Author's response to reviews

Title: Using intervention time series analyses to assess the effects of imperfectly identifiable natural events: a general method and example

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Author's response to reviews: see over
Response to reviewers of manuscript MS: 1401350736793188 – (Using intervention time series analyses to assess the effects of imperfectly identifiable natural events: a general method and example)

Reviewer 1

This reviewer’s primary concern is that the manuscript devotes too much space to the methods used and not enough space to discussion of the results. This paper is intended to document the methods used to examine a natural event with an imperfect time of onset, and the results given in the paper were presented in brief to give examples of the consequences of applying the method. The reviewer seems to have misunderstood the article as an original research report rather than a contribution to methodology. However, in order to make this point clearer the following has been added to the introduction:

The aim of this paper is to describe how these methods can be applied to indicator data to construct and test plausible theories of the consequences of a poorly identified unplanned intervention in ways that minimize the risk of drawing erroneous conclusions. We identify the major challenges that arise in applying standard ITSA methods to the analysis of such natural experiments and suggest methods for overcoming them. Examples from the Australian heroin shortage, a unique and expected event, are used for illustrative purposes only, results of such research which can be found elsewhere.

Reviewer 2

This reviewer also seems to believe that the article is presenting an analysis of a particular data set as an original research report, and as a consequence places too much emphasis on the presentation of the results. We have amended the introduction to the paper to make it clearer that our purpose is methodological description rather than reporting original research results. We refer interested readers to more detailed research reports on the heroin shortage.

Paragraph 3: published intervention experiments always involve a carefully timed or well-identified event, and generally literature on time series analysis methods frowns on the use of poorly-dated events [1]. Text to this effect has been inserted into the introduction.

Paragraph 4: The methods presented in this paper are an innovative use of Intervention Time Series Analysis (ITSA) rather than an innovative description of statistical methods for conducting ITSA. Statistical details have been avoided wherever possible, and reference is given to standard texts on the mathematics of time series analysis. Although the work is not intended as a review of time series methods, the authors have been unable to find any published work on ITSA with poorly-identified events in either the Web of Science, Medline or MathSciNet databases. The absence of such work is probably largely due to the strong advice against such research in standard literature, and it is for this reason that we have presented an innovative use of ITSA in analysing the effects of a unique natural experiment. The text has been amended to note this:

Many researchers recommend against the use of ITSA in such circumstances ([1]). We have been unable to identify any major published studies which perform ITSA on unplanned events.
with poorly identified time points, but the unique nature and large scale of unplanned events such as the Australian Heroin Shortage demanded an adaptation of these methods in order to better understand the effects of such events on various indicators of drug use and drug-related harm.

Our purpose in writing this article was not to discuss the interaction between heroin and cocaine markets in depth – this has been done elsewhere [2],[3]. This has been clarified in the introduction (see point 1 reviewer 1)

Discussion of the use of heroin market indicators such as heroin seizure purity and heroin price would be more relevant in a research report. Heroin seizure purity data in New South Wales, Australia is not collected consistently for all seizures and does not constitute a random sample of all such seizures [4, 5], so this data does not meet the criteria for ‘Indicator data’ laid out in the article. Data on price in New South Wales is not available as a time series, and the suitability of price data for ITSA has previously been criticized [1]. Although the reviewer’s point about the usefulness of this data and of possible covariates (such as arrest history and population subgroups) is well made, such analyses are secondary to the primary task of the paper (describing a new methodology), and the level of detail required is often not available for indicator data series. A comment regarding the limitations of these data series has been included in the paper:

*Indicator data often lack information on sub-populations and covariates, but notwithstanding their limited usefulness in the analysis of finely detailed hypotheses they remain of crucial importance in the analysis of major changes due to the types of unplanned events described here.*

**Paragraph 5:** The claim that our method is ‘detailed and exhaustive’ does not present a claim that our method is a ‘new statistical method’. We are presenting a research methodology, and this sentence has been changed to avoid confusion.

**Paragraph 6:** ‘mooted’ has been changed to ‘suggested’.

**Paragraph 7:** issues about the use of price and purity data are discussed above. This paper addresses the general methodological problem of how to identify the time point and construct simple models where limited flexibility and subjectivity in model-building minimises the risk of spurious findings due to incorrect dating of the event. Structural equation models for vectors of correlated outcomes are not simple models and introduce additional subjective researcher decisions which are likely to compound the effects of a poorly-identified time point. For this reason the paper does not discuss them, and leaves the extension of the method to these models for other researchers. The role of structural equation modelling in heroin market research is often raised by reviewers of time series papers, but very rarely actually used in practice, since the sort of data which is useful for modelling major policy interventions is usually much simpler, and the correlations between possibly related variables poorly understood. For example, this reviewer makes it clear that the links between heroin and cocaine markets are not well understood and multiple mechanisms can be postulated to explain these links. In the absence of a clear understanding of the mechanism by which these markets interact it would be unwise to try to test structural equation models to answer these questions.
Paragraph 8: reasons for not using purity data have been described above. A key part of the success of our proposed methodology is the use of Indicator Data, defined in the paper, and the type of surveillance data to which the reviewer refers does not fit this description. Data which qualifies as Indicator data is often collected on a very fine time scale, but this time scale requires aggregation into larger units or may not be available to the researchers. The discussion of these issues has been retained at the level of monthly data collection in order to reinforce the importance of indicator data as the natural data for these types of studies, and to maintain simplicity in the discussion of serial dependence. It should also be noted that time series analysis of data with daily or weekly intervals can require many more statistical tests for functions such as auto-correlation functions and partial auto-correlations, increasing the risk of spurious findings in the identification of the lag between the event and its effect on the series, and the serial dependence structure of the data. Monthly data usually requires only the first 12-15 lags of these functions to be identified, vastly reducing the risk of type I error at this stage of a modelling process whose major flaw is uncertainty in timing.

