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Cirrhosis mortality and per capita consumption of distilled spirits, United States, 1949-94: trend analysis

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Abstract

Objective To describe, evaluate, and suggest interpretations for an observed aggregate level relation between trends in mortality from cirrhosis and per capita consumption of distilled spirits in the United States.
Design Trend analysis using data on US cirrhosis mortality and per capita alcohol consumption.
Results There is a consistent long term trend relation between mortality from cirrhosis and per capita consumption of distilled spirits in the United States from 1949 to 1994. Two instances of comparatively sharp drops in the consumption of spirits earlier in the 1940s generated mixed results in predicting changes in cirrhosis mortality.
Conclusions An aggregate level relation between trends in long term cirrhosis mortality and the consumption of spirits falls considerably short of establishing a direct causal link between the two for individuals. Moreover, two sharp drops in the consumption of spirits generated only mixed results with respect to the short term trend in cirrhosis. Nevertheless, the observed relation between the consumption of spirits and cirrhosis mortality merits further investigation.

Introduction

This paper presents new epidemiological evidence of an aggregate level relation between trends in per capita consumption of distilled spirits and death from cirrhosis in the United States. Such data may help to understand why a long rise in the trend of deaths from cirrhosis after the second world war unexpectedly fell after 1973 even as the trend in total per capita consumption of alcohol continued to rise until the early 1980s. Although evidence of an aggregate level correlation between the consumption of spirits and death from cirrhosis falls short of showing a direct or causal relation between the use of spirits and the risk of cirrhosis for individuals, it suggests that there is value in pursuing further multidisciplinary investigations to discern the links between the consumption of specific alcoholic beverages and cirrhosis.

Mortality from cirrhosis in the United States rose by 75% from 1950 to 1973 (from 8.5 to 14.9 deaths per 100 000 population), accounting for 33 350 deaths in the peak year of 1973. After this time, cirrhosis mortality began a long, slow decline, falling to 7.9 deaths per 100 000 by 1993, roughly half of the 1973 rate and marginally below the rate in 1950 (fig 1a). The reasons why cirrhosis mortality fell and why the fall started when it did are unclear. A large fraction of cirrhosis mortality has long been associated in both medical and popular thinking with heavy drinking.[1 2] Do changes in American drinking practices account for changes in the trend? Per capita alcohol use also rose and then fell during the period after the second world war, increasing by 38% from the late 1950s to 1980 (from a mean of 7.57 litres of absolute alcohol to 10.45 litres for the drinking age population) and then falling by 20% from the early 1980s to the mid-1990s (to 8.36 litres) (fig 1a). However, the order of the peaks in time in the two trends is contrary to what would have been expected if the fall in alcohol consumption had caused the fall in cirrhosis mortality. The beginning of the decline in cirrhosis mortality in the mid-1970s preceded the beginning of the decline in consumption by seven or eight years, thus generating a transitional period (1973-80) when cirrhosis mortality was falling but per capita alcohol consumption was still rising.

Alcohol consumption should not, therefore, be eliminated as a possible explanation for the decline in cirrhosis mortality that occurred after 1973 in the

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United States. At least three factors may complicate the apparent relation between drinking and cirrhosis mortality when this relation is viewed through the medium of aggregate level trend statistics.[3 4] Firstly, statistics on per capita consumption do not provide a direct measure of the frequency of heavy drinking in a population. For example, statistics on per capita consumption may show an increase from one year to the next because the pool of drinkers in society has expanded (say, to include more youthful drinkers) rather than because the frequency of heavy drinking has increased. Secondly, contemporaneous changes in the availability or the efficacy of treatment for heavy drinking or cirrhosis may account for discrepancies in trends between per capita consumption and cirrhosis mortality. For example, a significant expansion in the alcoholism treatment system in the United States in the 1970s may have led to a decrease in cirrhosis mortality even as new or younger drinkers continued to drive per capita consumption rates upward. Thirdly, cirrhosis develops slowly, ordinarily requiring 15 to 20 years of heavy drinking before death occurs from the disease. Some analysts have suggested that changes in per capita consumption may require the passage of just as many years for the effects to be fully realised in changes in mortality from cirrhosis.[5–7] All three factors illustrate ways in which alcohol consumption may account for cirrhosis mortality even if the two societal trends are not always highly correlated.

