at preventing AUD due to the limited benefits they offer [2].

The literature currently identifies social network interventions, incentive-driven programs, culturally driven programs, and motivational interviewing as front-line non-pharmacologic interventions to simultaneously address isolation (risk factor) and accentuate community and familial engagement (protective factor).

A 2015 study on Yupik youth identified social network intervention as a promising systemic solution for AUD [14]. This study posits that increasing the density and closeness of family and elder ties could function as a protective factor against AUD [14]. A qualitative behavioral study on the Inupiaq revealed that in many communities, there exists a dissociation between a desire to live according to traditional subsistence practices preached by elders and a pressure to attend school and enter the wage economy [15]. This dissonance leads to many feelings of decreased self-worth and lack of direction [15]. Such positive intervention programs would ideally include services for high-risk youth and incorporate family treatment with the goal of building multigenerational legacies focused on promoting subsistence traditions [15]. Essentially, returning to the traditional Alaska Native community-oriented approach toward healing personal and family problems may bring about immense benefits in treating and preventing AUD [15]. Additionally, chronic alcoholic liver disease has been associated with initiating alcohol use at an early age with subsequent increases in consumption with age [16]. As a result, this technique may allow for early intervention and prevention to encourage abstinence until age appropriate and enhance protective factors.

Incentive-driven approaches centered around operant conditioning principles have also demonstrated success. Contingency management is a feasible low-cost approach to AUD treatment that utilizes positive reinforcers to promote and support abstinence. These abstinence programs endeavored to foster family relationships and integrate indigenous languages and practices, many of which have been lost due to forced assimilation [17]. This method is advantageous in the ability to customize rewards to uphold practical and cultural standards. A 2018 mixed-methods randomized controlled trial found focus groups prior to contingency management to be most effective when prizes are practical, implemented in a community context, and able to foster familial engagement [16]. This finding is corroborated by a recent randomized controlled trial of 158 Alaska Native adults diagnosed with AUD. In this study, cultural incentive-driven abstinence programs were identified as promising interventions [17]. Cultural incentives included gift cards for local businesses, fishing equipment, and local artwork [17].

Evidence for the prospective success of culturally driven therapy is the current use of tribal traditional healing. This therapy is advantageous within the Alaska Native subgroup due to its inherent emphasis on spirituality [18]. As a result, it is sought by many Alaska Natives and used regularly. One solution may be to merge biomedical treatment with traditional tribal healing methodology in an effort to provide holistic care that incorporates physical wellness with spiritual and cultural wellness as well. The concept of positive intervention with both biological and tribal healing was explored by a pilot study that combined dialectical behavioral therapy with traditional cultural treatment [19]. This study revealed a high rate of improvement among adolescents [19], which has been the key target demographic for early intervention strategies.

Motivational interviewing is another evidence-based therapy deemed consistent with Alaska Native values [20]. Studies suggest that wider dissemination of motivational interviewing within tribal treatment regimens may provide therapeutic benefits [20]. This is a patient-focused technique consisting of both a relational and technical aspect. The relational component consists of the interviewer establishing patient trust and rapport. The technical component then bolsters the individual's motivation for change and reinforces their decision [18]. Young urban patients diagnosed with AUD who engaged with this study credited both internal and external motivation in bringing about positive change in their lives [9].

Discussion

This review strongly corroborates the efficacy of an indigenous knowledge-driven and strengths-based intervention framework grounded in community and culture in addition to risk factor reduction for AUD. The implementation of indigenously informed and locally sustainable strategies is critical in the promotion of health and well-being, especially in the field of AUD treatment. Recent studies have termed this paradigm the "Qasgiq Model" of community intervention [21]. Historically a round extended kinship shelter, Qasgiq has come to represent the interdependent circle of family and community [21]. Under this model, early family and community intervention serves to provide skills, cultural strength, and values that act as protective factors [21]. Furthermore, increased participation in cultural activities and traditions may provide increased purpose and meaning to alcohol-dependent adults.

However, the complexities of regional and demographic variation may require a broader range of therapeutic approaches or only specific interventions to be implemented. Additional studies must explore cultural mechanisms and variations in alcohol use within subgroups, such as the Athabascan, Tlingit, and Aleut

populations. Furthermore, it is important to understand the granularity of behavioral patterns in these different groups to most effectively provide AUD care on both a population-specific and individualized basis.

Of note, there is a paucity of research examining drinking behavior in segments of the Alaska Native population, especially elders. This may partially be explained by a general distrust of behavioral health research following the Barrow Alcohol Study, notable for its ethics violations in cross-cultural research [22]. This study led to the propagation and widespread acceptance of the "intoxicated Indian" stereotype. Current treatment efforts should therefore aim to actively dismantle this myth. These studies underscore the importance of a collaborative and participatory framework for research and healthcare institutions. This requires fostering trusting relationships with community partners and appropriately contextualizing alcohol-related research results with respect to demographic and geographic factors [22].

Ultimately, research questions and treatment approaches should reflect local cultures, values, and experiences. In keeping with this approach, community partners have advocated for shifting to a strengths-based approach. This entails evaluating successful outcomes to accentuate protective factors in addition to addressing amenable risk factors [23]. Implementing such interventions in Alaska Natives may be especially worthwhile because despite having the highest levels of alcohol use, this population also seeks treatment for AUD at the highest rate of any other ethnicity [24]. As a result, there is great potential for improvement of AUD care in Alaska Native communities if they are provided with access to culturally competent specialized psychiatric care.

