

# Alcohol

## Science Summary

Alcohol consumption increases risk for breast cancer, as demonstrated by a large body of research. The more you drink, the higher your risk, and even light drinking increases risk. Very little research has specifically examined whether this finding is consistent across all racial and ethnic groups, although one study found that the risk associated with drinking was higher for Black women than for White women.

## What the Foundational Documents Say

Overall, the foundational documents, authoritative reviews, and meta-analytic studies support the assertion that alcohol consumption is causally related to breast cancer, and many studies support a dose-response based upon 10 grams/alcohol per day. A standard drink (12 ounces of beer, 5 ounces of wine, or one shot of liquor) has approximately 14 grams of alcohol.<sup>1</sup>

The AICR continuous update project reported that consuming alcoholic drinks probably increases risk of pre-menopausal breast cancer and that the evidence is convincing that alcohol consumption increases risk of post-menopausal breast cancer. In both pre- and post-menopausal breast cancer, the relationship between alcohol consumption was dose dependent. For each 10 grams of ethanol consumption per day, pre-menopausal risk increases by 5% and for post-menopausal breast cancer, risk of both ER+/PR+ and ER+/PR- breast cancer increases by 9%.<sup>2</sup>

Both the IBCERCC report<sup>3</sup> and IOM report<sup>4</sup> listed alcohol as a known risk factor for breast cancer, and the IOM indicated that alcohol has one of the clearest relationships to the disease. The CBCRP gaps document discussed alcohol as a recognized risk factor.

Several meta-analytic studies between 2002 and 2008 show that the overall data across studies confirms a link between breast cancer and alcohol consumption. These analyses found increased risk of 22% comparing drinkers and non-drinkers,<sup>5</sup> and a 27% higher risk of ER+ breast cancer and 14% higher risk of ER- breast cancer when comparing those with the highest levels of consumption with those with lowest consumption.<sup>6</sup>

Furthermore, these earlier meta-analyses suggested a dose-response with 7-10% increased risk per 10 grams per day of alcohol consumption,<sup>5,7</sup> with evidence of increased risk of both ER+ breast cancer (approximately 12% higher risk) and ER- breast cancer (approximately 7% higher risk) per 10 grams alcohol/day.<sup>6</sup> A 2003 review estimated that 8% of breast cancer cases could be attributed to alcohol consumption.<sup>8</sup>

A 2017 updated review by the same authors noted that the International Agency for Research on Cancer (IARC) found sufficient animal and epidemiological evidence to conclude that alcohol is causally related to breast cancer.<sup>9</sup> The IARC Monographs in both 2010 and 2012 offer detailed reviews of the literature to date regarding alcohol and breast cancer. They conclude that alcohol is causally related to female breast cancer and that the data on male breast cancer is inconclusive.<sup>10,11</sup>

### The Current State of the Evidence

Several meta-analyses and reviews since 2012 confirm the conclusions of the foundational documents. A 2015 meta-analysis of 16 studies found 28% higher risk among those with the highest consumption, when compared to the lowest consumption.<sup>12</sup>

A 2015 meta-analysis included 38 studies that specifically separated out people who never drank (abstainers) from occasional drinkers (which some other studies classified as abstainers), low-level, and high-level drinkers. They found 3% higher risk among occasional drinkers (<10g/week), 8% higher risk among low-level drinkers (<21g/day), 37% increased risk among hazardous-level drinkers (21-40g/day), and 34% higher risk among harmful-level drinkers (>40g/day), compared to abstainers.<sup>13</sup>

Several studies have included alcohol consumption as part of a healthy lifestyle index that includes other indicators, such as diet, smoking, physical activity, and body weight/BMI. In these studies, lower consumption of alcohol is considered healthier. These studies generally find that adherence to the index is protective and non-adherence increases breast cancer risk, regardless of the specific factors included in the index.<sup>14,15,16,17</sup> When these studies look specifically at alcohol consumption, controlling for the other factors, risk still appears to be increased. One study found 17% higher breast cancer rates among women who consumed more than 19.9 grams of alcohol/day.<sup>15</sup> Another study found alcohol intake in the range of 15-30 grams/day was associated with 79% higher breast cancer risk, compared to non-drinkers.<sup>18</sup>

