REVIEW ARTICLE
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Association between alcohol consumption and the risk of developing breast cancer: a systematic review

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ABSTRACT

Alcohol use is prevalent in many countries around the world and is a risk factor for several diseases, including cancer. Compared to other organs, breasts appear to be the most susceptible to the carcinogenic effects caused by alcohol. Therefore, the present study aims to verify the association between the consumption of alcoholic beverages and the risk of developing breast cancer (BC). A search was performed on the PubMed/Medical Literature Analysis and Retrieval System Online (MEDLINE), Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS), Cochrane, Clinical Trials, and Embase platforms, using descriptors relevant to the topic and published in the last 10 years. Of 675 articles, eight were included that described the relationship between alcohol consumption and BC, in Portuguese, English, and Spanish. Systematic reviews, case reports, and case series were excluded. The research was conducted by two independent reviewers between November and December 2024. The variables studied were menarche, primigravida, menopause, hormones, ethnicity, and alcohol consumption. The data were stored, synthesized, and presented descriptively. The final sample consisted of 306,204 participants. Menopause was the variable that had the greatest impact on the outcome. Alcohol appears to be harmful when consumed in excess of 5 g/day. The studies analyzed showed a positive relationship between alcohol and BC. These data are important to consolidate a literature that impacts the breakdown of the social culture of alcohol consumption, in which women are surrounded.

KEYWORDS: breast cancer; alcohol; menopause; risk factors; hormones.

INTRODUCTION

Alcohol use is prevalent in many countries around the world and is a risk factor for several diseases, including cancer. Possible mechanisms include the actions of acetaldehyde, inhibition of DNA methylation, oxidative stress, and changes in metabolism, as well as immune and hormonal functions. More than two million new cases of breast cancer (BC) are detected worldwide. Globally, there is a prevalence of almost 6.8 million cases. In women, this disease accounts for almost half of the tumors caused by alcoholic beverages[1,2].

In addition to the number of grams consumed per day, the consistency of which alcohol is consumed also influences risk. Having multiple drinks in a single day results in higher blood alcohol levels than having a single drink daily, which may trigger different metabolic pathways. Thus, women who report having seven drinks on the weekend but no alcohol consumption on weekdays may have a higher risk of BC when compared to those who consistently have one drink daily. Studies show that different patterns of alcohol consumption can have different effects on the development of BC, even when the total amount of intake is constant[3,4].

Alcohol is the greatest modifiable risk factor for BC, especially in women. It is estimated that almost 10% of all deaths from this disease are linked to the consumption of this substance. Although this is a low risk for an alarming concern in society, recent studies have shown that even low levels of alcohol can also be responsible for the development of cancer, because the neoplastic risk is dose-dependent. The positive association between them is described in more than 100 studies[5,6].

The high prevalence of this disease worldwide, together with the increase in alcohol consumption among young people, especially women, raises concerns about this association, given that there are 46.3 new cases per 100,000 inhabitants and more than 600,000 deaths annually worldwide due to BC. Despite this, the consumption of alcoholic beverages is socially accepted and often encouraged. The consequence is the tendency for the increase of this behavior in the population, which is a concern for health authorities. There is therefore an urgent need to develop greater

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knowledge and awareness of the current scenario, in addition to the creation of public policies aimed at preventing the disease and promoting health among consumers of alcoholic beverages. With this understanding in mind, this research was conceived[7].

Primary objective

To verify the association between the consumption of alcoholic beverages and the risk of developing BC, based on scientific literature.

Secondary objective

- To verify the association between the time of alcohol consumption and the development of BC.
- Identify the frequency of alcohol consumption in relation to the risk of developing BC.
- To verify the association between the amount of alcoholic beverage consumption and the risk of developing BC.

METHODS

Study design

This is a study with the design of a systematic review, based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol[8].

Eligibility criteria

Observational studies published from January 2014 to December 2024 that analyzed the association between alcoholic beverages and the development of BC, written in Portuguese, English, and Spanish, were included. Articles that had a theme that disagreed with the proposal in this work, systematic reviews, case reports, and case series were excluded.