No compelling evidence has emerged to show that the three factors we have noted actually account for the discrepancies in trends between total alcohol consumption and cirrhosis mortality. Survey data on trends in drinking patterns in the population do not indicate that a significant expansion in the pool of drinkers or a consistent decline in the frequency of heavy drinking occurred from 1973 to 1980.[8] Smart and Mann have suggested that the order of magnitude of the expansion in alcoholism treatment in the United States between 1979 and 1987 may have been sufficient to account for the concurrent decline in cirrhosis mortality.[9] However, Smart and Mann did not address the transitional period from 1973-80 when consumption was rising and cirrhosis mortality was falling; moreover, their analysis has highlighted some of the methodological problems involved in attempting to directly equate increases in the availability of treatment programmes with credible estimates of the supposed impact of treatment on cirrhosis mortality.[10] Although analyses based on time lags have been used to study data on discrepant consumption and changes in cirrhosis mortality in countries where changes in consumption preceded changes in cirrhosis—for example, in the United Kingdom[5] and Sweden[6]—the circumstance of a change in cirrhosis statistics preceding a change in consumption has worked against applying a similar approach to trends in the United States.

Another mode of linking cirrhosis mortality with alcohol consumption focuses on the relation between specific alcoholic beverages—distilled spirits, beer, and wine—and cirrhosis mortality. More than 30 years ago, Terris published an analysis of data on trends from the United States, Canada, and the United Kingdom suggesting that per capita beer consumption did not contribute to trends in mortality from cirrhosis.[11] Since wine consumption traditionally contributes only about one eighth of per capita total alcohol intake in the United States, Terris's exclusion of beer in his analysis implied that the consumption of spirits was the principal contributor to aggregate cirrhosis mortality. Some more recent studies have also drawn attention to the consumption of spirits and its relation to trends in cirrhosis mortality.[12–14] However, no paper has as yet examined either long term data on trends in the United States or the sharp, short term changes in the consumption of spirits which occurred in the 1940s.

Methods

Two kinds of relations in the trends between cirrhosis mortality and alcohol consumption were examined. Firstly, we compared the long term (1949-94) relation between cirrhosis mortality and the trend in total per capita alcohol consumption in the United States (which combines the consumption of all types of alcoholic beverages) and then we compared the long term relation with consumption trends for spirits, beer, and wine. Secondly, we evaluated changes in cirrhosis mortality occurring after two comparatively sharp drops in the consumption of spirits in the 1940s.

Sources of data

Data on national cirrhosis mortality and per capita alcohol consumption were analysed. Data were standardised by age to the US population in 1940, and total cirrhosis mortality for the 46 years from 1949 to 1994[15] were adjusted for the apparent impact of shifts in the coding of cirrhosis mortality in the international classification of diseases (ICD).[16] (These data are available on the *BMJ*'s website.) The year 1949 was selected as the starting point for the long term trend analysis because, as Terris originally noted,[11] the introduction of the ICD-6 (sixth revision) in 1949 had a comparatively large effect on the apparent mortality from cirrhosis; later revisions of the ICD had smaller and more easily corrected effects. Our use of total cirrhosis mortality, instead of the code for "cirrhosis with mention of alcohol," is common practice in the literature on the relation between alcohol and trends in cirrhosis and reflects prevailing reservations about the validity of subgroup discriminations in the coding of cirrhosis mortality.[17] Our particular focus on the question of whether the change in cirrhosis mortality may be accounted for by changes in alcohol consumption also allowed for the use of the total cirrhosis mortality variable.