A U.S. study of women under age 65 with private insurance or Medicaid, found that 12.3% of breast cancer cases among women aged 18-44 and 7.1% of breast cancer cases among women aged 45-64 could be attributed to alcohol consumption, and that \$148.4 million in estimated medical costs are attributable to alcohol related breast cancers.<sup>19</sup> Another study estimated that 4.9% of breast cancers could be avoided if alcohol consumption were eliminated completely.<sup>20</sup>

Research globally is less consistent. This may be due to variations in study quality, although nearly all recent studies adjusted models are based upon similar risk factors. These variations may also be due to different common patterns of drinking globally, other cultural factors, and genetics that are not captured via the common covariates.

Among women in Brazil, risk was almost five times higher among women under 50 who had consumed alcohol and nearly four times higher among women over 50.<sup>21</sup> In Italy, a study of alcohol consumption of more than 10 grams/day was associated with 30% higher risk of breast cancer.<sup>22</sup> A study of South Korean women found that ever consuming alcohol was associated with 19% higher risk of invasive breast cancer.<sup>23</sup>

A study from Japan found no effect for any alcohol-related factors.<sup>24</sup> In Southern Australia, researchers found correlations between alcohol consumption and breast cancer in a population-based study, but odds ratios were not elevated in a case-control study at any age.<sup>25</sup>

### Patterns of Drinking and Types of Alcoholic Beverages

Meta-analyses of light drinking also suggest increased risk. Pooled data from 110 studies of light drinking suggests 5% higher risk overall. Among studies from North America, estimates ranged from 2% to 9% higher risk.<sup>26</sup> A 2018 meta-analysis of 27 studies of very light (less than .5 drinks/day) and light (.5 to 1 drink/day), found 4% higher risk of breast cancer among very light drinkers, 9% higher risk among light drinkers, and 13% higher risk among moderate drinkers. This validates the idea that alcohol consumption is dose-dependent and suggests that any level of drinking may increase risk.<sup>27</sup>

In another meta-analysis of 26 studies specifically looking at wine consumption, overall risk was increased by 36% among those with the highest levels of consumption compared to the lowest. Among pre-menopausal women with the highest levels of wine consumption, risk was 79% higher, but there was no statistically higher risk among post-menopausal women. When the consumption of other alcoholic beverages was analyzed, there was no overall increased risk.<sup>28</sup>

A study from the United Kingdom found 27% increased risk per 10 units (standard drinks of any alcoholic beverage) of alcohol consumption per week and a linear association of nearly double risk per 10 units of consumption of spirits.<sup>29</sup>

In the Sister Study, a large cohort study of sisters of women diagnosed with breast cancer, binge drinking (defined as drinking four or more drinks at one time) was associated with 29% higher risk of breast cancer compared to low-level drinking. Among modest drinkers who binged, risk was 25% higher than low-level drinkers who never binged. Finally, blackout drinking was associated with 39% higher risk. All analyses controlled for other key risk factors.<sup>30</sup>

Alcohol dependency (defined as attendance at alcohol treatment centers) was associated with more than tripled breast cancer risk in a Danish study.<sup>31</sup>

## Race/Ethnicity

One study found that drinking more than 14 drinks/week was associated with 78% higher risk overall. However, among Black women only, having 14 or more drinks nearly tripled the risk of breast cancer.<sup>14</sup>

Another study sought to understand whether alcohol consumption and dietary factors partially explained racial disparities in breast and other cancers. They found that, while nutrition and physical activity adherence both partly explained differences in breast cancer rates between Black and White women, alcohol did not explain the different incidence rates.<sup>32</sup>

A 2017 study looked at the association of alcohol and breast cancer risk in the AMBER Consortium, a cohort of Black women drawn from several different projects. They found 33% higher overall breast cancer risk among Black women who drank 14 or more drinks per week, compared to 0-4 drinks per week. When they looked at specific breast cancer subtypes, having more than 7 drinks/week was associated with increased risk of four subtypes: ER-, PR-, HER2- and triple-negative. Increased risk was in the range of 28-39% for all four subtypes.<sup>33</sup>

