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The temporal relationship between per capita alcohol consumption and harm: A systematic review of time lag specifications in aggregate time series analyses

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Abstract:

Background: Changes in per capita alcohol consumption are temporally linked to changes in rates of alcohol-related harm. Methodological approaches for analysing this relationship have been suggested, however, the problem of time lags is not well-addressed. This study provides a review of time lag specifications, looking at a) time to first effect on harm, b) time to full effect and c) the functional form of the effect accumulation from first to full effect to inform modelling of the relationship between changes in aggregate alcohol consumption and changes in rates of harm.

Methods: Bibliographic databases were searched and citation and reference checking was used to identify studies. Included studies were time series analyses of the relationship between aggregated population alcohol consumption and rates of alcohol-related harms where time lag specifications had been derived or tested.

Results: 36 studies were included with liver cirrhosis, heart disease and suicide dominating the evidence base. For a large number of alcohol-related harms, no literature was identified. There was strong evidence of an immediate first effect following a change in consumption for most harms. Recommended lag specifications are proposed for a set of alcohol-attributable harms.

Conclusions: Research on time lag specifications is under-developed for most harms although we provide suggested specifications based on the findings of the review. Greater methodological attention needs to be given to the rationale for choosing or applying lag specifications and the inherent complexity of the time lag process. More consistent and transparent reporting of methodological decisions would aide progress in the field.

Key words: alcohol consumption; harm; time-series analysis; time lag; temporal relationship

1. Introduction

Average levels of alcohol consumption in the population are widely recognised as a relevant public health indicator. Such aggregate levels of consumption have been associated with the incidence and prevalence of a range of alcohol-related harms including morbidity and mortality from various health conditions and also rates of crime, unemployment and workplace absences (2009). These associations can be seen in cross-sectional studies; however, stronger evidence comes from time series analyses showing that changes in per capita alcohol consumption are temporally linked to changes in rates of alcohol-related harms. Although methodological approaches for such analyses have been suggested (Norström & Skog 2001; Rehm & Gmel 2001) debates on aspects of applying these continue. One such aspect is the time lag problem.

Given that much alcohol-related harm is the accumulated result of years of harmful individual drinking behaviours, the full effect of changes in consumption may not be immediately apparent in harm data. Instead, the effect of changes in aggregate consumption may be delayed and distributed over a number of years. In response to this problem, it is commonplace to incorporate a lag structure into time series analyses to ensure the full long-term effect is captured.

Studies which have explored time lags in depth have tended to focus on liver cirrhosis and have found that, despite the anticipated long-term effect, much of the impact on cirrhosis mortality rates occurs in the first year following a change in consumption (Kerr et al. 2000; Skog 1984). This somewhat paradoxical finding of immediate effects at the aggregate level on a harm which develops after many years of heavy drinking at the individual level can be clearly observed in the sharp falls in cirrhosis deaths following alcohol rationing in Paris during World War Two (Norström 1987).

The notion of critical thresholds has typically been used to explain this paradox (Norström 1987; Norström 1989; Skog 1980). It is postulated that, at any given time, there are a group of people with advanced liver cirrhosis for whom a change in alcohol consumption could prompt or prevent liver failure. It is changes in the mortality rate within this group which are often used to explain the rapid effects of changes in aggregate alcohol consumption (Norström & Skog 2001). Simultaneous changes in alcohol consumption amongst those who are not at this critical threshold also need to be accounted for and Skog (1984) and Norström (1987) have obtained consistent results modelling lag structures specifying both short- and long-term effects for the UK and Sweden respectively. However, other work has suggested time series models accounting only for a short-term effect adequately fit the data (Kerr et al. 2000; Roizen et al. 1999).

The primary concern of this paper is to provide the first systematic review of aggregate time series lag structures which have been applied to different alcohol-related harms with a focus on three pieces of information: the time to first effect, the duration to full effect and the functional form of the accumulation of effect. Referred to hereafter as the lag specifications, these pieces of information are illustrated in Figure 1.

2. Methods

The search was conducted across the following databases between December 2010 and February 2011: ASSIA, Campbell Collaboration, CINAHL, Econlit, IBSS, Embase, Medline, PsychINFO, Scopus, Social Care Online, Sociological Abstracts, Web of Knowledge and World Political Science Abstracts.

The full search terms can be seen in the online Appendix 1. The search was conducted in three stages using a set of alcohol terms combined in turn with three sets of terms relating to lags. These three sets were progressively less precise to account for the anticipated diffuseness of the literature with lags typically not mentioned in abstracts. A search of the first twenty pages of Google Scholar results using the same search terms and reference and citation checking of all relevant studies were used to identify further studies.

Search results were first assessed by title and then abstract. This process was initially undertaken independently on small samples of papers by two researchers with high rates of agreement obtained. Studies not rejected at this stage were obtained and read in greater depth to assess relevance.

Inclusion criteria were that studies should 1) be aggregate level time series analyses with sufficient data points to assess lag specifications; 2) examine effects of changes in alcohol consumption on rates of alcohol-attributable health, crime or employment harms; 3) conduct analyses of at least one of the three lag specifications of interest. The main exclusion criteria were that 1) studies should not simply include lag specifications without mentioning any testing of alternative specifications and 2) that lag specifications should be empirically analysed, not simply inferred from inspection of time series graphs or raw data.

Data extraction was undertaken by the lead author. The key data extracted were location of study and time period, modelling approach employed, specific consumption and harm measures used, the lag specifications and the method used for deriving them

No meta-analysis was attempted as the resulting lag specifications are insufficiently homogenous in structure or varied in duration for this to be meaningful.

3. Results

The results of the literature search are shown in Figure 2. Of 3,342 studies initially identified, 18 were included in the narrative synthesis with a further 18 studies identified through reference and citation checking of those studies. Reporting of the results is structured as follows: a summary of the different methods used to derive lag specifications and their implications are presented first, followed by the lag specifications used for liver

cirrhosis, heart disease and suicide in turn. Finally, a brief summary of results for other harms is presented. For each harm section, the results for time to first effect are discussed first followed by the results for the functional form and finally the time to full effect. The full results can be seen in the online Appendix 2.

3.1 Methodological findings

The most widely used approach to modelling population-level time series relationships between alcohol consumption and alcohol-related harm is ARIMA modelling, also referred to as the Box-Jenkins method, (Box & Jenkins 1976), and this was used by almost all of the studies identified. This method allows analysts to regress the harm series onto the consumption series whilst controlling for a range of statistical features commonly found in time series which may bias parameter estimates. These include underlying trends in the data, autoregression of the time series and autocorrelation of error terms. ARIMA modelling also permits easy inclusion of consumption levels from previous years as additional predictors of current levels of harm in the regression equation. Therefore, a common approach is to weight the coefficients of these lagged consumption terms to specify the lagged effects of consumption on harm – the lag structure. .

The basic ARIMA model estimating the influence of alcohol consumption on alcohol-related is as follows:

$$\nabla \ln H_t = b\nabla Aw_t + c\nabla D_t + \nabla \ln N_t$$

Where ∇ indicates the series has been differenced to account for shared underlying trends between the consumption and harms series which may bias correlations; $\ln H_t$ is the natural logarithm of the harm series at time t; b is the effect of a weighted alcohol series (Aw_t) on harm; c is the effect of confounders (D_t) on harm and N_t is the noise term which may include autoregressive or moving average parameters (see Box & Jenkins 1976).

The weighted alcohol series contains the lag structure such that:

$$b\nabla Aw_t = w_0 A_t + w_1 A_{t-1} + w_2 A_{t-2} + \ldots + w_j A_{t-j}$$

Where w terms are the different effects of the lagged alcohol consumption series A.

Although most studies employed ARIMA modelling, this was not always the case and where lag specifications differed between studies, a key explanation is found in different methodological approaches to deriving specifications. Although rarely discussed in the literature, the methods employed have important implications for the lag specifications which are chosen and also for which lag parameters are being derived within the analysis and which must be implicitly or explicitly selected a priori.