Sources for data collection

The platforms chosen to collect data were PubMed/Medical Literature Analysis and Retrieval System Online (MEDLINE), Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS), Cochrane, Clinical Trials, and Embase. The search was conducted between November and December 2024.

Search strategy

The search was based on the question formulated according to the Patient/Problem, Intervention, Comparison, and Outcome (PICO) strategy, in which the patients are people who consume alcoholic beverages (P), the intervention is the development of BC (I), in which it is compared with people who do not consume alcohol (C), in order to know the influence of the substance on the risk of BC (O). The searches were carried out on electronic platforms using Boolean operators. The research question––"What has the scientific literature discussed about alcohol consumption and the increased risk of developing BC?"––was formulated in accordance with the PRISMA protocol, guiding the search strategy: (breast cancer) AND (alcohol). Results were limited to studies published between January 2014 and December 2024, and were in English, Portuguese, or Spanish. Only primary studies were considered. In addition to this search strategy, there are those references found manually from the selected articles.

Study selection

The studies were initially pre-selected by reading the titles and abstracts by two independent reviewers, who did not have access to each other during this stage of the review. After completing this stage, the studies were read in full to ensure compliance with the previously established criteria. Disagreements in selection were resolved by consulting a third experienced reviewer.

Data collection process

Extraction was done by reading the studies in full, including the authors, country, and year of the study. The reviewers also analyzed the scientific journals in which they were published, the study designs, sample sizes, and the objectives of each article. Important data and variables were extracted and stored in a form in Microsoft Excel.

Variables

The variables of interest are the amount of daily alcohol intake, the type of alcoholic beverage, the relationship between the time of consumption and the development of BC, and its classification according to the estrogen receptor (ER) tumor. These variables were also evaluated by the other author.

Methodological bias

Following the PRISMA protocol, some mechanisms were used to assess the methodological quality and risk of bias of the selected studies. They were used by two independent reviewers, who performed the analysis individually and without communication. For cohort studies, the Joanna Briggs Institute (JBI) Checklist for Cohort Studies was used, while for case–control studies, the JBI Checklist for Case Control Studies was used. These checklists consist of instruments for analyzing biases in the following domains: patient selection, comparability of study groups, methods for measuring exposure, identification of biases and use of strategies to deal with them, methods for evaluating outcomes, adequate follow-up time, strategies adopted to minimize loss to follow-up, and adequacy of statistical analysis[9,10].

Synthesis methods

The data were tabulated and stored in a Microsoft Excel spreadsheet created by the authors exclusively for this purpose. The data were then processed for descriptive presentation.

RESULTS

Identification and study selection

After applying the inclusion criteria obtained during this period, a total of 968 articles were obtained, of which 248 were from the PubMed/MEDLINE platform, 40 articles from the Clinical Trials platform, 19 from the LILACS platform, 266 articles from the Cochrane platform, 395 articles from the Embase platform, and 0 from the SciELO platform. The details of the selection process for this review are shown in Figure 1.

Analysis of the methodological quality of articles

As mentioned in the Methodology subtopic, cohort studies were analyzed based on the JBI Checklist for Cohort Studies, while case–control studies were analyzed according to the JBI Checklist for Case Control Studies. All articles had their methodological quality above the minimum standard of 70% of the criteria met[9,10].

General characteristics of the studies analyzed

The characteristics of the selected articles are described in Table 1. The period in which they were published was between 2014 and 2021. They originated from three continents, with Brazil and the United States having the most publications. There was a predominance of observational case–control studies (five articles). The studies analyzed aggregate a sample of 306,204 participants, with prospective cohort studies accounting for 96.6% of the sample[11-15].

Objectives and variables of specific studies

Among the articles analyzed, the age range was between 20 and 90 years. The main variables studied were menarche, primigravida, menopause, estrogen and progesterone hormones, race/ethnicity, and type, quantity, and frequency of alcohol consumption. Regarding the main outcomes, seven studies indicated the relationship between alcohol intake and the development of BC as positive; however, one study showed no association. Menopause was the variable that had the greatest impact on the outcome[11,13,15,16].