## Subtypes

Several studies suggest an association between alcohol consumption and ER+ breast cancer. A study in the U.K. found 9% higher risk of ER+ breast cancer among drinkers, but no effect for ER- breast cancer.<sup>34</sup> Similarly, a Norwegian study found 14% higher risk of luminal A (ER+ and/or PR+) breast cancer among those who drank three or more glasses of wine per week. Another study found that those who drank at the time of their diagnosis were 35% more likely to be diagnosed with ER+ breast cancer than HER2+ breast cancer, and that there was no differential risk for triple-negative breast cancer.<sup>35</sup>

As noted above, in one study of Black women, alcohol consumption was associated with about 1/3 higher risk of ER-, PR-, HER2-, and triple-negative BC.<sup>33</sup> Due to the lack of additional studies examining disparities in subtypes of breast cancer stratified by race and ethnicity, it is not clear if different patterns would be found in different communities.

A large U.S. cohort study found trend effects for both invasive ductal and lobular breast cancer. Consuming more than 20 grams of alcohol per day was associated with 26% higher risk of invasive ductal cancer and 43% higher risk of invasive lobular cancer.<sup>36</sup>

## Nuances and Emerging Considerations

### Interactions with Hormone Replacement Therapy and B vitamins

There is some evidence that the effects of alcohol intake may interact with pharmaceutical hormones, and that B vitamins may ameliorate some of the risk of alcohol intake in some cases. In one study of Hormone Replacement Therapy (HRT) use and alcohol consumption, both increased risk independently (combined estrogen/progestin HRT nearly doubled risk, estrogen alone increased risk by 40%, and alcohol consumption increased risk by 25%). Among those on HRT who also consumed alcohol, risk was more than doubled.<sup>37</sup>

Intake of Vitamin B9 (folate) may be protective. Alcohol consumption as reported in 10g/day dose increments increased risk by 11% among those with low folate (Vitamin B9) intake.<sup>38</sup>

### Family History and BRCA Status

Alcohol consumption may affect risk more notably among women with a family history of breast cancer. In one study, each 10 grams of alcohol consumed per day increased risk by 4% among those with no family history of breast cancer but increased risk by 16% among those with a family history.<sup>39</sup> A 2019 study of BRCA carriers found that alcohol consumption was not associated with risk among women with BRCA1 or BRCA2 mutations.<sup>39</sup>

### Genes, Mechanisms, and Metabolomics

Studies and reviews have suggested multiple mechanisms for alcohol's effects on breast cancer risk. One experimental study randomly assigned 51 post-menopausal women to three different daily doses of alcohol consumption in a crossover study design. Each woman was randomly assigned to 0 grams/day, 15 grams/day or 30 grams/day for 8 weeks, and then switched to another dose, cycling through all three conditions. Estrogen metabolism was disrupted with alcohol consumption as consumption increased from 0 to 15 grams/day to 30 grams/day.<sup>40</sup>

One review suggested that acetaldehyde, which is a carcinogenic metabolite of alcohol, may increase circulating hormones, and that this may be one mechanism that explains the link between alcohol consumption and breast cancer specifically.<sup>41</sup> A study of triple-negative breast cancer cells in culture found that even low concentrations of alcohol (0.025-0.1% v/v) led to cellular proliferation (growth and multiplication), migration, and invasion into the growth medium. These changes were associated with alcohol-induced oxidative stress.<sup>42</sup> One study used emerging data on metabolomics to understand the link between 617 metabolites from 55 foods, food groups, and vitamin supplements and breast cancer risk. Of these metabolites, 12 of the 617 were related to alcohol consumption. Ten of these 12 alcohol-related metabolites were among the top 20 metabolites linked to breast cancer.<sup>43</sup>

Studies of gene-environment interactions have shown mixed results. In one study, a polygenic risk score was calculated based upon the presence of 77 single nucleotide polymorphisms. Of several environmental factors studied, alcohol had the strongest multiplicative effect on breast cancer risk. In other words, breast cancer risk was increased most strongly among women with the highest score based upon combined genetic polymorphisms associated with breast cancer who also consumed alcohol.<sup>44</sup> Other studies found no interactions between alcohol and genetic variants, despite seeing increased breast cancer risk with alcohol consumption.<sup>45</sup>