Four main approaches to deriving specifications were identified and are outlined below with a summary provided in Table 1.

The first approach, employed initially by Skog (1984) and subsequently by Norström (1987), draws on aetiological literature and a proposed risk function for liver cirrhosis to hypothesise

a distributed lag structure with both short- and long-term effects operating over many years and taking the form:

$$\omega = p\lambda_1^t + (1-p)\lambda_2^t$$

Where ω is the total lag weight at time t, λ_1^i is the short-term effect at time t, λ_2^i is the long-term effect at time t and p is the balance of total effect between the short- and long-term effect where $p \leq 1$ and $p \geq 0$. Skog then derived parameters to fit this pre-specified structure for Britain giving the lag structure:

$$\omega = 0.85 * 0.6^t + (1-0.85) * 0.95^t$$

Norström (1987) subsequently replicated Skog's findings by selecting the same form of lag structure and re-estimating its parameters for the Swedish context, obtaining the lag structure:

$$\omega = 0.80 * 0.5^t + (1-0..8) * 0.93^t$$

Although comprehensive, Skog's approach is complex, requiring inferences drawn from analyses across multiple data sources and has not been attempted in the published literature for other harms. For this reason, we distinguish it from other approaches.

The second approach is more widely used and involves iteratively testing the significance of lagged consumption terms in regression equations (usually ARIMA regression equations but in some cases generalised linear model regression equations) to assess the effects of consumption in each previous year on current levels of harm. Significant terms are then included in the final regression equation. Although, the derivation of a functional form for the lag structure is usually not an explicit aim of this process, such a structure is implied by the relative size of each consumption year's coefficient in the regression equation.. Skog and Elekes (1993) extend this analysis by using a Koyck model (Johnson 1984) to derive a functional form, however, no other study did so. This second approach to empirically deriving lag specifications is more straightforward than Skog's (1984) method; however, identification of long-term lags is hampered by the difficulty of testing the significance of small effect sizes seen at longer lags. As a result, studies using this approach tend to identify only short-term lag structures and this may be considered an inherent bias.

The third approach is to select a functional form a priori and then compare model fit or the total effect of consumption on harm for different times to full effect, thus obtaining a lag duration. The functional forms selected and times to full effect tested are often based on those used in previous studies or theoretical assumptions, although the selection process is rarely discussed in detail. This approach is again relatively straightforward; however, it makes assumptions about the transferability of lag structures across contexts and harms. For example, Norström's (1987) cirrhosis lag specifications, which were derived for Northern Europe, were used for Eastern European data (Ramstedt 2007) and for pancreatitis (Ramstedt 2004). Whether different consumption histories or disease processes challenge the validity of transferring specifications, this is, again, rarely discussed in the text. An advantage of this

approach is that it allows longer lags to full effect to be specified as the focus is on model fit and total effect size rather than the significance of individual consumption terms.

A final approach is to test the significance of correlations between harm series and the consumption series at various lags. Best practice suggests this should be done using differenced data (Norström & Skog 2001) although this is not always adhered to. This approach is the weakest of the methods as it has the same difficulties in identifying longer lags as the second approach and does not derive or imply a functional form for the lag structure.

As noted above, most papers offer little or no explanation of why they have chosen a particular method. However, when reading the results below, the limitations of each approach should be borne in mind when interpreting the lag specifications which have resulted. No approach can be said to be inherently superior as, for example, Skog's approach is comprehensive but beyond the scope of many analyses, testing the significance of regression terms is straightforward but has a bias for shorter lag durations and selecting lag structures a priori offers grounding in previous research but justifications for the validity of selections are rarely readily available.

3.2 Liver cirrhosis

The most sophisticated work on lag specifications has been undertaken for liver cirrhosis with eight studies identified covering a broad range of developed nations (Corrao 1998; Corrao et al. 1997; Kerr et al. 2000; Norström 1987; Ramstedt 2007; Roizen et al. 1999; Skog 1984; Ye & Kerr 2011) and Eastern Europe (Corrao 1998; Corrao et al. 1997; Roizen et al. 1999). Methods used for selecting lag structures were the Norström/Skog approach (Norström 1987; Skog 1984), significance testing of regression terms (Kerr et al. 2000; Roizen et al. 1999) and comparison of overall effect size or model fit (Corrao 1998; Corrao et al. 1997; Ramstedt 2007; Ye & Kerr 2011). Where sufficient specifications and information were available, the lag structures are shown in Figure 3.

Most studies used lag specifications which modelled an immediate effect and, where tested, change in current aggregate drinking was found to have a significant effect on cirrhosis rates within the first year following the change (Corrao 1998; Corrao et al. 1997; Kerr et al. 2000; Roizen et al. 1999). Evidence from Eastern Europe was contradictory with studies finding the first effect was lagged by more than five years (Corrao 1998; Corrao et al. 1997) whilst Ramstedt (2007) modelled an immediate effect. Limitations relating to the use of undifferenced time series in the Corrao studies and specifying immediate effects a priori in the Ramstedt study mean neither finding can be considered robust evidence; thus further validation of the time to first effect is needed for Eastern Europe.

Four of the cirrhosis studies attempted to derive a functional form for the lag structure (Kerr et al. 2000; Norström 1987; Roizen et al. 1999; Skog 1984). In all cases the greatest single year effect was seen in the first year with effects of declining magnitude seen in subsequent

years. The size of the first year effect showed some consistency with Skog (1984), Norström (1987) and Kerr et al. (2000) finding approximately 60 per cent of the total effect is seen in the first year if Skog and Norström's lag durations are truncated to the same length as Kerr et al.'s. A smaller first year effect of 23 per cent was derived by Roizen et al. (1999) and the reasons for this disparity are unclear. One possible explanation may lie in Roizen et al.'s national-level US data being less robust to random error than Kerr et al.'s pooled state-level US data.

The duration to full effect was estimated by four studies (Kerr et al. 2000; Ramstedt 2007; Roizen et al. 1999; Ye & Kerr 2011) and, additionally, the lag structures of both Skog (1984) and Norström (1987) imply the full effect is distributed over as many as 40 years. Roizen et al. (1999) and Kerr et al. (2000) found only short-term lagged consumption term were significant in their regression equations and, consequently, the lag duration was truncated to two years and one year respectively. In contrast Ye and Kerr (2011) and Ramstedt (2007) tested the effect size of Norström's (1987) lag structure with lag durations of zero and five years, with Ramstedt also testing a ten year lag model. In both cases the five year lag models showed larger effects than alternatives, although the differences may be insignificant for some of the wide range of modelling techniques explored by Ye and Kerr. Given the difficulty of identifying small individual effect sizes at longer lags (Norström & Skog 2001), this review gives greater weight to those studies comparing different lag durations rather than testing individual terms and concludes that lags of at least five years may be necessary to capture the full effect of changes in aggregate alcohol consumption on rates of cirrhosis mortality. However, it should be noted that the number of specific lag durations tested was limited and evidence in this area can therefore only be considered as indicative at this stage.

3.3 Heart disease

Eight studies addressed ischaemic heart disease (IHD) with data again taken from a range of developed countries (Hemstrom 2001; Kerr et al. 2011; Kerr & Ye 2007; Laporte et al. 1980; Schmidt & Popham 1981; Skog 1983) and Eastern Europe (Razvodovsky 2009a, 2010a). Lag specifications were selected using comparison of overall effect size or model fit (Hemstrom 2001; Kerr et al. 2011) and cross correlation of differenced (Razvodovsky 2009a, 2010a; Skog 1983) or undifferenced (Laporte et al. 1980; Schmidt & Popham 1981) time series. One study selected lagged specifications using unspecified testing (Kerr & Ye 2007). Where sufficient specifications and information was available, the lag structures are shown in Figure 4.