Limitations of this literature review include factors influencing epidemiological rates over an individual's life span. This includes but is not limited to recovery with and without treatment, maturing out of AUD in those surviving to older age, incarceration for AUD-related crimes, death due to AUD-related causes, and moving out of Alaska to another state. All of the aforementioned factors limit the ability to accurately assay prevalence among age groups, and thus such comparisons have been excluded from this analysis. Another shortcoming is the presence of cultural heterogeneity within the Alaska Native subgroup. The standard reporting of Alaska Natives as an entire population is subject to misinterpretation and overgeneralization. Differences in language, customs, and culture lead to a large variance in alcohol use among tribes and geographical locations [18].

As data in this field is limited, we can draw attention to how the change in DSM criteria for AUD has correlated with research on this population over the years. It appears that rates of diagnosis of AUD among natives had been increasing even prior to the change of the DSM language in 1994, but since then, more data has been collected on help-seeking behaviors and changing the approach in lieu of a culturally contextualized one [25]. More recently, data shows that Alaska Native populations with AUD, being male, and aged 35-64 were statistically significant correlates of seeking treatment or help for AUD [24]. Based on older studies, there is scant data indicating the prevalence of seeking treatment for AUD among Alaska Natives, but much of the literature focuses on violent death and adverse outcomes rather than also focusing on rates of help-seeking in this subpopulation.

From the DSM-IV to the DSM-5, the addition of cravings to the diagnostic criteria for AUD may be thought of as a perceived beneficial change as it incorporates physiological aspects of addiction, outside of tolerance and withdrawal, into the definition. This change allows for open discussion techniques to decrease use for physiological benefit rather than focusing on harm reduction counseling [8]. Removing the criteria of legal problems specifically may also introduce a wider selection of individuals with cognitive, functional, and socioeconomic protective factors [8]. The consolidation of the diagnoses from abuse and dependence to AUD also appears to lessen the stigma associated with the volitional activity of consuming alcohol and instead allows us to place the patient on a continuum of pathologic severity and give significance to the non-modifiable risk factors that do exist [8]. Additionally, the change from polysubstance dependence to each individual named disorder allows each disorder to be treated as its own entity and, therefore, more appropriately treated according to specific evidence.

Important methodological limitations of this review include the reliance on primarily cross-sectional studies for data collection. The majority of works on this topic contain analysis of qualitative data with variation in outcome measures. There is also variation within evaluated exposures, as well as heterogeneity among chosen group demographics resulting in an inability to conduct higher-order statistical syntheses of results. This renders comparison among studies in the form of a systematic review difficult. This also results in a lack of quantitative effect measures and summary statistics regarding treatment efficacy. Although all included studies were qualitatively assessed as "high quality," they all notably lacked comparability (Figure 1). As such, this increases the overall risk of bias. As a result, this body of evidence has considerably less certainty when compared to forms of more objective quantitative analysis. Furthermore, this body of work cannot be used to advocate for the efficacy of one treatment regimen over another. Instead, this work should be used as a framework to highlight important risk factors and current trends in effective non-pharmacologic treatment measures.

Conclusions

 $Treatment\ of\ AUD\ in\ the\ Alaska\ Native\ subgroup\ remains\ an\ urgent\ issue.\ This\ study\ finds\ that\ multifaceted$

approaches encompassing early social network intervention, incentive-driven programs, culturally driven programs, and motivational interviewing may be efficacious as front-line non-pharmacotherapeutic interventions in the treatment of AUD in Alaska Native communities. The literature also finds that treatment efforts that are elder-led and indigenous-knowledge-driven may be associated with improved outcomes. Furthermore, a focus should be placed on mitigating isolation as a risk factor while accentuating protective factors. It is important to note that many risk factors associated with AUD are a product of systemic manipulation that will likely require more than social intervention programs to rectify. While a broad range of therapies is likely required, we advocate for the exploration of positive intervention programs with pharmacologic and nonpharmacologic treatment strategies that have shown to be efficacious in treating Alaska Natives struggling with AUD.

Appendices



PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	N/A
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Y
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Υ
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Υ
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Y
Synthesis of results	6	Specify the methods used to present and synthesise results.	N/A
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Y
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).	Υ
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).	Υ
Interpretation	10	Provide a general interpretation of the results and important implications.	Y
OTHER			
Funding	11	Specify the primary source of funding for the review.	Υ
Registration	12	Provide the register name and registration number.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

FIGURE 2: PRISMA 2020 checklist for abstracts



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist Item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	N/A
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Pg. 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pg. 2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pg. 2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pg. 3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pg. 3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Pg. 3, 5
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.	Pg. 3
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 investigators, and if applicable, details of automation tools used in the process.	Pg. 3
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.	Pg. 3
	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.	Pg. 3
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.	Pg.3
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.	Limitations
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)).	Limitation
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Limitation
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Limitations
	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.	Limitation
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Limitations
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Limitations
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Limitations
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Limitations

FIGURE 3: PRISMA 2020 checklist (title-methods)



PRISMA 2020 Checklist

Section and Topic	item #	Checklist Item	Location where item is reported
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.	Pg. 5
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Pg. 5
Study characteristics	17	Cite each included study and present its characteristics.	Pg. 7
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Pg. 6
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.	Limitations
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Limitations
syntheses	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.	Limitations
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Limitations
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Limitations
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Limitations
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Limitations
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pg.8
	23b	Discuss any limitations of the evidence included in the review.	Pg.10
	23c	Discuss any limitations of the review processes used.	Pg.10
	23d	Discuss implications of the results for practice, policy, and future research.	Pg. 9
OTHER INFORMA	TION		
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Title Page
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Title page
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
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.	N/A

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FIGURE 4: PRISMA 2020 checklist (results-other)

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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