Type, quantity, and frequency of alcohol intake

The most common types of drinks were wine, beer, and distilled spirits. Among the spirits, Japanese shochu was also evaluated (180 ml of Japanese sake=22.8 g of alcohol). The amount was divided in relation to the grams of alcohol consumed per day or week. Regarding alcohol consumption frequency, it was categorized from "non-drinkers" to "high consumption," which varied from more than 4–7 drinks per day or 30 g per day. In the study by Wang *et al.*, a standard drink was considered to contain 12.8 g of alcohol for beer, 11 g for wine, and 14 g for distilled spirits per serving. In contrast, Strumylaite *et al.* used a standard of 10 g of alcohol for each serving

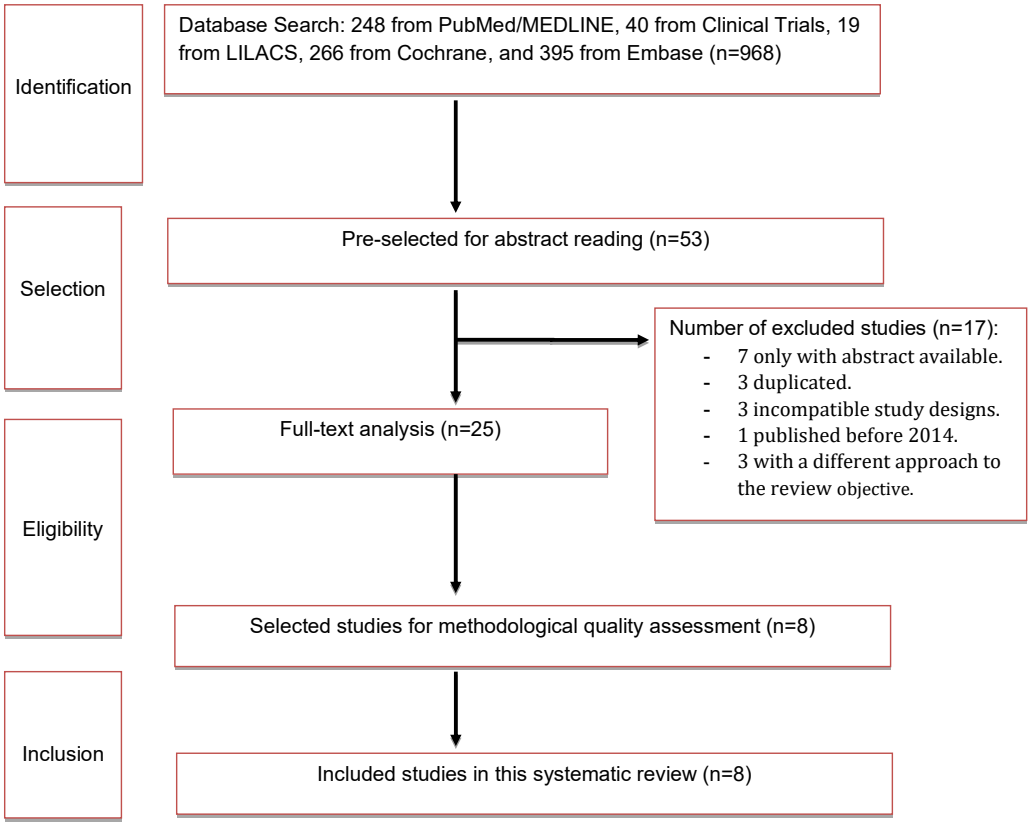


Figure 1. Study selection flowchart, December 2024, Salvador, BA.

of drink, with 250 ml for beer, 120 ml for wine, and 32 ml for spirits. Other studies did not indicate the amount of grams per serving[13,15,17].

Influence of alcohol consumption

Seven studies presented data that alcohol increases the risk of BC. Of these articles, one indicated that the positive relationship depended on the type of hormone receptor the woman had. The other showed that the increase was not significant. Only one article did not show this relationship[11-18].

Alcohol consumption, breast cancer, and menopause

Two studies showed a higher risk of developing BC from premenopausal alcohol intake, and two studies also presented consistent data for a higher risk of BC in postmenopausal women. Four studies did not find any association. Among the studies, it was found that in both pre-menopause and post-menopause, the most common type of BC was ER+ and progesterone receptor negative (PgR–). There was no evidence of interaction in relation to menopause for negative hormone receptors (ER– or PgR–) for the development of BC. The characteristics are described in Table 2[11-18].

