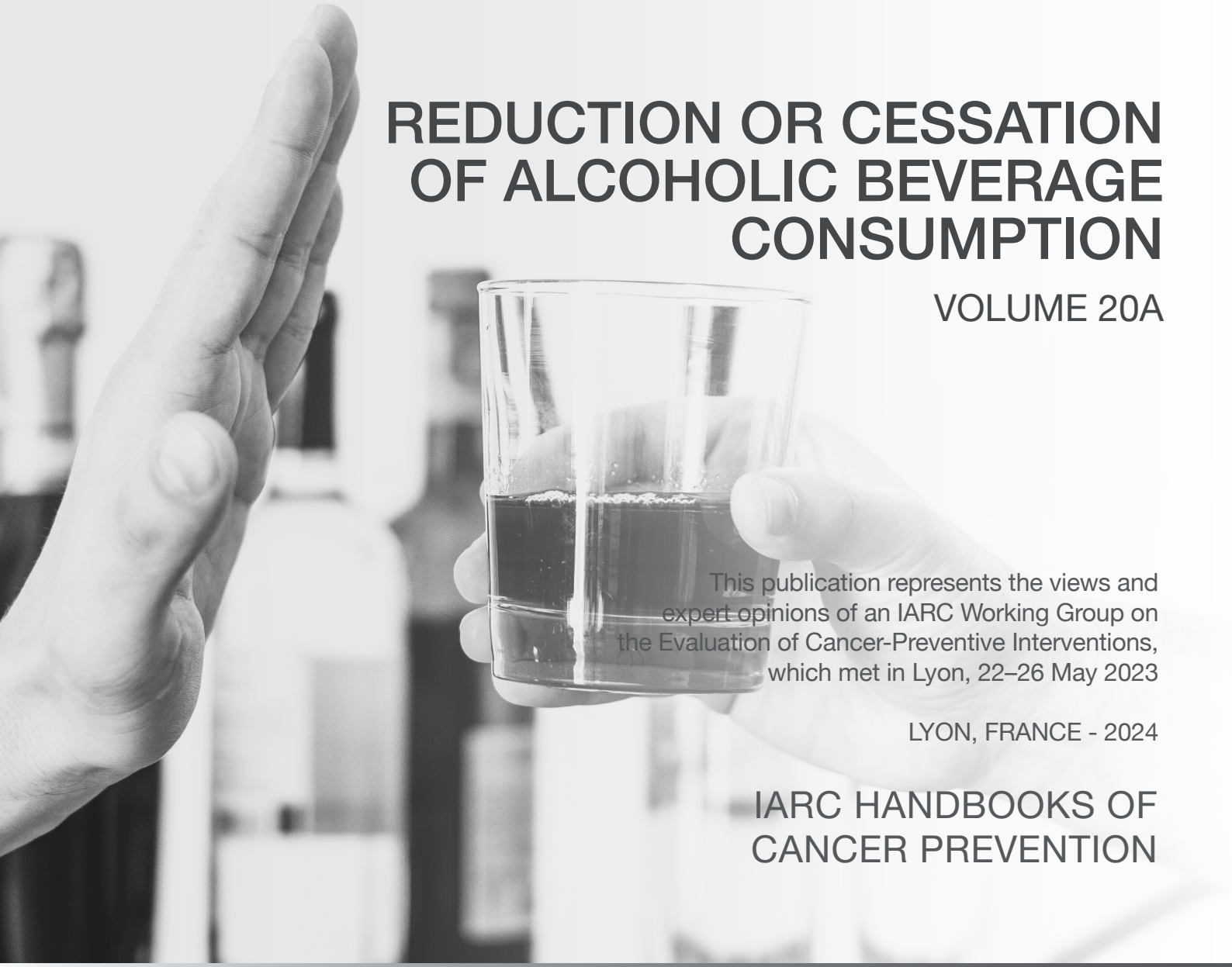
IARC HANDBOOKS



REDUCTION OR CESSATION OF ALCOHOLIC BEVERAGE CONSUMPTION

VOLUME 20A

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Cancer-Preventive Interventions, which met in Lyon, 22–26 May 2023

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IARC HANDBOOKS OF CANCER PREVENTION

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5. EVALUATIONS

5.1 Associations of reduction or cessation of alcoholic beverage consumption with cancer risk in humans

5.1.1 Oral cancer

There is *sufficient evidence* that reduction or cessation of alcoholic beverage consumption reduces the risk of oral cancer.

Rationale. In the most influential study, the large international pooled analysis, long-term cessation was associated with a lower risk of oral cancer compared with continuing consumption even after adjustment for the amount of alcohol consumed, pack-years of smoking, and other risk factors. There was consistent evidence of a reduced risk for long-term cessation in strata of higher amounts of consumption. Furthermore, consistent with smoking modifying the carcinogenic effect of alcohol, the risk for long-term alcohol cessation was lower in the current-smoking stratum than in the other smoking strata. The reduced risk for long-term cessation overall was weaker but remained after adjustment for duration of smoking cessation. Moreover, in most other studies reviewed, alcohol cessation was associated with a lower risk compared with continuing consumption.