Most of the studies found significant effects on heart disease rates in the first year and no evidence of a lag to first effect in any context. The exception was LaPorte et al. (1980) which found a five year lag to first effect for beer consumption and no significant effects for other alcohol measures. Given the consistency across the other studies, it is likely this result can be attributed to the analysis using undifferenced time series with their associated biases (Gruchow et al. 1983).

Five of the studies found no evidence of, or did not test for, a lag to full effect and consequently included no lag structure (Kerr & Ye 2007; Laporte et al. 1980; Razvodovsky 2009a, 2010a; Skog 1983). Where lag structures were used, there was limited information provided as to why these were selected. Both Kerr et al. (2011) and Hemström (2001) employed distributed geometrically declining lag structures (i.e. lag structures where the lag weight allocated to each lagged year i equalled x^i). Kerr et al. derived a distributed lag structure where x equalled 0.7 through testing which is not detailed in the paper, whilst Hemström employed a lag structure where x equalled 0.8 which was derived in a study of cigarette smoking and all-cause mortality (Hemstrom 1999). As with the liver cirrhosis lag structures, both of these loaded the greatest effect onto the first year with declining loads on subsequent lagged years.

Systematic disagreement was found with regard to the duration to full effect. Studies which used cross-correlation of differenced time series found no significant lags to full effect; however, those studies which compared a zero lag model to one with five or six years lag (Hemstrom 2001; Kerr et al. 2011) found the longer lag durations gave the better model fit. This is again in line with the implications of the methodological results discussed above relating to identifying small effect sizes at longer lags.

3.4 Suicide

Suicide represents something of a special case in the time lags literature as it straddles the boundary between chronic harms, which are assumed to be subject to lagged effects, and acute harms, which are not. An individual may commit suicide both following a single bout of heavy drinking and also as a result of suicidal ideation attributable to chronic heavy drinking (Mäkelä 1996). Ten studies relating to suicide were identified with the study locations covering Russia (Pridemore & Chamlin 2006; Razvodovsky 2009c, 2009d, 2010b; Stickley et al. 2011), Belarus (Razvodovsky 2007b, 2009b, 2011), Hungary (Skog & Elekes 1993) and Finland (Mäkelä 1996). Methods for estimating lag specifications were cross-correlation of differenced time series (Pridemore & Chamlin 2006; Razvodovsky 2007b, 2009b, 2009c, 2009d, 2010b, 2011; Stickley et al. 2011) and significance testing of regression terms (Mäkelä 1996) with one study extending this approach by using Koyck models (Skog & Elekes 1993).

In all studies, an immediate effect of changes in aggregate consumption on the suicide rate was found. In five of these studies, the total effect occurred in the first year and no lagged effects were identified (Pridemore & Chamlin 2006; Razvodovsky 2007b, 2009d; Stickley et al. 2011). Only one of the studies reported sufficient data to describe a lag structure. Skog and Elekes (1993) found 33 per cent of the total effect occurred in the first year, followed by 45 per cent at one year's lag with the remaining 22 per cent distributed over later lags of around five years. The remaining four studies found a lag to full effect of just one year (Mäkelä 1996; Razvodovsky 2009c, 2010b, 2011).

In line with expectations regarding the relationship between suicide and acute and chronic drinking, the studies which identified no lagged effects were all those which used proxies for acute drinking as their consumption measure whereas studies which identified lagged effects all used mean consumption measures.

3.5 Other harms

In addition to those harms discussed above, smaller numbers of studies were found which tested lag specifications for overall alcohol-related mortality (Skog 1987), pancreatitis (Ramstedt 2004), diabetes (Razvodovsky 2008a), delirium tremens (Skog & Melberg 2006), drink-driving related incidents (Wagenaar 1985), homicide (Razvodovsky 2007a, 2008b; Stickley & Razvodovsky 2011), work absences (Norström 2006) and various forms of violent and sudden alcohol-related mortality (Razvodovsky 2010b; Skog 1986). As above, different approaches for selecting lag specifications were used, namely comparison of overall effect size or model fit (Ramstedt 2004), cross-correlation of differenced time series (Razvodovsky 2007a, 2008a, 2008b, 2010b; Skog 1986; Skog & Melberg 2006; Stickley & Razvodovsky 2011; Wagenaar 1985) and unspecified or unsuccessful testing in two cases (Norström 2006; Skog 1987).

Immediate effects were specified for all of the above studies, although not all studies actually tested for the presence of these effects. A range of lag structures were applied, however, only the Wagenaar (1985) study of drink-driving derived its lag structure. Others transferred lag structures derived for other harms to a new context. For example, Ramstedt's (2004) analysis of pancreatitis mortality used Norström's (1987) cirrhosis lag structure and Norström's (2006) study of work absence used a 0.7 geometrically declining lag structure derived for all-cause mortality (although Norström notes that efforts to derive a work absence-specific lag structure were unsuccessful). The duration to full effect was tested in several studies and results ranged from zero years to five years; however, as above, the specification of this duration appeared partially dependent on the means used to derive it with shorter durations found when significance testing was employed.

3.6 Harms not covered

Studies testing lag specifications were not found for many alcohol-related harms including alcohol-related cancers and strokes, wholly alcohol-attributable chronic conditions with low incidence such as alcoholic polyneuropathy and alcohol-induced pseudo-Cushing's syndrome and alcohol-attributable crime or workplace harms. It was also noteworthy that no studies addressed aggregate alcohol-related morbidity, although one excluded study of time lags in policy effects on hospitalisations was identified (Jarl et al. 2010). We make suggestions for lag specifications for these harms in the discussion section and table 2 below.

4. Discussion

The above review presents current knowledge on the different ways of deriving time lag specifications when modelling the effects of aggregate alcohol consumption on rates of various alcohol-related harms. Although consistency across studies is limited, some recommendations can be made about valid lag specifications for different harms. These are presented at the start of the discussion followed by some general comments on deriving, modelling and reporting lag specifications.

The results highlight that substantial work on lag specifications has only been conducted for liver cirrhosis, heart disease and suicide mortality, with the latter primarily examined in the context of Eastern Europe with its particular drinking culture. For these harms, the evidence indicates that immediate effects from a change in alcohol consumption should be expected at the aggregate level. The theoretical rationale is well established in the case of liver cirrhosis mortality and relates to the notion of critical thresholds whereby individuals with advanced cirrhosis are particularly sensitive to consumption changes (Norström & Skog 2001). For suicide the immediate effect is attributed to the role of acute intoxication in prompting the suicidal act. However, for heart disease, the rationale is ill-addressed and better links need to be made between the aetiological and aggregate time series literature to explain this finding. A range of lag structures and durations to full effect are applied and Figure 5 demonstrates how different lag structures can substantially alter the rate at which the total effect accumulates. The lag structures used typically specified the immediate effect as the greatest single year effect, with declining effects attributed to subsequent years[1]. However, a justification for this is only found in the empirical work of Skog (1984) and Norström (1987) on liver cirrhosis. The substantial variation found in durations to full effect is partly a product of methodological decisions, but for liver cirrhosis, models which have specified lag durations of five or more years have typically found these specifications fit the data better and show larger overall effect sizes than short-term lags, although only limited exploration of this has been undertaken. In the case of heart disease, there is less evidence or agreement and work remains to be done to establish appropriate lag durations. For suicide, a lag duration of one year is repeatedly found for the Eastern European context.