Alcohol consumption and hormonal expression

From the analysis of the articles, it was found that two studies had no data on the relationship between hormone expression and BC risk. Only one study did not show a consistent association. Majority of the studies reported an increased risk of BC in hormone receptor-positive compared with hormone receptor-negative women. The characteristics are described in Table 3[11-18].

DISCUSSION

Alcohol consumption is a well-established risk factor for BC. This association has been confirmed by many epidemiological studies and is accepted by the International Agency for Research on Cancer. Among the results found in this systematic review, divergence was found on some points regarding the carcinogenic influence of the substance on the mammary glands. Of the eight articles selected, seven studies showed a positive relationship between alcohol and the development of BC. The study by Vargas *et al.* stated that alcohol consumption at a daily dose of ≥5 g/day, beginning at an early age and persisting into adulthood, significantly increases the chances of BC. Although studies such

Table 1. General characteristics of the studies, December 2024, Salvador, BA.

Author/Year	Country of publication	Journal of publication	Title	Study design	Sample
Portela *et al.*[11]	Brazil	*Mastology*	Association between alcohol consumption and breast cancer development: a case-control study	Case–control study	69 cases and 71 controls
Vieira *et al.*[12]	Brazil	*Asian Pacific Journal of Cancer Prevention*	Alcohol Consumption as a Risk Factor for Breast Cancer Development: A Case-Control Study in Brazil	Case–control study	406 cases and 1,100 controls
Strumylaite *et al.*[13]	United States	*Journal PLOS One*	The Association of Low-To-Moderate Alcohol Consumption with Breast Cancer Subtypes Defined by Hormone Receptor Status	Case–control study	585 cases and 1,170 controls
Park *et al.*[14]	United States	*International Journal of Cancer*	Alcohol consumption and breast cancer risk among women from five ethnic groups with light to moderate intakes: the Multiethnic Cohort Study	Prospective cohort study	85,089 patients analyzed
Wang *et al.*[15]	United States	*Springer Science+Business Media*	Alcohol Consumption and Risk of Breast Cancer by Tumor Receptor Expression	Prospective cohort study	106,037 patients analyzed
Donat-Vargas *et al.*[16]	United Kingdom	*British Journal of Cancer*	Trajectories of alcohol consumption during life and the risk of developing breast cancer	Case–control study	1,278 cases and 1,278 controls
Takizawa *et al.*[17]	Japan	*The Tohoku Journal of Experimental Medicine*	Alcohol Consumption and Breast Cancer Risk According to Hormone Receptor Status in Japanese Women: A Case-Control Study	Case–control study	1,256 cases and 933 controls
Sánchez-Bayona *et al.*[18]	Spain	*Journal Nutrients*	Binge Drinking and Risk of Breast Cancer: Results from the SUN ("Seguimiento Universidad de Navarra") Project	Prospective cohort study	104,932 patients analyzed

Source: own author.

as those by Strumylaite *et al.* and Vieira *et al.* presented results similar to the previous article, they suggested that the carcinogenic effect of alcohol on the mammary glands is enhanced by female hormones and, consequently, influenced by the hormonal cycle. In contrast, Portela *et al.* did not present scientific evidence supporting a correlation[11-18].

Regarding the influence of alcohol on the development of BC, Portela *et al.* found no data to suggest that the effects of alcohol are cumulative over time. Furthermore, a protective effect was observed in moderate wine intake (<1 dose/day), inferring that the harmful effect of alcohol was partially reduced due to the antioxidant agents present in the grapes in the drink. The study by Takizawa *et al.* also did not suggest such a clear positive association between the history of alcohol consumption and BC risk, even after calculating the odds ratio for heavy (>50 g/day) and occasional (≥30 g/day) drinking. The other six studies strongly

Table 2. Alcohol consumption, breast cancer, and menopause, December 2024, Salvador, BA.