Total per capita consumption and figures for the consumption of specific beverages are expressed in absolute alcohol equivalents, which were calculated in our source by dividing the total number of gallons sold by estimates of the alcohol content of specific beverages and then by the population aged 15 and older (before 1971) or 14 and older (1971-94).[18] Although the mean alcohol content of distilled spirits declined marginally after 1973, our estimates of the consumption of spirits have not been adjusted for this factor.[19 20]

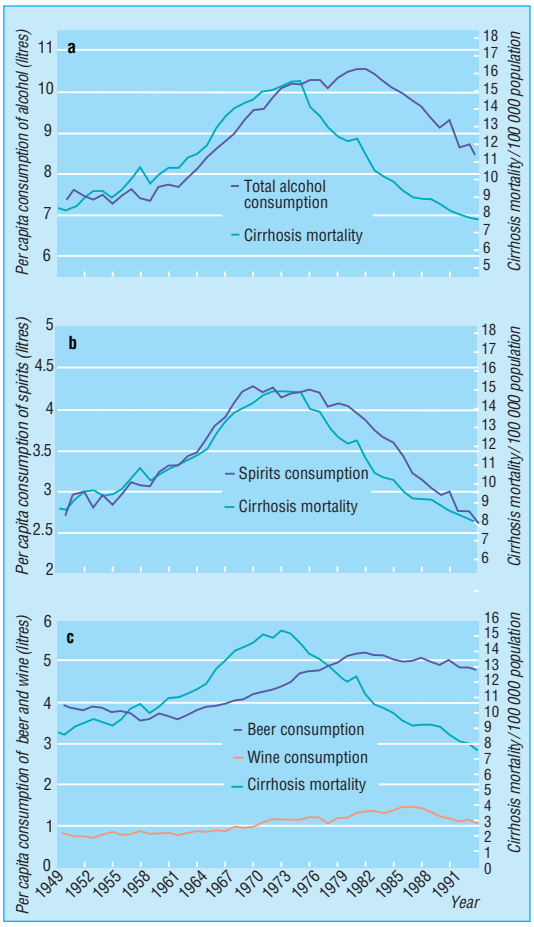

Fig 1 Mortality from cirrhosis and total per capita consumption of (a) total alcohol, (b) distilled spirits, and (c) beer and wine, in the United States, 1949-94

Results

Time series analysis, 1949-94

The trend in cirrhosis mortality is compared with the trends in four variables of alcohol consumption (total alcohol consumption, spirits consumption, beer consumption, and wine consumption) in figure 1. These curves show that the consumption of spirits has a stronger association with cirrhosis mortality than total per capita consumption of alcohol, beer, or wine. Pearson's product moment correlation coefficient expresses the degree of covariation in a pair of standardised variables. The relation between the consumption of spirits and cirrhosis mortality generated the highest correlation coefficient (spirits, r=0.94; total alcohol, r=0.50; beer, r=−0.03; wine, r=0.05).

Autoregressive integrated moving average models provide a more sophisticated statistical approach to the evaluation of trend data.[21 22] These models assess associated trends for the impact of current and past values of the independent variable and for a dependent variable's impact on itself. Two autoregressive models were developed: one for the relation between the consumption of spirits and cirrhosis mortality and the other for the relation between total alcohol and cirrhosis mortality. The model for spirits generated a better predictive fit than the total alcohol model (spirits model, adjusted r^2=0.47; total alcohol model adjusted r^2=0.32). Both models used only short term, lagged effects (current year consumption, previous year, and the year before that). (Additional information about the models is available on the *BMJ*'s website).

Drops in the consumption of spirits

Epidemiologists have long been wary of aggregate level correlations between a pair of long term, slowly changing trends—like the observed correlation between cirrhosis mortality in the United States and the consumption of spirits during 1949-94—because of the possibility that unmeasured third factors may account for both trends. In the period immediately preceding our long term analysis there were two relatively sharp, one year drops in the consumption of spirits, one occurring from 1942 to 1943 and the other from 1946 to 1947. These provided an opportunity to examine whether the aggregate level association derived from the longer term trends could predict the impact of changes in the consumption of spirits on cirrhosis mortality in the more demanding environment of sudden and marked change in the variable for the consumption of spirits.

The apparent per capita consumption of spirits fell by 22% from 1942 to 1943 and by 23% from 1946 to 1947. These are the only instances of one year drops in the consumption of spirits in the 1940s and the only instances of comparatively large one year declines in the consumption of spirits from 1940 to 1994. By comparison, there were 20 instances of one year declines in the consumption of spirits from 1949 to 1994, and among these the mean drop in consumption was 3%, 18 of the 20 were declines of less than 5%, and the two largest declines were of less than 10%. Because the consumption of spirits and rates of cirrhosis before 1949 did not contribute to the construction of the model for spirits, the sharp declines in the consumption of spirits in 1942-3 and 1946-7 represent fresh data suitable for independent testing of the model's ability to predict trends in cirrhosis mortality.

