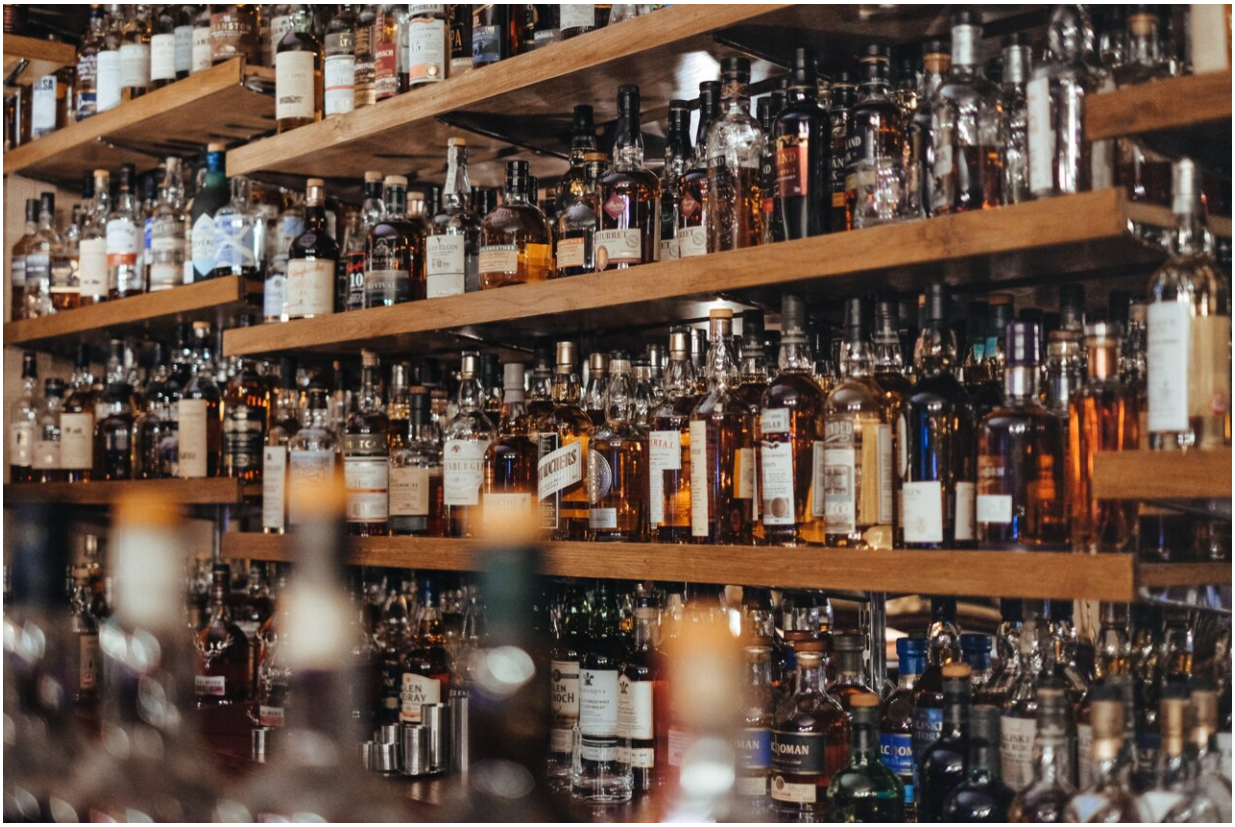
Genetic study provides evidence that alcohol accelerates biological aging

July 26 2022



Credit: Unsplash/CC0 Public Domain

The short-term effects of excessive drinking are well known, but to date it has been less certain whether alcohol also accelerates the aging process.

Traditionally, investigating this has been challenging due to the lack of reliable methods to measure biological aging. In addition, it was not clear from observational studies whether alcohol was the true cause of any effect, or if it was linked to other factors, such as socio-economic status.

Today, researchers from Oxford Population Health have published results from a new genetic-based analysis which suggest that alcohol directly accelerates aging by damaging DNA in telomeres. The findings are published today in *Molecular Psychiatry*.