The overall findings of the review describe a fairly underdeveloped knowledgebase, with a lack of any literature on a large number of major alcohol-attributable harms such as cancers and stroke. For alcohol-related morbidity, specifying temporal effects such as lag times is complicated by the fuzzy nature of the state of morbidity, inconsistent recording practises and difficulties in linking the timing of diagnoses with disease progress. Consequently, morbidity

[1] For example, Kerr et al. [23] use a geometric lag structure of the form $w = 0.7^i$ where w is the lag weight at time i. For a five year lag, 36% of the total effect would occur in the first year with 25%, 18%, 12% and 9% occurring in the four subsequent years respectively.

lag specifications have generally not been addressed, despite some attention being given to the area in policy evaluations and avoidable cost studies (Herttua et al. 2011; Jarl et al. 2010).

Our motivation for reviewing time lag specifications was to inform the selection of specifications for use in a model of the effects of alcohol policies on alcohol consumption and related harms (Purshouse et al. 2009). Existing versions of the model assume no time lags for acute harms and all chronic conditions specify an immediate effect with linear functional form and ten years to full effect. As an addendum to this paper, we present in Table 2 what we consider to be our current 'best evidence' specifications for the full set of health harms modelled. These specifications would be used for all population groups for both mortality and, in the absence of better information, also morbidity. For cancers, selection was informed by a study of the change in head and neck cancer risk following drinking cessation (Rehm et al. 2007). For other harms where evidence was not found in the review, specifications were selected in consultation with clinicians. This involved considering the processes by which alcohol causes each harm, comparing processes for harms with time lag evidence and those without and, in line with these comparisons, modifying the specifications for harms with evidence to provide specifications for those without. Lag specifications were truncated at a maximum of twenty years to reflect the longest expected running time of our model. This process is clearly prone to subjectivity and we welcome discussion of our suggestions.

One reason for the lack of attention given to time lags in the literature is that modelling them is a challenging task. It requires investigation of the aetiological and disease literature to inform and rationalise decisions, with awareness given to the relevance of both initial volume and patterns of consumption, the exposure period required for disease development, evidence of protective effects, the influence of competing risks, the risks for different social groups and the functional form of those risks. At the population level, attention needs to be given to age, period and cohort trends which may also distort temporal processes. It may also be necessary to address whether the lag response differs for consumption increases and decreases. Such complexity may be acting as a barrier to further investigation, particularly as time lags are typically only one element of most time series analyses (Rehm & Gmel 2001).

One area needing further work is the rationale for applying lag specifications. Where specifications are used, it is rare for their meaning to be explicitly considered in print. Little attention has been given to establishing a rationale for immediate effects where the critical threshold explanation used for liver cirrhosis may not apply. The widely-used practice of transferring lag specifications between contexts (Ramstedt 2003; Ramstedt 2007) or between harms (Hemstrom 2001; Ramstedt 2004), is typically undertaken without reflection being offered on how particular drinking cultures and histories may shape the nature of lag responses. A more specific area meriting further attention is the protective effect against heart disease associated with moderate consumption. That this has not been addressed is perhaps unsurprising as the effect has primarily been studied at the individual level, however, any proposed rationale for heart disease lag specifications may need to account for the j-shaped individual-level risk function.

Greater reflection is also needed on how methodological decisions play a substantial role in determining which lag specifications are selected. Where lag structures or durations have been derived using significance testing, longer-term lags to full effect are rarely identified. Although it is possible this reflects the true nature of the effect, Norström and Skog (2001) argue it is due to the difficulties of significance testing for the small effect sizes inherent to longer-term lags.

With these considerations in mind we recommend the following to ensure better theoretical and empirical validation of lag specifications. Where possible, a comprehensive approach such as that undertaken by Skog (1984) and Norström (1987) should be used. This allows the identification of more complex lag structures which incorporate both short- and long-term effects as well as achieving improved model fit and longer lag times. Incorporating such complex lag structures has costs in terms of parsimony and the impact on overall effect estimates may be small; however, where there is a strong interest in modelling the distribution of lagged effects across individual years, the trade-off may be beneficial. More generally, it would be a valuable addition to the field if further in-depth empirical work along these lines were undertaken, particularly for harms other than liver cirrhosis and with an additional focus on how lag specifications may be affected by the individual and population-level contexts we discuss above.

If this more complex approach is not possible and structures are selected a priori, authors should be aware of how different approaches to selecting or deriving lag specifications may impact on their findings. In particular, we recommend that they should be explicit in justifying their selection and their source of lag structures, in noting where potential challenges to validity may lie and, in light of these acknowledgments, they should signpost when caution needs to be employed when interpreting results. When selecting lag durations using empirical methods, analysts should look beyond simply significance testing of regression terms and, instead, examine patterns in the sign of cross-correlations of lagged years which may indicate consistent effects despite a lack of statistical significance. They should also test model fit and overall effect size using different lag durations to explore whether longer lag durations may be appropriate.

5. Limitations

The main limitation of the review was the difficulty in identifying relevant studies as lag specifications were commonly not referred to in abstracts. Reference and citation checking and professional networks were invaluable in limiting this; however, it is possible studies may have been omitted due to non-identification.

6. Conclusions

Time lag specifications for aggregate time series analyses of the impacts of changes in alcohol consumption on alcohol-related harms are underdeveloped for most harms. For liver cirrhosis, heart disease and suicide some recommendations can be made including the expectation of immediate, front-loaded effects. In general however, greater research attention needs to be given to the rationale for choosing or applying particular lag specifications and the inherent complexity of the processes which aggregate to create time lag effects.

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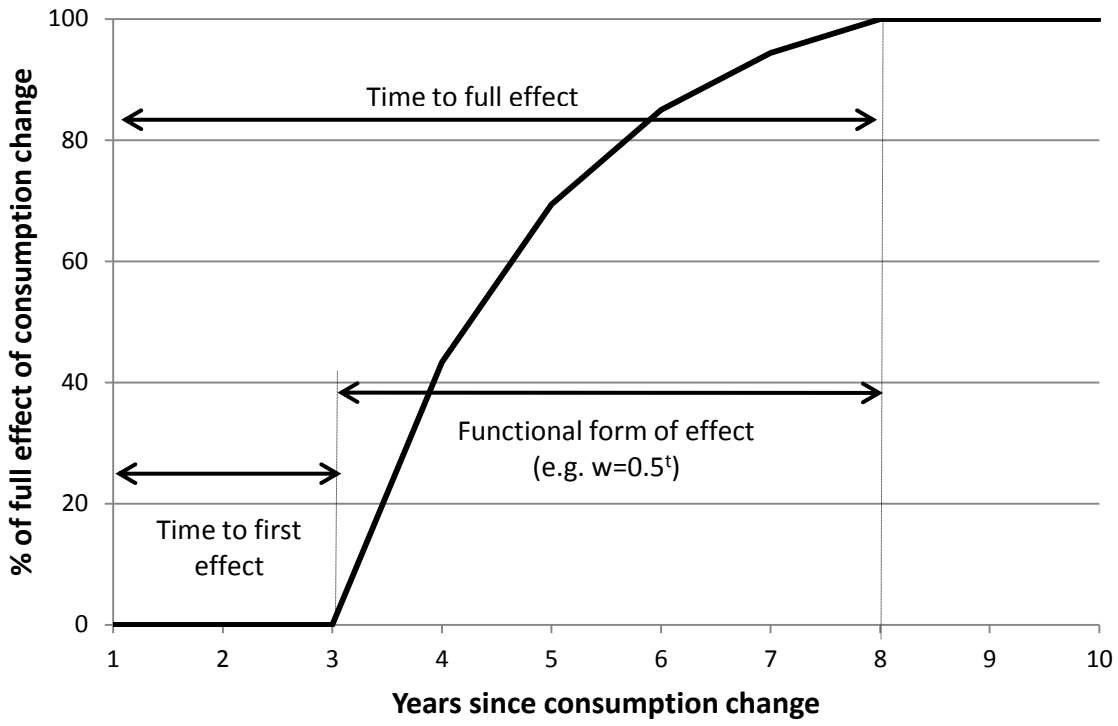