The two predictive tests generated only mixed results, however. Figure 2 plots the consumption of spirits, the model's predicted cirrhosis curve, and the observed cirrhosis curve from 1940 to 1950 adjusted to ICD-9 coding. We have used the "static" predictive mode, which allows the model to make its prediction of cirrhosis mortality for each successive upcoming year using the observed cirrhosis mortality in the preceding year and the observed amount of spirits consumed in the current year, the previous year, and the year before that. This requires that the model be given sufficient

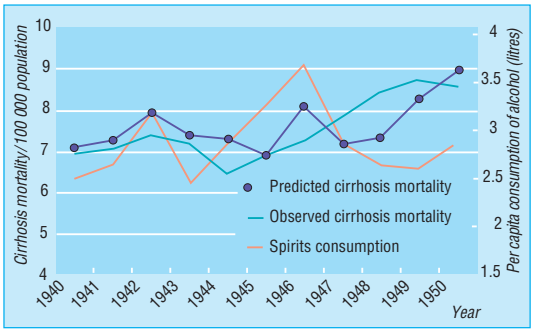

Fig 2 Per capita consumption of spirits, predicted mortality from cirrhosis (adjusted), and observed mortality from cirrhosis in the United States, 1940-50

lead time to establish its frame of reference for predictions. We have satisfied this requirement by starting the model in 1938, five years before the first sharp drop (1942-3) in the consumption of spirits. Both drops in consumption followed periods of rising consumption, and hence the model's predictions for the time after the drops included the lagged effects of the previous rising trend.

The model for the consumption of spirits seems to perform reasonably well in relation to the first sharp drop in consumption (1942-3); it correctly predicts a downward trend for cirrhosis in 1943 and 1944. The predicted curve is displaced upward, however, by the model's over prediction of a rising trend in cirrhosis for 1942-3. The model also places the lowest point of the fall in cirrhosis after 1942 in 1945, one year after the lowest point was actually reached. The model's predictive performance in relation to the second sharp drop in spirits consumption (1946-7) is considerably less successful. The model predicts a sharp decline in cirrhosis in 1947, a slight upward rebound in 1948, and a steep upward trajectory in 1949 and 1950. In fact, however, cirrhosis mortality climbed steeply in 1947 and 1948. The change in cirrhosis mortality in 1949 occurred after the change from ICD-5 to ICD-6. A sharp decline in unadjusted cirrhosis mortality in 1949 is eliminated once the unadjusted 1949 mortality is adjusted to the ICD-9 standard.

Some cautions should be noted in connection with these two tests of the model for the consumption of spirits. The decline in the consumption of spirits in 1942 occurred during the second world war as a result of the US War Production Board's commandeering of all distilled spirits to wartime uses, such as the production of synthetic rubber and explosives.[23] Widespread wartime hoarding of scarce consumer goods may have altered the usual peacetime relation between consumer purchasing and the actual consumption of spirits.[24] The decline in the consumption of spirits in 1946-7, moreover, may have reflected a broad shift from wartime to postwar consumer behaviour, thus also introducing a measure of unreliability into the usual relation between purchasing and actual consumption. Also, time series analyses address the description of statistical regularity over many years of data, and so spot checks of predicted and actual results for short term trends do not definitively confirm or negate the trend models.