Author/Year	Association with menopause
Portela *et al.*[11]	No association was found between BC, alcohol consumption, and menopause.
Vieira *et al.*[12]	Menopause was defined as age ≥45 years. The data highlight the role of alcohol in premenopausal women, suggesting that the association between alcohol consumption and breast cancer may be at least partially mediated by the estrogen pathway.
Strumylaite *et al.*[13]	In the general sample, we found no significant interaction between alcohol consumption and menopausal status. Menopause was was defined as age ≥ 45 years.
Park *et al.*[14]	In this large multiethnic population, alcohol consumption of ≥5 g/day was associated with an increased risk of postmenopausal breast cancer. The increased risk with high-alcohol intake was consistently found among African American, Japanese American, Latino, and White women––but not among Native Hawaiian women––and appeared to be independent of ER/PR status.
Wang *et al.*[15]	Menopausal women who did not use alcohol were less likely to develop breast cancer. There was no clear linear trend in alcohol consumption and the chance of BC.
Donat-Vargas *et al.*[16]	An increasing positive association between alcohol and breast cancer risk was consistently observed, particularly in postmenopausal women and for the HER2-negative luminal subtype (70% of cases).
Takizawa *et al.*[17]	The age at menopause ranged from 48 to 54 years. No consistent association was found between breast cancer, alcohol intake, and menopause.
Sánchez-Bayona *et al.*[18]	The risk of premenopausal breast cancer increased markedly for women in the heavy drinking category. Project SUN participants were relatively young, which may partially explain the low incidence of breast cancer, especially postmenopausal breast cancer.

Source: own author.

Table 3. Hormonal expression and breast cancer, December 2024, Salvador, BA.

Author/Year	Hormonal expression
Portela *et al.*[11]	Not informed in the article.
Vieira *et al.*[12]	Not informed in the article.
Strumylaite *et al.*[13]	A higher risk of developing breast cancer was observed in positive hormone receptors (ER+ and PR+) have, while there was no evidence for negative hormone receptors (ER– and PR–).
Park *et al.*[14]	No indication of an association between alcohol consumption and breast cancer by hormone receptor status was found in the study population. This finding suggests that the interaction between alcohol consumption and breast cancer development is not fully explained by estrogen-mediated action.
Wang *et al.*[15]	When considering each tumor marker separately, no significant heterogeneity was found between alcohol consumption and breast cancer risk. However, increasing alcohol intake was positively associated with an increased risk of AR+, ER+, or PR+ breast cancer, but not AR–, ER–, or PR– breast cancer. For example, each 11 g increase in alcohol (approximately one drink) per day was associated with a 10% increased risk. However, there was no apparent dose–response relationship for AR– breast cancer.
Donat-Vargas *et al.*[16]	There is an increased risk of breast cancer in ER+/PR+ tumors.
Takizawa *et al.*[17]	The study demonstrates a slightly increased risk of ER+/PgR+ cancer among women who consumed ≥15 g/day of alcohol. The risk of ER+/PgR– tumor was higher for premenopausal women (p=0.01). This analysis did not include risk assessment for ER–/PgR+ due to the small number of cases.
Sánchez-Bayona *et al.*[18]	There is a consistent association between alcohol consumption and hormone receptor-positive tumors, while an inconclusive or no association with hormone receptor-negative tumors.

Source: own author.

pointed to a carcinogenic relationship with alcohol consumption. The study by Vargas *et al.* suggested that the substance can accumulate over a lifetime, which implies a greater chance of developing cancer in consumers of high concentrations that persist for years. The study also argued that zero or low intake throughout life has a weak association with BC, an idea also supported by Wang *et al.*[11-18].

Furthermore, Vieira *et al.* observed that women under 50 years of age had a three times greater risk of developing BC associated with alcohol intake compared to women over 50 years of age. These data highlight that the influence of alcohol on BC in premenopausal women may be at least partially mediated by the estrogen pathway, although this is still not very clear in the literature. Studies such as those by Park *et al.* stated that a daily intake of ≥5 g of alcohol already increases the risk of BC, and similar results were also found in the systematic review of Jun *et al.* According to them, there is no safe level of alcohol consumption, since even light consumption has a dose–response effect on the tumor. However, heavy alcohol consumers have a higher risk. These data were also confirmed in the aforementioned article, since the group in which intake was higher (≥30 g/day) presented a 53% increase in risk after adjustments for potential confounding variables. These conclusions were similar to those of the meta-analysis study by Seitz *et al.*, which found a 4% increase in the risk of BC by consuming up to one alcoholic drink per day. The risk more than doubles and can rise up to 50% when associated with heavy consumption of the substance, as well as an intrinsic risk of a family history of the neoplasia[12,14,19,20].