Figure 1: Time lag specifications for the effect of consumption change on harm

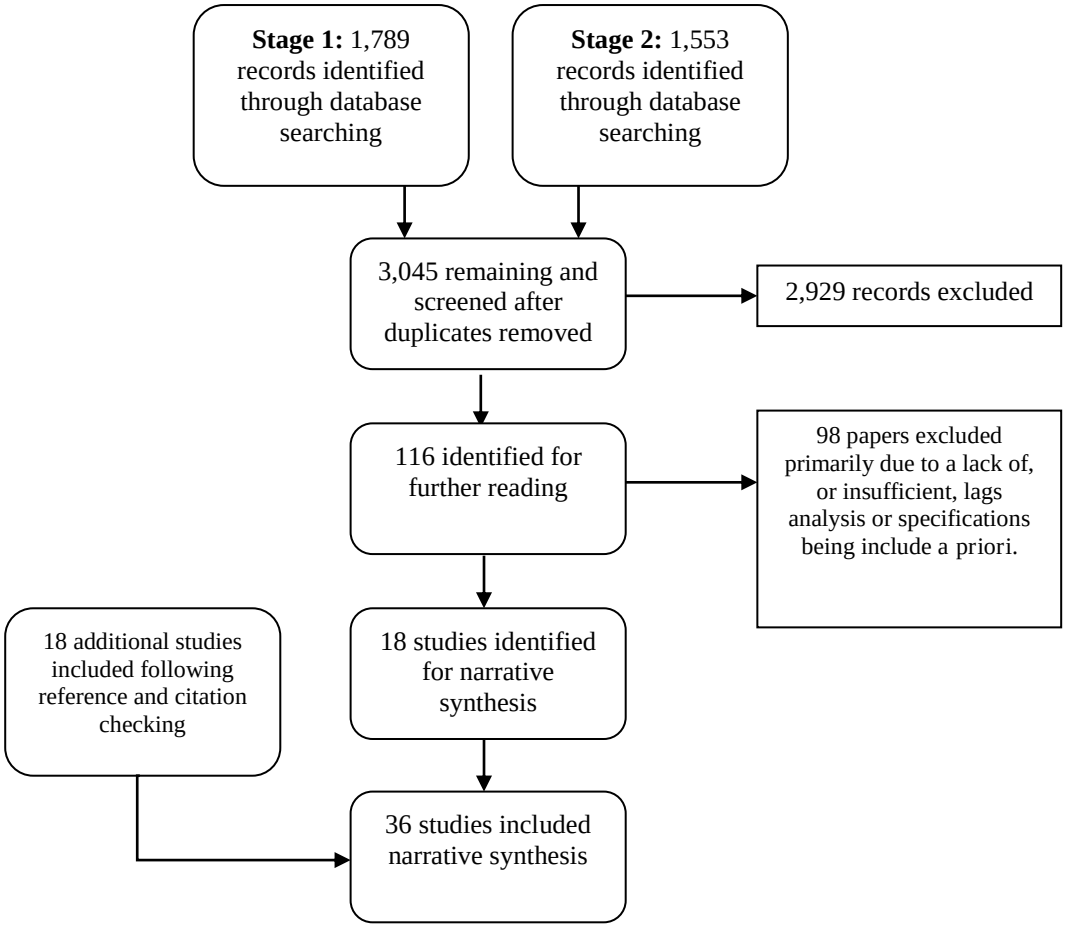

Figure 2: PRISMA Flow diagram of review results

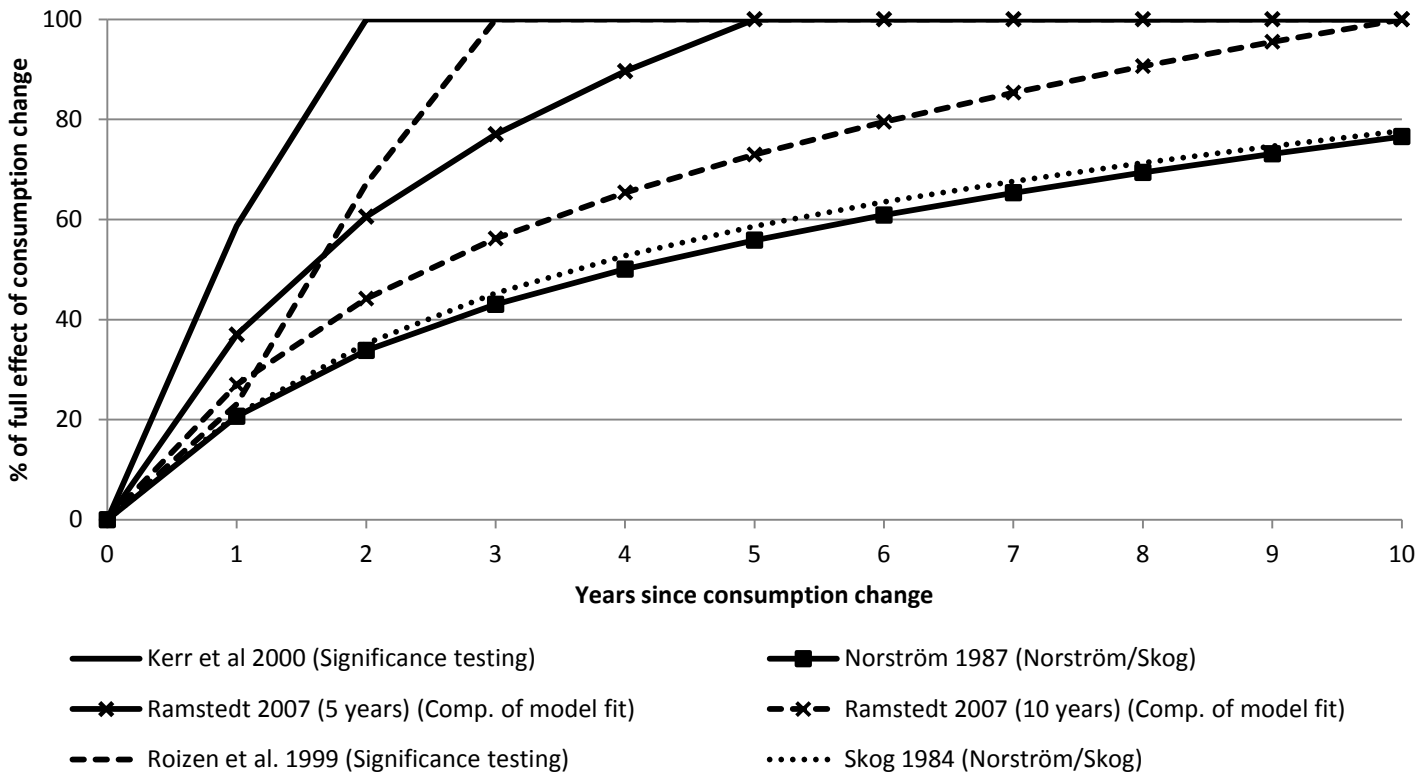

Figure 3: Accumulation of effect as described by lag specifications in liver cirrhosis studies (where sufficient specifications were provided)

Figure 4: Accumulation of effect as described by the lag specifications in ischaemic heart disease studies (where sufficient specifications were provided)