5.1.2 Pharyngeal cancer

There is *inadequate evidence* that reduction or cessation of alcoholic beverage consumption reduces the risk of pharyngeal cancer.

Rationale. In the most influential study, the large international pooled analysis, long-term cessation was not associated with a lower risk of oropharyngeal and hypopharyngeal cancer combined after adjusting for alcohol consumption, smoking status, duration of smoking cessation, and other risk factors. These findings contrast with that for oral cancer, for which the risk was lower. Results from studies of cessation and risk of pharyngeal cancer were inconsistent within and between pharynx subsites.

5.1.3 Laryngeal cancer

There is *limited evidence* that reduction or cessation of alcoholic beverage consumption reduces the risk of laryngeal cancer.

Rationale. Long-term alcohol cessation was associated with a lower risk of laryngeal cancer in the large international pooled analysis; however, this association was not as strong as that observed for oral cancer. There was a lower risk of laryngeal cancer associated with alcohol cessation compared with continuing consumption in the three individual hospital-based case–control studies and in two cohort studies, but not with alcohol reduction or cessation in

another large cohort study. Furthermore, given the strength of the association between smoking and risk of laryngeal cancer, bias due to smoking cessation could not be ruled out with reasonable confidence.

5.1.4 Oesophageal cancer

There is *sufficient evidence* that reduction or cessation of alcoholic beverage consumption reduces the risk of oesophageal cancer.

Rationale. In the only study of reduction of alcohol consumption, the median follow-up time was only 6.4 years, which may not be adequate for observing reduced cancer risks. Among six of nine studies of duration of cessation, including an influential meta-analysis, long-term cessation was associated with a substantially lower risk of oesophageal cancer. The large number of studies supporting an inverse association helps to rule out chance. Similarly, consistent results across study designs help to rule out selection bias and information bias. Furthermore, confounding due to smoking and the amount of alcohol consumed also could be ruled out with reasonable confidence.

5.1.5 Colorectal cancer

There is *limited evidence* that reduction or cessation of alcoholic beverage consumption reduces the risk of colorectal cancer.

Rationale. In the most influential study, a large cohort study in multiple European countries with two prospective measurements of alcohol consumption, reduction of alcohol consumption was associated with a lower risk of colorectal cancer. Other cohort studies of reduction of alcohol consumption, one of which used retrospective assessment of alcohol consumption and one that had assessment only 2 years apart, did not show reduced risks. In one case–control study, the relative risks of colorectal cancer decreased with longer duration of cessation, whereas in a cohort study of colon cancer and rectal cancer mortality, there was no consistent evidence of reduced risk. Overall, there are inconsistencies among studies of alcohol reduction and cessation, and few studies of duration of cessation.

5.1.6 Liver cancer

There is *inadequate evidence* that reduction or cessation of alcoholic beverage consumption reduces the risk of liver cancer.

Rationale. In the only study of reduction of alcohol consumption, no evidence of a lower risk of liver cancer was observed. In a cohort study of individuals with alcohol-related liver disease, compared with continuing consumption, cessation was associated with a lower risk of liver cancer. In contrast, relative risks for duration of cessation and cessation were near to or greater than 1 in all other studies comprising participants without alcohol-related liver disease. For most of the studies, bias due to reverse causation or competing risk could not be ruled out.

5.1.7 Breast cancer

There is *limited evidence* that reduction or cessation of alcoholic beverage consumption reduces the risk of breast cancer.

Rationale. The body of evidence suggests that cessation of alcohol consumption may be associated with a lower risk of breast cancer compared with continuing consumption, and a lower risk was observed in the Working Group meta-analysis. This association may be limited to hormone receptor-positive tumours. Given the consistent, but modest and imprecise, inverse associations between alcohol cessation and risk of breast cancer observed, and the few studies with analyses by hormone receptor status, chance and bias could not be ruled out with reasonable confidence.

5.2 Mechanistic data

There is *sufficient evidence* from mechanistic studies that alcohol cessation reduces alcohol-related carcinogenesis.

This evaluation is based on evidence for the three mechanisms listed here.

5.2.1 Local exposure to genotoxic concentrations of acetaldehyde after ethanol ingestion

There is *strong evidence* that cessation of alcoholic beverage consumption results in an immediate reduction or elimination of the ingested ethanol and its conversion to acetaldehyde in the oral cavity, and subsequent local exposure to this carcinogenic metabolite in the upper aerodigestive tract and colon. It also reduces or eliminates the systemic distribution of ethanol and later conversion to acetaldehyde throughout the body; this is particularly relevant in the oral cavity among individuals with reduced ALDH2 enzyme activity.

5.2.2 DNA damage

There is *strong evidence* that cessation of alcoholic beverage consumption results in a decrease in acetaldehyde-induced DNA damage – although this has only been validated in blood and in the context of chronic heavy consumption; a reduction or elimination of acetaldehyde–DNA adduct formation in the oral cavity has also been observed.

5.2.3 Intestinal permeability and microbial translocation

There is *strong evidence* that cessation of alcoholic beverage consumption reverses changes in intestinal permeability and microbial translocation in the intestine. However, these data were limited to studies among individuals with chronic heavy consumption, and the role of these changes in alcohol-induced carcinogenesis remains unclear.