Discussion

What sort of connection between the consumption of spirits and cirrhosis mortality is suggested by the data we have presented? Several possibilities should be considered. Spirits consumption in itself may not be "doing the work" in the observed relation. Instead, the amount of spirits consumed may be acting as an indicator of the changing acceptability of heavy drinking in American society. The consumption of spirits may also have gained a special aggregate level relation with cirrhosis by being the preferred beverage of heavy drinkers or alcoholics.[25] Our data also do not exclude the possibility of an underlying cohort effect in which the rise and fall of cirrhosis mortality before and after 1973 represents the "mortality trail" through its course of an American generation of comparatively heavier drinkers who prefer spirits. Neither, of course, is the possibility of a direct relation between the consumption of spirits and risk of cirrhosis specifically excluded. The higher alcohol concentrations of spirits (in unmixed drinks) and the potential for causing a faster rise in blood alcohol concentrations may give rise to comparatively greater hepatic insult and damage.[26] Such an effect would be exacerbated if, as has been reported, those who drink spirits tended to consume greater mean amounts of alcohol per drinking occasion[27 28] and more often drink without eating.[29 30]

Key messages

- US cirrhosis mortality peaked in 1973 but alcohol consumption did not peak until the early 1980s
- Both shifts in the distribution of US drinking patterns (which are not reflected in per capita consumption statistics) and the increase in the availability of treatment for alcoholism have been suggested as potential sources of the decline in cirrhosis
- The trend in the consumption of distilled spirits from 1949 to 1994 shows a close, aggregate level association with cirrhosis mortality
- This aggregate level relation suggests that research is needed into the link between the effects of specific alcoholic beverages and cirrhosis

Conclusion

The reported aggregate level relation between the consumption of spirits and cirrhosis mortality in the United States cannot be directly generalised to other nations; this includes wine drinking cultures that historically have high rates of cirrhosis. Therefore, this finding is context specific and also suggests the value of paying further attention to contextual factors in the relation between alcohol and cirrhosis. Nevertheless, the observed aggregate level relation in the United States undoubtedly warrants more investigation. Additional epidemiological and biomedical research is needed into the cirrhosis causing effects of specific alcoholic beverages.

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Contributors: RR initiated the research with his observation of the stronger association between the consumption of spirits and mortality from cirrhosis. He has been responsible for many of the core ideas and writing the paper. WCK was responsible for generating the ARIMA results and participated in some of the writing of the paper. KMF participated in discussions concerning core ideas and the writing of the paper. All authors will act as guarantors of the paper.

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What is meant by intention to treat analysis? Survey of published randomised controlled trials

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Abstract

Objectives To assess the methodological quality of intention to treat analysis as reported in randomised controlled trials in four large medical journals.
Design Survey of all reports of randomised controlled trials published in 1997 in the *BMJ, Lancet, JAMA,* and *New England Journal of Medicine.*
Main outcome measures Methods of dealing with deviations from random allocation and missing data.
Results 119 (48%) of the reports mentioned intention to treat analysis. Of these, 12 excluded any patients who did not start the allocated intervention and three did not analyse all randomised subjects as allocated. Five reports explicitly stated that there were no deviations from random allocation. The remaining 99 reports seemed to analyse according to random allocation, but only 34 of these explicitly stated this. 89 (75%) trials had some missing data on the primary outcome variable. The methods used to deal with this were generally inadequate, potentially leading to a biased treatment effect. 29 (24%) trials had more than 10% of responses missing for the primary outcome, the methods of handling the missing responses were similar in this subset.
Conclusions The intention to treat approach is often inadequately described and inadequately applied. Authors should explicitly describe the handling of deviations from randomised allocation and missing responses and discuss the potential effect of any missing response. Readers should critically assess the validity of reported intention to treat analyses.

Introduction

"Intention to treat" is a strategy for the analysis of randomised controlled trials that compares patients in the groups to which they were originally randomly assigned. This is generally interpreted as including all patients, regardless of whether they actually satisfied the entry criteria, the treatment actually received, and subsequent withdrawal or deviation from the protocol. However there is a debate about the validity of excluding specific cases within each of these categories from an intention to treat analysis.[1] Clinical effectiveness may be overestimated if an intention to treat analysis is not done.[2]

The intention to treat approach has two main purposes. Firstly, the approach maintains treatment groups that are similar apart from random variation. This is the reason for randomisation, and the feature may be lost if analysis is not performed on the groups produced by the randomisation process. For example, in a trial comparing medical and surgical treatment for stable angina pectoris, some patients allocated to surgical intervention died before being operated on.[3] If these deaths are not attributed to surgical intervention using an intention to treat analysis, surgery seems to have a falsely low mortality (table 1). Secondly, intention to treat analysis allows for non-compliance