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Moderate Alcohol Consumption and Cancer - Low Cancer Risk, Major Uncertainties

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Cancer is among the most complex groups of diseases in modern medicine, encompassing more than 50 cancer types and over 200 subtypes. This heterogeneity makes broad generalizations about individual risk factors such as moderate alcohol consumption difficult. The scientific evidence is based predominantly on observational studies, which can identify statistical associations but cannot establish causality. The interpretation of results is complicated by confounding, reverse causation, multiple forms of selection bias (including abstainer bias, non-starter bias, and recall bias), as well as complex risk patterns. Compared with cardiovascular diseases, the quantitative impact of moderate alcohol consumption on cancer risk appears to be smaller [1].

1. Current State of The Evidence

The Available Epidemiological and Modelling Evidence Indicates The Following

Epidemiological evidence indicates no consistent association between moderate alcohol consumption and overall cancer risk. Indications of statistical associations mainly concern a few specific cancer types. The most consistent association is observed for breast cancer in women, although the effect size remains small [2-4]. For other tumour types - including cancers of the oral cavity, pharynx, oesophagus, colon and rectum, and larynx - the evidence is inconsistent, and current systematic reviews and meta-analyses have produced partly contradictory results [2-5].

Modelling studies estimate that in 2020 approximately 103,000 of around 18.1 million new cancer cases worldwide (about 0.6%) could theoretically be attributed to moderate alcohol consumption. These estimates are based on assumptions and are subject to considerable uncertainty [2]. Overall, the absolute individual risk remains low. Genetic factors further modify the association. While no additional effect of moderate alcohol consumption has been observed in women with a hereditary increased risk of breast cancer [6], certain genetic variants affecting alcohol metabolism can substantially increase the risk of cancers of the oral cavity, pharynx, and oesophagus even at low levels of consumption, moderately increase the risk of liver cancer, and slightly increase the risk of colorectal cancer [7]. Knowledge of individual genetic predispositions may therefore be relevant for prevention and risk assessment.

2. Key Controversies

Research In This Area Remains Controversial, Largely Due to Methodological Limitations of Observational Studies

A central issue is the inaccurate assessment of alcohol consumption: many individuals substantially underestimate their intake up to 75%. Studies indicate that this can lead to an overestimation of cancer risk associated with light to moderate drinking. In a large U.S. cohort of more than 127,000 participants, the observed increase in risk disappeared after correction for underreporting [8].

Some studies have also reported potential protective effects of moderate alcohol consumption for certain cancer types, such as lung or kidney cancer [9,10], findings that are generally attributed to residual confounding.

The classification of moderate alcohol consumption as a carcinogen is based primarily on high-dose data from animal experiments and cellular studies. Whether these findings can be extrapolated to low levels of consumption in humans is unclear and remains a subject of debate [11]. Direct evidence of cell-damaging effects of moderate amounts of alcohol in humans is, in any case, lacking.

3. Limits of Causal Evidence

Randomized controlled trials (RCTs) are considered the gold standard for establishing causal relationships. However, the world's first randomized controlled trial on moderate alcohol consumption (MACH15, costing approximately USD 100 million) was regrettably terminated prematurely in 2018 [12,13]. The study was criticized for conflicts of interest and for focusing

on cardiovascular endpoints while neglecting cancer outcomes [13-15]. A commentary in the European Journal of Preventive Cardiology countered the criticism (16): substantially larger sample sizes would have been required to study alcohol-related cancers (e.g., about 350,000 participants for breast cancer), which was logistically and financially not feasible. Nevertheless, systematic recording of adverse events among the 7,800 participants could have provided indications of cancer risk.

4. Conclusions

Evidence for a definitive association between moderate alcohol consumption and cancer remains inconclusive.

For eight of over 200 cancer types and subtypes - particularly breast cancer - weak to moderate statistical associations exist, but the absolute risk remains low.

Targeted, pragmatic RCTs focusing on cardiovascular endpoints - which occur far more frequently than cancer - could yield valuable insights into moderate alcohol-related risks by systematically recording all adverse events including rare cancer. This represents currently the most practically feasible approach.

In the future, genetic information may play an increasingly important role in personalized prevention and risk assessment

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