### Breast Density

The relationship between breast density and alcohol consumption is explored more fully in the breast density section of this report. However, it is worth noting that the research is inconclusive. For example, one study found no relationship in breast density associated with alcohol consumption.<sup>46</sup> Another study found that women who consumed alcohol were almost twice as likely to have dense breasts.<sup>15</sup> A third study found no overall effect of alcohol consumption on breast density; however, among women with past hormone therapy, those who consumed more than 5 grams of alcohol/day had denser breasts.<sup>47</sup>

## Take-Home Message

- Alcohol is causally related to breast cancer, in a dose-dependent manner.
- Risk appears to be higher among heavy drinkers and binge drinkers, but even light drinkers have elevated risk compared to non-drinkers.
- Few studies have explored whether these patterns hold across different racial and ethnic groups. However, results from one study suggest that the risk associated with drinking may be more elevated among Black women than White women.

## Alcohol: Context for Interventions

California is the fourth largest wine producer in the world<sup>48</sup> and home to more than 1,000 craft breweries.<sup>49</sup> Despite this, California is not one of the highest high-risk alcohol consuming states: it ranks 22nd in binge and heavy drinking.<sup>50</sup> Still, indirect costs of excessive drinking (lost work productivity, healthcare expenses, criminal justice, and motor vehicle crash costs) amount to \$35 billion per year, more than in any other state.<sup>51</sup>

Per capita, Californians drink 2.33 gallons of ethanol in alcoholic beverages a year.<sup>52</sup> This is slightly over the 2.1 gallons per person per year goal (the equivalent of about 448 standard drinks per person per year<sup>53</sup>) set out in the federal Office of Disease Prevention and Health Promotion's Healthy People 2020 report.<sup>54</sup> The 2015-2020 U.S. *Dietary Guidelines for Americans* recommends that if alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and two drinks per day for men—and only by adults of legal drinking age. The Guidelines also recommend that individuals who do not already drink alcohol should not start.<sup>55</sup>

However, research on breast cancer risk related to alcohol consumption brings into question whether this level is still too high. For instance, the World Cancer Research Fund recommends not drinking any form of alcohol (this includes wine, beer, and all forms of liquor) in order to reduce risk of breast and other cancers.<sup>56</sup> Shifting the drinking habits of Californians, whether to one drink a day or total abstinence, will require more education and a cultural shift away from ubiquitous access to alcohol, especially in social settings.

This is no simple task. While there is a great need to raise awareness about the link between breast cancer risk and alcohol consumption, actually changing women's behavior will be difficult. One study found that a mass media campaign was successful in raising awareness about the connection to breast cancer and significantly increased people's support of policies intended to reduce alcohol consumption, but this awareness did not affect the study subjects' motivation to change their drinking habits.<sup>57</sup>

Addressing alcohol consumption among youth is especially important. The National Institute of Alcohol Abuse and Alcoholism notes that alcohol is the most widely abused substance among America's young people.<sup>58</sup> While California's minimum drinking age has been 21 since the end of Prohibition,<sup>59</sup> a 2018 report found that nearly 21%

of youth aged 12-20 in California had consumed alcoholic beverages in the past month.<sup>60</sup> Better enforcement of the minimum drinking age is needed.

In addition to the many ways that drinking can increase risky behavior while under the influence, drinking at a young age sets the stage for long-term challenges: adolescents who start drinking before 15 years of age are at four times the risk of developing alcohol dependence as those who start drinking after 20 years of age.<sup>61,62,63</sup> Among U.S. youth who drink, approximately 50% of those 12 to 14 years of age and 72% among those 18 to 20 years of age drink heavily.<sup>64</sup> Young people who have higher exposure to alcohol marketing appear to be more likely to initiate alcohol use and engage in binge and hazardous drinking.<sup>65</sup>

Fortunately, policies to reduce alcohol consumption have been shown to be effective. In fact, having stronger alcohol policies in general, even those that do not target youth specifically, reduces the likelihood of youth alcohol consumption<sup>66</sup> and heavy/binge drinking overall.<sup>67</sup> Raising prices and reducing availability (e.g., reducing the number of sales outlets) were found to be helpful in reducing binge drinking in particular.<sup>68</sup> In general, stand-alone education programs about the risks of alcohol have been less successful, but a combination of policy approaches and education has potential to reduce alcohol consumption.<sup>68</sup>