Telomeres are repetitive DNA sequences that cap the end of chromosomes, protecting them from damage. Telomere length is considered an indicator of biological aging, since 50-100 DNA bases are lost each time a cell replicates. Once telomeres become too short, cells can no longer divide and may even die. Previous studies have linked shorter telomere lengths with several aging-related diseases including Alzheimer's disease, cancer, and coronary artery disease.

In this analysis, the researchers investigated the association between alcohol intake and telomere length in over 245,000 participants in the UK Biobank. They used a genetic approach called Mendelian Randomisation (MR), the first time this has been applied to investigate the effects of alcohol on aging. This method uses 'genetic proxies' to predict the level of exposure for each participant.

For this study, the researchers used genetic variants that have previously been associated with alcohol consumption and alcohol use disorders in large-scale genome-wide association studies.

To complement the MR analysis, the researchers also performed an observational assessment, based on the participants' self-reported weekly alcohol intake at recruitment.

In the observational analysis, there was a significant association between high alcohol intake and shorter telomere length. Compared with drinking less than 6 units of alcohol a week (about two large 250ml glasses of wine), drinking more than 29 units weekly (about ten 250ml glasses of 14% alcohol by volume wine) was associated with between one and two years of age-related change on telomere length.

Individuals who had been diagnosed with an alcohol-use disorder had significantly shorter telomere lengths compared with controls, equivalent to between 3 and 6 years of age-related change.

Similarly, in the MR analysis, higher genetically-predicted alcohol consumption was associated with shorter telomere length. An increase from 10 units to 32 units per week was associated with the equivalent of 3 years of aging.

However, the association between genetically-predicted alcohol consumption and telomere length was only significant for those drinking more than 17 units per week. This suggests that a minimum amount of alcohol consumption may be required to damage telomeres.

The MR analysis also found a significant association between genetically-predicted alcohol-use disorder and telomere length, equivalent to around 3 years of aging.

Most of the participants were current drinkers, with only 3% being never drinkers and 4% being previous drinkers. 51% were men, 49% were women, and the average age was 57 years.

Study lead, Dr. Anya Topiwala from Oxford Population Health, says that "These findings support the suggestion that alcohol, particularly at excessive levels, directly affects telomere length. Shortened telomeres have been proposed as risk factors which may cause a number of severe

age-related diseases, such as Alzheimer's disease. Our results provide another piece of information for clinicians and patients seeking to reduce the harmful effects of excess alcohol. Furthermore, the dose of alcohol is important—even reducing drinking could have benefits."

For both the observational and MR analysis, telomere lengths were measured using leucocytes (immune system cells) from the participants' DNA samples collected when participants were first recruited to the UK Biobank.

In the MR analysis, alcohol intake was estimated by screening DNA samples for 93 genetic variants that have previously been associated with weekly alcohol consumption, besides 24 variants that have previously been linked to a diagnosis of an alcohol use disorder. Because these genetic variants are randomly allocated and fixed before birth, the results give greater confidence that alcohol directly affects telomere length, rather than a different factor being responsible.

Although these results do not conclusively prove that alcohol directly affects telomere length, two findings from the study support this being the case. 1) Effects were only found in current drinkers, and not previous or never-drinkers; 2) The most influential genetic variant in the MR analysis was AD1HB, an alcohol metabolism gene.

According to the research team, a potential biological mechanism to explain alcohol's influence on telomere length is increased oxidative stress and inflammation. The process which breaks down ethanol in the body can both produce reactive oxidative species that damage DNA and reduce levels of antioxidant compounds that protect against oxidative stress.

Dr. Richard Piper, Chief Executive of Alcohol Change UK, says that they "welcome all research into the effects of alcohol on the human

body. This particular study shows clear links between consuming alcohol and aging, and points towards a possible link between alcohol and Alzheimer's. The researchers are transparent that this study does not prove a causal link, but they also make a well-argued case about the likely biological mechanism. In general, there is an ever-larger body of science showing how, exactly, alcohol causes so much ill-health and so many early deaths."

More information: A. Topiwala et al, Alcohol consumption and telomere length: Mendelian randomization clarifies alcohol's effects, *Molecular Psychiatry* (2022). DOI: 10.1038/s41380-022-01690-9

Provided by University of Oxford