As for menopause, it was the variable that had the greatest impact on the outcome. Alcohol is strongly linked to hormone-sensitive cancers, which include prostate and testicular cancers in men and breast, ovarian, and endometrial cancers in women. In addition to this, it is also believed that the mechanisms of action are greater for women, due to greater aromatization, impaired estrogen metabolism in the liver, and stimulation of adrenal steroidogenesis. The studies by Vieira *et al.* and Bayona *et al.* both associated BC with premenopausal women, with Vieira *et al.* attributing the risk partly to the influence of the estrogen pathway, while Bayona *et al.* linked it to excessive consumption of the substance. On the other hand, Vargas *et al.* linked BC to postmenopausal women, especially in women who were obese or overweight, due to to increased enzymatic expression of aromatase in the breast and increased local estrogen production. In addition, the low amount of body fat serves as a protective factor against neoplastic risk, since the ovaries no longer function to produce female hormones, and the main source of estrogen in postmenopausal women would be adipose. While in the study by Park *et al.*, the association with postmenopausal women was observed at alcohol intakes greater than 5 g/day. However, four other studies found no association between alcohol consumption and menopausal status[11-18,21,22].

Regarding hormonal expression, several aspects of alcohol consumption and the risk of developing BC are still under scientific discussion. Among them are the effects of BC defined by the status of the ER and PR. Among the studies, five reported an increased risk for hormone receptor-positive (ER+/PR+) BC. Hormone receptor-negative tumors presented an inconclusive or negative association, mainly due to the lack of documented cases. Other studies have not indicated any association of serum ethanol and BC by hormone receptor status in the study population, suggesting that cancerous development is not fully explained by estrogen-mediated action. In short, unlike other organs, breast carcinogenesis is stimulated by even very low levels of ethanol that would not necessarily affect other tissues. Therefore, small concentrations of alcohol significantly increase serum estrogens, according to the meta-analysis by Seitz *et al.*[13,15-19].

As analyzed in a mixed-method research in the study by Sinclair *et al.*, women's knowledge about alcohol being a modifiable risk factor for BC is low, and this lack of understanding indicates that women are not well equipped to assess the consequences of their own alcohol intake. Understanding the risks requires health professionals to work to foster a broader cultural change around alcohol use. With this understanding, future research should consider the benefits of abstaining from alcohol or drinking responsibly about the harmful effects of this carcinogenic substance. More studies are also needed to understand the best way to incorporate a prevention habit that includes providing clear information, considering that consolidated literature enriches arguments for health professionals to alert the population and, especially, women[23].

The limitations of this study are related to the fact that the sample consisted of observational studies, in which it was impossible to infer causality from the reviewed articles, as well as to a recall bias due to the interview methodology. In addition, not all articles fully presented the points analyzed in this review and, when present, the data were described differently, which made it impossible to conduct a meta-analysis associated with the systematic review. Although this study includes the risk of bias related to the subjective analysis of articles, it provides the best possible evidence with the available data based on the overall assessment of a careful team following systematic review criteria.

CONCLUSIONS

After analyzing the studies included in the sample of this systematic review, it was possible to verify the existence of a positive association between the consumption of alcoholic beverages and the risk of developing BC. The studies indicated that alcohol consumption is already harmful when consumed above 5 g/day, since breast tissue is more sensitive than other organs in the body, meaning that a small dose would not necessarily cause neoplastic damage in a different location.

The authors also emphasize that alcohol consumption alone does not define the risk of BC; it depends on other variables, such as menopause and hormonal expression. These findings are essential to corroborate the literature on this extremely important topic, since it has a major impact on the lives of women who are surrounded by the social culture of alcohol consumption.

AUTHORS' CONTRIBUTIONS:

SSC: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Visualization, Writing – original draft, writing – review & editing. GNC: Data curation, Software, Visualization, writing – review & editing. MNF: Supervision, Validation. MGS: Methodology, Supervision, Validation.

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