Overall, there are many evidence-based approaches to reduce alcohol consumption (See Text Box: The American Society of Clinical Oncology's Recommendations to Reduce Alcohol Consumption); California has embraced a few of these measures, but there are many others that the state could adopt. Compared to other states, California has relatively low taxes on alcoholic beverages: In dollars per gallon, distilled spirits are taxed at \$3.30 (20th in the country), beer at \$0.20 (25th in the country), and \$0.20 for wine (tied with Texas for the lowest).<sup>69</sup> The higher the tax, the more drinking can be expected to go down, especially for younger drinkers.<sup>70</sup> Local governments in California could also use their zoning powers to limit the number of alcohol outlets and the hours of sale.<sup>71,72</sup> One Australian study of 20- and 22-year-olds found that "for each increase in liquor stores over time, alcohol consumption increased by 1.22g/day or 8%, and for each additional club license, consumption increased by 0.90g/day or 6%."<sup>73</sup> Another important piece is improving the public's understanding that the risks of alcohol consumption are both short-term (e.g. higher rates of motor vehicle accidents and neighborhood violence near high concentrations of retail alcohol outlets<sup>74</sup>) and long-term (e.g. increased risk for breast and other cancers over a person's lifetime). Women need to be empowered with the knowledge of the health risk so that they can make informed decisions.



## The American Society of Clinical Oncology's Recommendations for Evidence-Based Approaches to Reducing Alcohol Consumption

Below are some of the evidence-based approaches to reducing cancer risk from alcohol consumption recommended by the American Society of Clinical Oncology (ASCO):<sup>75,76</sup>

1. Clinical strategies of alcohol screening and brief intervention: Health care providers can screen adults, including pregnant women, for excessive alcohol use to identify people whose levels or patterns of alcohol use place them at increased risk of alcohol-related harms.
2. Regulate alcohol outlet density: Using regulatory authority to reduce the number of alcohol outlets in a given area (i.e. density) has proven to be an effective strategy for reducing excessive alcohol consumption.<sup>77,78,79,80</sup>
3. Increase alcohol taxes and prices: Increasing taxes, and therefore the overall price of alcohol, has been shown to reduce levels of excessive consumption and related health harms.<sup>81,82,83</sup>
4. Maintain limits on days and hours of sale: Evidence from several studies has demonstrated the positive impact that reducing the number of days or hours that alcoholic beverages are sold generally results in a decrease in related harms.<sup>84,85</sup>
5. Enhance enforcement of laws prohibiting sales to minors: The minimum legal drinking age is 21 years in all U.S. states. Enhanced enforcement of the minimum legal drinking age can reduce sales to minors (younger than 21 years) in retail settings (such as bars, restaurants, liquor stores), thereby helping to reduce youth access to alcohol.<sup>86</sup>
6. Restrict youth exposure to advertising of alcoholic beverages: Early onset of drinking has been associated with an increased likelihood of developing dependence on alcohol later in life,<sup>87</sup> and studies have demonstrated that youth exposed to more advertisements also show increases in drinking levels.<sup>88,89</sup>

In addition to these strategies, ASCO supports "efforts to eliminate pinkwashing in the marketing of alcoholic beverages. Pinkwashing is a form of cause marketing in which a company uses the color pink and/or pink ribbons to show a commitment to finding a cure for breast cancer. Given the consistent evidence that shows the link between alcohol consumption and an increased risk of breast cancer, alcoholic beverage companies should be discouraged from using the symbols of the battle against breast cancer to market their products".<sup>90</sup>

The global alcohol industry spends more than \$4 billion each year marketing its products.<sup>91</sup> Federal law allows alcohol companies to largely self-regulate how they advertise. One voluntary industry guideline is to only advertise to an audience that can be reasonably expected to be at least 70% of legal drinking age.<sup>92,93,94,95</sup> However, the industry often does not comply with this guideline.<sup>96</sup>



Alcohol consumption increases risk for breast cancer. The more you drink, the higher your risk, and even light drinking increases risk.