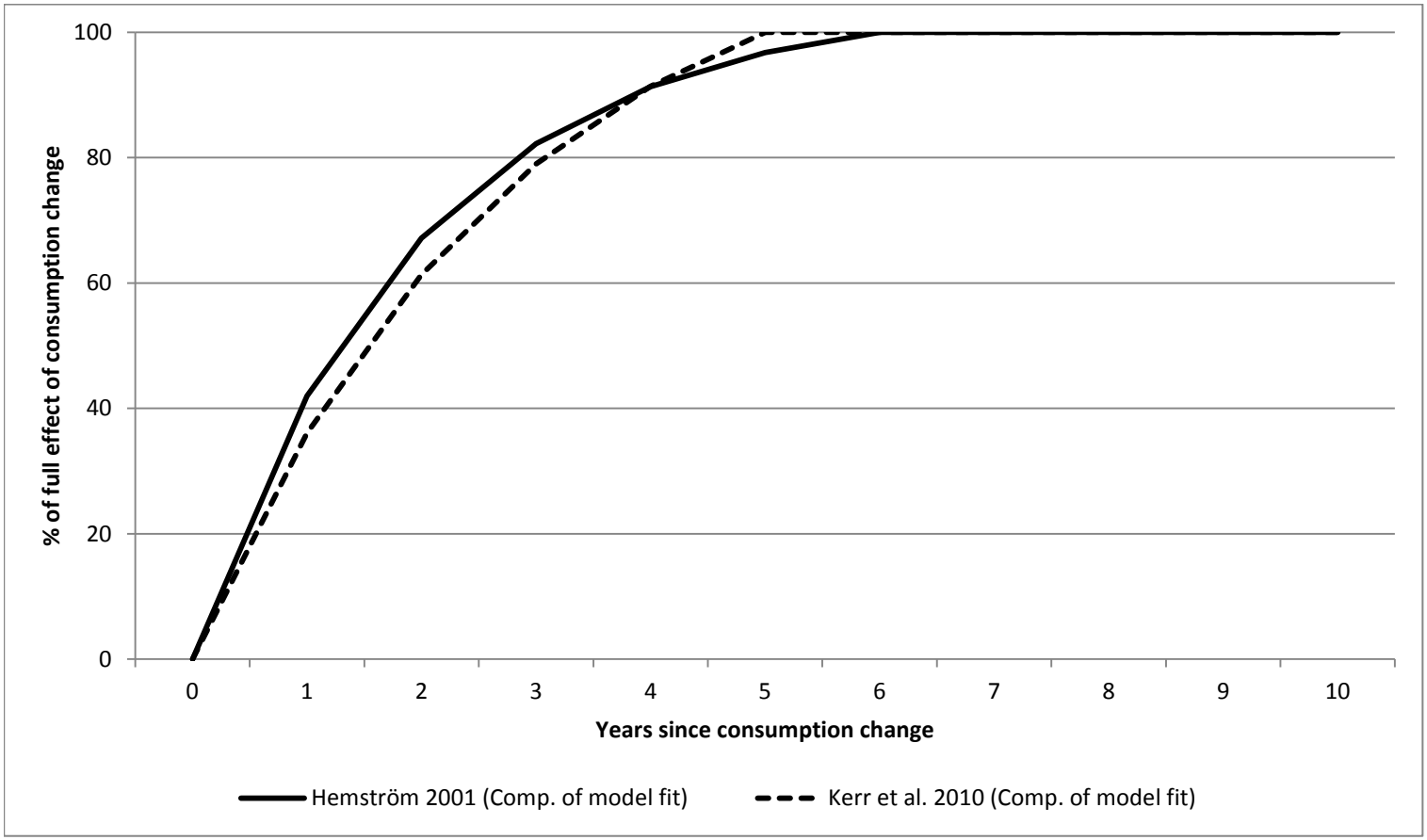

Figure 5: Accumulation of effect under different lag structures for a twenty year lag period

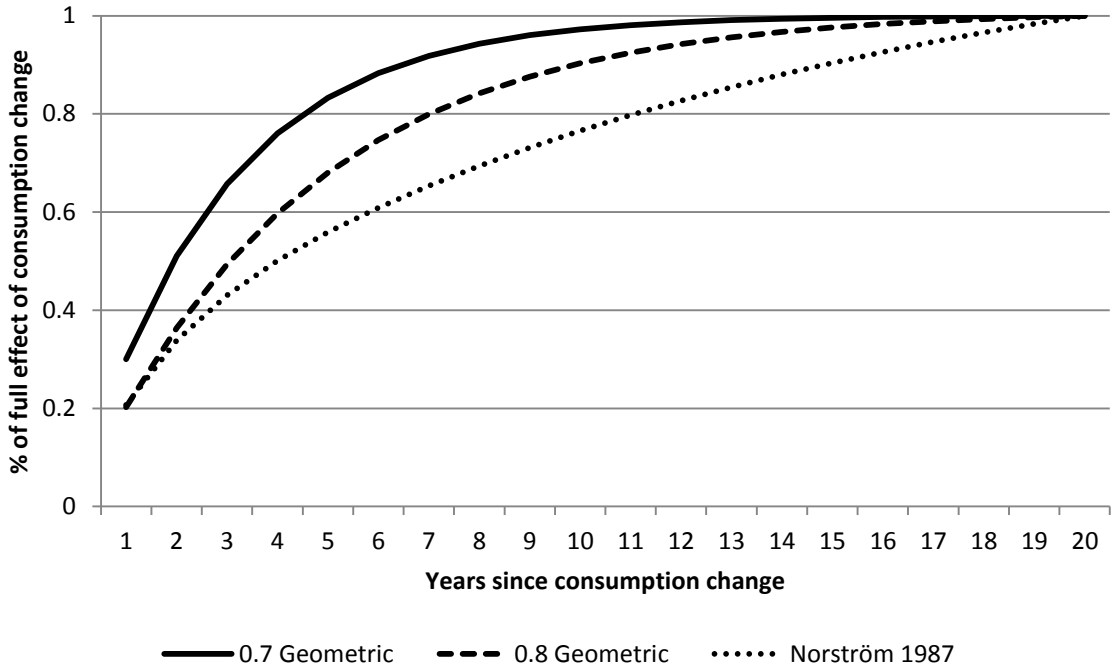

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Table 1: Approaches to selecting lag specifications

Method	**Specifications**		
	Time to first effect	**Time to full effect**	**Functional form**
Norström/Skog approach	Derived[1]	Derived	Derived
Significance testing of lagged regression terms	Derived	Derived	Implied[2]
Comparison of effect size and model fit	Selected a priori[3]	Derived	Selected a priori
Cross-correlation of time series	Derived	Derived	Not specified

[1]Derived specifications are those identified through analysis as part of the study.
[2]Implied specifications are those not directly derived but which are the result of selecting other parameters.
[3]Selected a priori specifications are those not resulting from analysis within the study and are usually based on earlier studies or theoretical considerations.

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Table 2: Proposed time lag specifications for chronic alcohol-related health harms

Harm	**ICD10 code**	**Time to first effect**	**Time to full effect**	**Functional form**
Alcohol-induced pseudo-Cushing's syndrome	E24.4	Immediate	20 years	Linear
Degeneration of the nervous system	G31.2	Immediate	20 years	Linear
Alcoholic polyneuropathy	G62.1	Immediate	20 years	Linear
Alcoholic myopathy	G72.1	Immediate	20 years	Linear
Alcoholic cardiomyopathy	I42.6	Immediate	20 years	Linear
Alcoholic gastritis	K29.2	Immediate	10 years	0.5 geometric
Alcoholic liver disease	K70	Immediate	20 years	Norström[1]
Chronic pancreatitis	K86.0	Immediate	20 years	0.8 geometric
Malignant neoplasm of lip, oral cavity and pharynx	C00-C14	10 years	20 years	Linear
Malignant neoplasm of oesophagus	C15	10 years	20 years	Linear
Malignant neoplasm of colon	C18	10 years	20 years	Linear
Malignant neoplasm of rectum	C20	10 years	20 years	Linear
Malignant neoplasm of liver and intrahepatic bile ducts	C22	10 years	20 years	Linear
Malignant neoplasm of larynx	C32	10 years	20 years	Linear
Malignant neoplasm of breast	C50	10 years	20 years	Linear
Diabetes mellitus (type II)	E11	Immediate	10 years	0.8 geometric
Epilepsy and status epilepticus	G40-G41	Immediate	5 years	0.6 geometric
Hypertensive diseases	I10-I15	Immediate	10 years	0.8 geometric
Ischaemic heart disease	I20-I25	Immediate	10 years	0.7 geometric
Cardiac arrhythmias	I47-I48	Immediate	10 years	0.8 geometric
Haemorrhagic stroke	I60-I62, I69.0-I69.2	Immediate	10 years	0.7 geometric
Ischaemic stroke	I66, I69.3, I69.4	Immediate	10 years	0.7 geometric
Oesophageal varices	I85	Immediate	20 years	Norström[1]
Gastro-oesophageal laceration-haemorrhage syndrome	K22.6	Immediate	5 years	Linear
Unspecified liver cirrhosis	K74, K74	Immediate	20 years	0.8 geometric
Cholelithiasis	K80	Immediate	5 years	Linear
Acute and chronic pancreatitis	K85-K86.1	Immediate	20 years	0.8 geometric
Psoriasis	L40 excludes L40.5	Immediate	10 years	0.5 geometric
Intentional self-harm	X60-X84	Immediate	5 years	0.4 geometric
Tuberculosis	A15-A19	Immediate	5 years	0.4 geometric
HIV/AIDS	B20-B24	Immediate	20 years	Linear

