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Don’t blame it on the sunshine, don’t blame it on the moonlight, don’t blame it on good times, blame it on the sociocultural factors

Peter Jepsen (1, 2)

Matthew J. Grainge (3)

1. Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark.
2. Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark.
3. Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, Nottingham UK, NG5 1PB.

In this issue of HEPATOLOGY, Ventura-Cots and colleagues present their study arguing that colder weather and fewer sunlight hours increase alcohol consumption and thus cause alcoholic cirrhosis (1). "Causality" is a key concept for this study. A recent review on the topic highlighted two nicely articulated definitions provided by Lilienfeld ('a factor may be defined as a cause of a disease, if the incidence of the disease is diminished when exposure to this factor is likewise diminished') and Pearl ('X is a cause of Y if Y listens to X and decides its value in response to what it hears') (2). In the context of the Ventura-Cots paper, we of course cannot modify the weather to determine its causal effect on alcohol, but it is conceivable that an individual could move, or be moved, to a different climate whilst all other factors affecting alcohol consumption remained the same. If the individual then 'listened' to the change in climate and changed his or her alcohol consumption in response to that, we would accept that as a causal effect of the climate. However, that is not what happened in the Ventura-Cots study. First, some factors affecting alcohol consumption could not be accounted for, so what we think was caused by the climate could in fact have been caused by those other factors—confounding, that is. Second, this was not a study of individuals, but of communities.

The possible role of confounding is shown in Figure 1 in the form of a directed acyclic graph (DAG) for the Ventura-Cots study, as interpreted by the editorialists. A DAG is a tool to visualize and understand causal structures whilst pointing to sources of confounding and other biases (3). The figure shows the exposure (temperature and sunlight), the outcomes (alcohol consumption and alcoholic cirrhosis), and the causal chain linking them: Temperature and sunlight affect seasonal variation and the risk of mood-related disorders; they affect alcohol consumption; and alcohol consumption in turn affects the risk of alcoholic cirrhosis. Moreover, a colder climate increases the risk of harm from alcohol consumption because alcohol inhibits the physiological response to exposure to cold weather. These arguments are all discussed by the authors (1). They also discuss the potential confounding pathways shown in Figure 1: geographic location affects not only

temperature and sunlight, but also sociocultural factors such as religion, culture, and education. All of these factors affect alcohol consumption and are consequently sources of confounding. Ideally, that confounding could be eliminated by conditioning on geographic location or on sociocultural factors. However, conditioning on geographic location is not feasible; location is so tightly linked to temperature and sunshine that it does not make sense to separate one from the other, except in the laboratory. It is more feasible to condition on sociocultural factors, i.e. examining the association between climate and alcohol consumption while holding sociocultural factors constant. Ventura-Cots and colleagues attempt that, by conducting the analysis within the United States. However, religious beliefs and alcohol policies vary considerably even within that one country, so unfortunately the result of that analysis does not settle the issue of determining which of the factors (sociocultural or climate) are responsible for the association between geographic location and alcohol consumption.

What other countries could have been examined? It would have to be a country that spans a long distance in North-South direction, yet is homogenous with respect to sociocultural factors—Chile, perhaps (https://en.wikipedia.org/wiki/Chile)? A 2015 study examined regional variation in standardized mortality ratios attributable to alcohol within Chile, and there was no apparent North-South trend (4). Mortality peaked in the south-central and southern regions, not in the southernmost Magallanes region. Alcohol sales were not greater in the high-mortality regions, but wine is produced there, and the authors speculated that home-made or illegal alcohol contributed to the high alcohol-related mortality there (4). They did not explicitly examine the regions' climate as an alternative explanation, so the effects of sociocultural factors and climate could not be disentangled in the Chilean study, either.

Ventura-Cots and colleagues did not study individuals, but aggregate data from all individuals within a community. It is consequently possible that the associations they found do not exist at all

within the individual person, even if persons in colder climates are more susceptible to alcoholic liver disease *on average*. The causal mechanism claimed by the authors (the green arrows in Figure 1) involves biologic processes operating within the individual, not at the community level (5). This means that the authors place themselves at risk of 'the ecological fallacy', but of course no fallacy occurs if the findings by Ventura-Cots and colleagues can be replicated using individual-level data (6). Such an individual-level study would need to have individual-level data on location of residence (for which climatic data could be extracted); religion, culture, education, and other sociocultural confounding factors; and alcohol-related outcomes. On top of that, there would have to be substantial variation in climate in order to demonstrate any effect of climate.

Incidentally, a study from Ireland, published in 2013, did use individual-level data to identify factors associated with drinking among students (7). The authors of that study wrote: "Irish weather is far from uniform. Variation in rain is pronounced with heavier rainfall concentrated along the West Atlantic coast and in the more mountainous areas. In contrast, sunshine shows a rather marked increase as one moves from the North-West to the South-East. In spite of common folklore, we find no effect of Irish weather on the drinking of the students." In their conclusion, they further stated that "Overall, our results point to a pattern of transmission of parental drinking and sibling drinking affecting both actual alcohol consumption and standards for what is considered normal or acceptable drinking behavior. Our results also point to complex deep-rooted cultural and historical factors that facilitate alcohol consumption and explain variation even among the student sample." Thus, this Irish study found that sociocultural factors were important, whereas climatic ones were not. That does not rule out the possibility that climate exerts an effect on a grander scale, of course, but it counters the argument put forward by Ventura-Cots and colleagues.

So, how does the present study advance our management of alcoholic liver disease? The paper ends with the recommendation that "public health measures aimed at preventing excessive alcohol

consumption should focus on regions with colder climates" (1), and that is true, even if we do not fully understand *why* those who live in colder climates drink more alcohol, on average. Public health measures to prevent the development of alcoholic liver disease through minimum-pricing or reduced access to alcohol will indeed be more successful in colder climates than in warmer ones, but sociocultural factors could help us further narrow down the target regions. For example, Ventura-Cots and colleagues found that the 'inequality-adjusted human development index' predicts average alcohol consumption in a community, so it would be sensible to target more developed communities than less developed ones. Many areas of the world, including most of the Western countries ravaged by alcohol liver disease, fit the description of a cold and dark, yet developed place. Let the preventing begin.

References

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Figure Legend

Figure 1. Directed acyclic graph illustrating the editorialists' interpretation of the causal mechanisms proposed by Ventura-Cots and colleagues. The exposure of interest is 'temperature and sunlight', and the outcomes are 'alcohol consumption' and 'alcoholic cirrhosis'. The green arrows indicate the proposed biological mechanisms that explain why, in the individual person, the exposure causes the outcome. The purple arrows indicate the alternative mechanisms, i.e., the confounding pathways, that might contribute to the association between exposure and outcomes.