## INTERVENTIONS

**Overarching Goal:** Significantly expand public education on the link between breast cancer risk and alcohol consumption and expand support and incentives to reduce consumption of alcoholic beverages for girls and women.

### Intervention Goal 1

Greatly improve public knowledge of the link between alcohol and breast cancer risk.

**Objective 1:** Launch a state-wide public education campaign explaining the breast cancer risk from alcohol consumption.

- **Strategy 1:** Require the California Department of Public Health, in consultation with other relevant stakeholders, to develop effective public health messages to raise awareness of the link between breast cancer risk and drinking and to reduce alcohol consumption.
- **Strategy 2:** Develop a distribution plan for the public health messages about drinking and breast cancer that includes public service announcements and various social media platforms.

**Objective 2:** Revise the *Health Education Curriculum Framework for California Public Schools, Transitional Kindergarten Through Grade Twelve*, which already covers the subject of alcohol use, to specifically include the connection between alcohol consumption and breast cancer risk.<sup>97</sup>

**Objective 3:** Develop educational materials on the breast cancer-alcohol connection in multiple languages that can be easily adapted to the needs of different communities and distribute them widely through health clinics, community events, and other outreach opportunities.

### Intervention Goal 2

Strengthen, fully implement and, where appropriate, enforce measures to reduce alcohol consumption (modeled after American Society of Clinical Oncology's recommendations).

**Objective 1:** Adopt alcohol screening and education in clinical settings.

- **Strategy 1:** Medical institutions can expand alcohol screening practices from primarily focusing on reducing heavy drinking and addiction to be more inclusive of education on the dose-dependent link to breast cancer risk and other health concerns.

**Objective 2:** Regulate alcohol outlet density.

- **Strategy 1:** Cities should reduce the number of permits to sell alcohol in retail outlets, bars, or restaurants and ensure that permits that are granted are not concentrated in vulnerable communities.<sup>98</sup>

**Objective 3:** Increase alcohol excise taxes and designate some of the revenue for alcohol consumption reduction and education activities.

- **Strategy 1:** Raise the California state excise tax on the sale of distilled spirits, beer, and wine to a level comparable to the highest state excise tax rates in the nation.
- **Strategy 2:** Commit a substantial portion of the funds raised from the tax increase toward efforts to educate the public about the health impacts of drinking alcohol, including the impact on breast cancer risk.

### Intervention Goal 2 (continued)

Strengthen, fully implement and, where appropriate, enforce measures to reduce alcohol consumption (modeled after American Society of Clinical Oncology's recommendations).

**Objective 4:** Maintain limits on days and hours of sale of alcohol.

- **Strategy 1:** Oppose efforts (including legislation) to extend bar hours. Legislation to change closing time for bars from 2 a.m. to 4 a.m. in certain cities has been introduced in California on at least two occasions.<sup>99</sup>

**Objective 5:** Enhance enforcement of laws prohibiting supplying alcohol to minors, both by vendors and adults buying alcohol for minors.

- **Strategy 1:** Ensure local police departments are fully trained and funded to enforce the minimum drinking age of 21. Community members and community-police advisory boards should be fully engaged in setting priorities in how to best enforce this law.
- **Strategy 2:** Increase capacity for campus police or security to enforce the minimum drinking age of 21.

**Objective 6:** Restrict youth exposure to advertising of alcoholic beverages.<sup>100</sup>

- **Strategy 1:** Cities should prohibit alcohol advertising within 500 feet of all schools, playgrounds, and other places where youth are likely to be present.<sup>101</sup>
- **Strategy 2:** College campuses should further limit and consider banning all advertising of alcoholic beverages.<sup>100</sup> For example, currently California State University allows advertising of beer and wine, but not distilled spirits. This rule could be expanded to be inclusive of all alcoholic beverages.<sup>102</sup>

### Intervention Goal 3

Expand research on the link between alcohol consumption and breast cancer.

**Objective 1:** Support research to better understand the effectiveness of interventions, including educational messages, to reduce alcohol consumption in response to breast cancer risk.

**Objective 2:** Support research to better understand the mechanisms of how alcohol consumption increases breast cancer risk.

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