Appendix 1: Search strategy

1. Alcohol* OR drink* OR drunk* OR drank* OR liquor OR beer* OR wine* OR spirit* OR "malt beverage*" OR smok* OR cigar* OR tobacco NOT (radiat* OR mice OR rats OR pollut* OR hydro* OR MRSA OR staphylococcus OR pregnan*)
2. Alcohol* OR drink* OR drunk* OR drank* OR liquor OR beer* OR wine* OR spirit* OR "malt beverage*" OR smok* OR cigar* OR tobacco NOT (radiat* OR mice OR rats OR pollut* OR hydro* OR MRSA OR staphylococcus) AND (Miscarri* OR abort*)
3. #1 OR #2
4. Lag w/3 struct* OR delay w/3 effect* OR time w/3 lag* OR distribut* w/3 lag* OR laten* w/3 period* OR latent* w/3 effect*
5. Declin* w/3 effect* OR "time-limited" w/3 effect* OR decay* w/3 effect* OR tempor* w/3 effect* OR sustain* w/3 effect* OR perman* w/3 effect* OR ARIMA OR ARMA
6. "long* term" w/3 effect* OR "short* term" w/3 effect* OR full w/3 effect* OR contemporaneous w/3 effect* OR immediate w/3 effect*
7. #3 AND #4
8. #3 AND #5
9. #3 AND #6

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Appendix 1: Data extraction table

Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Cirrhosis mortality papers							
Corrao, 1998	Eastern Europe: Bulgaria, Hungary, Poland, Romania, former Czechoslovakia, Yugoslavia, East Germany. Europe as a whole 1970-89	Age-period-cohort analysis with regression to establish latency periods	Moving average of per capita alcohol consumption for population aged 15+ Standardised cirrhosis mortality rate	Comparison of model fit	E. Europe: 5 years Rest of Europe: Immediate	Method cannot estimate	Method cannot estimate
Corrao, 1997	22 European countries, grouped into northern, eastern, southern and western Europe 1961-89	Pooled time series using Poisson regression	Per capita alcohol consumption for population aged 15+ Cirrhosis mortality rate	Comparison of model fit	N. Europe: 1 year E. Europe: 6 years S. Europe: 2 years W. Europe: Immediate	Method cannot estimate	Method cannot estimate
Kerr et al., 2000	Australia, Canada, New Zealand, UK, USA 1953-93	Pooled time series using generalised estimating equations	Per capita alcohol consumption (total and beverage-specific) Standardised cirrhosis mortality rate for population aged 15+	Significance testing of lagged regression terms	Immediate	One year	Not specified
Norström, 1987	Sweden 1931-80	ARIMA	Per capita alcohol consumption Male liver cirrhosis mortality	Norström/Skog approach	Immediate	Zero years	$w_i = 0.80 * 0.50^i + 0.20 * 0.93^i$

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Ramstedt 2007	Eastern Europe: Belarus, Poland, Russia, Ukraine, Bulgaria, former Czechoslovakia, Hungary, Romania, former Yugoslavia Be: 1970-2003 Po: 1959-97 Ru: 1959-98 UK: 1965-2000 Bu: 1961-2003 Cz: 1950-91 Hu: 1950-2002 Ro: 1962-2002 Yu: 1961-90	Pooled time series using ARIMA	Per capita alcohol consumption (with adjustments for under-recording) Standardised total cirrhosis mortality rate for population aged 15+	Comparison of model fit	Immediate	Tested: Zero years: Total effect of 1L increase in consumption = 3.5% increase in cirrhosis Five years: Total effect of 1L increase in consumption = 9.1% increase in cirrhosis Ten years: Total effect of 1L increase in consumption = 7.8% increase in cirrhosis	See Norström, 1987 (specified a priori)
Roizen et al. 1999	USA 1949-94	ARIMA	Per capita alcohol consumption (total and beverage specific) Standardised total cirrhosis mortality rate for population aged 15+ Controls: ICD changes	Significance testing of lagged regression terms	Immediate	Two years	Not specified
Skog, 1984	UK 1902-75	ARIMA	Per capita alcohol consumption Live cirrhosis mortality	Norström/Skog approach	Immediate	Approximately 40 years	$w_i = 0.85 * 0.60^i + 0.15 * 0.95^i$

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Ye & Kerr, 2011	47 USA states (missing Alaska, Hawaii, Mississippi, Oklahoma) 1950-2002	Pooled time series using ARIMA, generalised estimating equations, generalised linear models, fixed effects models and multi-level modelling	Per capita alcohol consumption (total and beverage-specific) Standardised cirrhosis mortality rate	Comparison of effect size/model fit	Immediate	Tested: Five years: Total effect of 1L increase in consumption = 8% increase in cirrhosis Zero years: Total effect of 1L increase in consumption = 5% increase in cirrhosis	See Norström, 1987 (specified a priori)
Heart disease mortality papers							
Hemström, 2001	15 European countries 1950-95 (Spain: 1962-94)	ARIMA	Per capita alcohol sales for population aged 14+ (beers and spirits data missing 1960-4) Standardised IHD mortality rate Controls: ICD changes; per capita cigarette consumption (lagged); outliers	Comparison of effect size/model fit	Immediate	Tested: Six years and Zero years Insufficient reporting to provide comparison.	0.8 geometric (specified a priori)
Kerr & Ye, 2007	USA 1955-2002	ARIMA and Vector Error Correlation models	Per capita alcohol consumption (total beverage-specific) Standardised IHD mortality rate for population 15+ Controls: Per capita cigarette consumption; cirrhosis mortality rate; per capita sugar sweetened soft drink consumption; ICD changes	Unspecified	Immediate	Zero years	No time lag

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Kerr et al., 2011	USA (national and state-level) 1950-2002	Pooled times series using ARIMA Panel models using generalised least square models	Per capita alcohol consumption (total and beverage-specific) Standardised IHD mortality rate Controls: per capita tobacco consumption; standardised cirrhosis mortality rate; ICD changes	Comparison of effect size/model fit	Immediate	Five years	0.7 geometric (specified a priori)
LaPorte et al., 1980	USA 1950-75	Correlational	Beverage-specific consumption Age-adjusted ASHD mortality rates Controls: Cigarette consumption; Fat consumption	Cross-correlation of undifferenced time series	Immediate (beer) Effect not significance (other beverages)	Five years (beer) Effect not significant (other beverages)	Method cannot estimate
Razvodovsky 2009a	Belarus 1970-2005	ARIMA	Total alcohol sales (total and vodka) Myocardial infarction mortality rate Controls: Per capita cigarette sales	Cross-correlation of differenced time series	Immediate	Zero years	No time lag
Razvodovsky, 2010a	Russia 1970-2005	ARIMA	Per capita alcohol sales (total and beverage-specific) Age-adjusted, sex-specific cardiovascular mortality rate	Cross-correlation of differenced time series	Immediate	Zero years	No time lag

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Schmidt & Popham, 1981	19 developed countries 1950-77	Time series correlation	Per capita alcohol consumption IHD mortality rate	Cross-correlation of undifferenced time series	Immediate to 2 years lag	Method cannot estimate	Method cannot estimate
Skog, 1983	Norway 1951-80	ARIMA	Per capita alcohol sales (15+) Ischemic heart disease mortality Controls: Intervention model of unreliable data for 1978	Cross-correlation of differenced time series	Immediate	Zero years	No time lag
Suicide papers							
Mäkelä, 1996	Finland 1950-91	ARIMA	Per capita alcohol sales (15+) Age-specific male suicide rate (15+) Controls: Marriage, Divorces, Unemployment	Significance testing of lagged regression terms	Immediate	One year	Not specified
Pridemore & Chamlin, 2006	Russia 1956-2002	ARIMA	Sex-specific combined alcohol psychosis, cirrhosis and poisoning and chronic alcoholism rates per 100,000 Age-standardised sex-specific homicide mortality rate per 100,000; Age-standardised sex-specific suicide rate per 100,000	Cross-correlation of differenced time series	Immediate	Zero years	No time lag

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Razvodovsky, 2007b	Belarus 1970-2005	ARIMA	Alcohol psychoses rate Suicide rate	Cross-correlation of differenced time series	Immediate	Zero years	No time lag
Razvodovsky, 2009c	Russia 1970-2005	ARIMA	Alcohol sales per capita (total and beverage-specific) Age-adjusted, sex-specific suicide rate	Cross-correlation of differenced time series	Immediate	One year	Not specified
Razvodovsky, 2009d	Russia 1956-2005	ARIMA	Age-adjusted, sex-specific alcohol poisoning mortality rate Age-adjusted, sex-specific suicide rate	Cross-correlation of differenced time series	Immediate	Zero years	No time lag
Razvodovsky 2010b	Russia 1980-2005	ARIMA	Per capita alcohol sales (total and beverage-specific) Violent mortality rate plus individual mortality rates for each of alcohol poisoning, homicide, suicide and accidents or injury	Cross-correlation of differenced time series	Immediate	Zero years: Homicide, fatal alcohol poisoning (total alcohol); violent mortality, accidents/injuries, suicide, fatal alcohol poisoning (vodka) One year: Violent mortality, accidents/injuries, suicide (total alcohol); homicide (vodka)	Not specified

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Razvodovsky, 2011	Belarus 1980-2005	ARIMA	Per capita alcohol consumption Total, BAC positive and BAC negative suicide mortality rate per 100,000	Cross-correlation of differenced time series	Immediate	Total suicide rate: Zero years BAC positive suicide rate: One year BAC negative suicide rate:: no relationship	Not specified
Skog & Elekes,1993	Hungary 1950-90	ARIMA Granger's causal test	Per capita alcohol consumption (total population Suicide rate per 100,000 (total population)	Significance testing of lagged regression terms extended with Koyck models	Immediate	Two years	33% of effect in first year 45% of effect at one year lag
Stickley et al. 2011	Russia 1870-94 1956-2005	ARIMA	Alcohol consumption per capita (Tsarist only); Alcohol poisoning mortality rates per 100,000 Suicide rate per 100,000 Alcohol poisoning mortality rates per 100,000 (Tsarist only)	Cross-correlation of differenced time series	Immediate	Suicide: Zero years Alcohol poisoning: One year	Not specified
Homicide and other violent mortality papers							
Razvodovsky, 2007a	Russia 1956-2005	ARIMA	Alcohol poisoning mortality rates Age-adjusted, sex-specific homicide rates	Cross-correlation of differenced time series	Immediate	Zero years	No time lag
Razvodovsky, 2008b	Belarus 1970-2005	ARIMA	Alcohol psychoses mortality rate Homicide rate	Cross-correlation of differenced time series	Immediate	Zero years	No time lag

Study	Location and	Modelling technique	Consumption,	Derivation	Time to first effect	Number of lagged years to full	Lag structure

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	period		harm and control measures	method		effect	
Razvodovsky 2010b	Russia 1980-2005	ARIMA	Per capita alcohol sales (total and beverage-specific) Violent mortality rate plus individual mortality rates for each of alcohol poisoning, homicide, suicide and accidents or injury	Cross-correlation of differenced time series	Immediate	Zero years: Homicide, fatal alcohol poisoning (total alcohol); violent mortality, accidents/injuries, suicide, fatal alcohol poisoning (vodka). One year: Violent mortality, accidents/injuries, suicide (total alcohol); homicide (vodka)	Not specified
Skog, 1986	Norway 1930-80	ARIMA	Per capita consumption (15+) Violent deaths mortality rate	Cross-correlation of differenced time series	Immediate	Zero years	No time lag
Stickley & Razvodovsky, 2011	Russia 1970-2005	ARIMA	Per capita alcohol consumption (Total and beverage specific) Age-adjusted, sex-specific homicide rates per 100,000	Cross-correlation of differenced time series	Immediate	Zero years (total alcohol) One year (vodka)	Not specified

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Miscellaneous papers							
Norström, 2006	Sweden 1936-2002	ARIMA	Per capita alcohol sales for population aged 15+ Sickness absence rate per insured person Sickness absence according to Labour Force Survey Controls: percentage of workforce unemployed, real wages, changes in recording practices of sickness absence rate	No derivation – derivation of lag structure attempted but results were largely insignificant, inconsistent or implausible	Immediate	Five years	0.7 geometric
Ramstedt, 2004	14 western countries: Finland, Norway, Sweden, Austria, Belgium, Denmark, Netherlands, Ireland, UK, West Germany, France, Italy, Spain, Canada, with grouping for northern, mid- and southern Europe 1950-95	Pooled time series ARIMA	Per capita alcohol sales for population aged 15+ Age-adjusted acute, chronic and combined pancreatitis mortality rates for population aged 15+ Controls: ICD changes	Comparison of effect size/model fit	Immediate	Tested: Five years: 1L increase in consumption = 25% increase in pancreatitis Zero years: 1L increase in consumption = 15% increase in pancreatitis	See Norström 1987 (specified a priori)
Razvodovsky, 2008a	Russia 1956-2005	ARIMA	Age adjusted sex-specific alcohol poisoning mortality rate Age-adjusted, sex-specific diabetes mortality rate	Cross-correlation of differenced time series	Immediate	Zero years	No time lag

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Study	Location and period	Modelling technique	Consumption, harm and control measures	Derivation method	Time to first effect	Number of lagged years to full effect	Lag structure
Skog, 1987	Norway 1930-80	ARIMA	Per capita consumption (15+) Alcohol-related disease mortality (Liver cirrhosis, alcoholic psychoses, alcoholism, pancreatitis, cancers of the upper digestive tract and pancreas)	Unspecified	Immediate	Approximately 80 years	$w_i = 0.1 * \sum (0.9^i * Alc_{t-i}) + 0.5_i * \sum (0.5^I * Alc_{T-I})$
Skog & Melberg, 2006	Denmark 1911-31	ARIMA/Rational addiction	Beverage specific per capita sales Delirium tremens GNP (income proxy)	Cross-correlation of differenced time series	Immediate	1 year	65% in first year (spirits) No time lag (beer)
Wagenaar, 1984	Michagan, USA 1972-80	ARIMA	Total wholesale beverage-specific alcohol sales Total of officer-reported drinking driver incidents involving property damage or injury-producing motor vehicle crashes	Cross-correlation of differenced time series	Immediate (beer) 1 month (wine)	5 months: Property damage (beer) 1 month: Injury (beer); property damage, injury (wine)	Method cannot estimate