Paragraph 9: this sentence has been changed to refer to the collection rather than publication of the data: For example data on overdose deaths and nonfatal overdoses are not made public for a year or more after collection.

Paragraph 10: the method of transfer functions for ARIMA modelling handles a great deal of the discussion the reviewer has presented here, and is another part of the attractiveness of ARIMA time series modelling for ITSA. These transfer functions modify simple step, pulse or change of slope functions to represent a range of possible effects, including the ‘ramping up’ and ‘exponential decay’ described by the reviewer. They can even be used to model damped oscillations if required. These functions have the advantage of applying the fine detail of the response to the intervention based on the available information in the data series (rather than a researcher’s prior expectations), which makes them ideal for the situation described in the paper. Simple functions such as slope or step functions are also much more statistically viable than triangles, exponential growth curves, etc. and more easily modelled, and references have been given in the paper which discuss this matter extensively. In any case, the fundamental question asked by researchers is not ‘was the change triangular or decaying exponential’ but ‘was the change permanent or temporary’ with the less interesting secondary questions of ‘if permanent, did the change take time to occur’ and ‘if temporary, did the change take time to disappear’. The ARIMA method with transfer functions clearly separates these two questions, with the subsidiary questions being treated by the significance tests of the transfer functions and the main questions being handled by the significance tests of the slope and step themselves. Again, references have been given in the paper which describe the details of the modelling process, and our main concern has been to present the ways in which this process is complicated by unplanned interventions and the best methods for reducing the risk of spurious conclusions in the primary and secondary questions. Text has been inserted into the paper in the section headed “Modelling the effects of planned and unplanned interventions” which reflects these facts:

These transfer functions modify simple step, pulse or change of slope functions to represent a range of possible effects that include a long-term change which occurs after a period of ‘ramping up’, and a sudden increase followed by (possibly oscillating) ‘exponential decay’. Such a modeling process separates the primary question - ‘was the change temporary or permanent’ - from the secondary question: ‘what was the precise shape of the identified short
or long term change?’ The test of the step or pulse term is used to answer the first question and the transfer functions are used to answer the second question.

(inserted in the second paragraph of this section, near the end).

**Paragraph 11:** Publications elsewhere have discussed the first point of this paragraph. We do not agree with the reviewer’s second point that ‘how much substitution there was and why’ is ‘the real question of this paper’. This topic has been discussed elsewhere [6]. The real question of this paper is how best to model sudden interventions when the date of those interventions is not clearly understood. Further discussion of points such as ‘how much substitution there was and why’ would muddy the distinction between the paper as a methodological description and the conclusions which can be drawn from the simple example presented.

**Paragraph 12:** this discussion is better suited to a paper on the Australian Heroin Shortage, rather than a paper on the methods used.

**Paragraph 13:** the increase in cocaine possession offences, while smaller numerically than the decrease in heroin possession offences, was considerably larger as a percentage of the series (200% increase for cocaine vs. 45% decrease for heroin), and these figures have been included in the paper (pages 12 and 13). The wider implication of these differences in response is a topic best reserved for policy discussion, rather than a paper aimed at elucidating a methodology.

**Paragraph 14:**

The counter-factual for the example presented is: ‘What would have happened if the shortage had not occurred?’ The example and the methods here aim to describe only the consequences of the event, and little information can be gained by including a discussion of this counterfactual in the paper.

**Reviewer 3**

Reviewer 3 correctly points out the confusion caused by including an example which uses a statistical method not described properly in the methods, namely a method which is not an ARIMA time series. This alternative statistical approach was alluded to in the methods but not clearly described. The methods have been changed to give a more detailed description of this method and the reasons it should be applied. This change (rather than presentation of a different example) was made for two reasons:

1) the methodology described in the paper, while ideally suited to ARIMA time series, does not preclude the use of other methods when ARIMA methods are not suitable. The brief references to the major alternative method (linear models with serial dependent residuals) in the original manuscript were a confusing oversight of the authors

2) Although the alternative methods alluded to here are not as commonly used, their use in the heroin shortage project was necessary for the example given in this paper, which is a particularly interesting example of the considerable benefits to be obtained from the analysis of unplanned events with major consequences
The revised methods (in the section “Modelling the effects of planned and unplanned interventions”) make clear the two statistical approaches that are commonly used for time series analyses and the benefits and drawbacks of each. The changes are not detailed here. This change does not affect the substantive conclusions or purpose of the paper, since it simply elaborates upon a method already alluded to in the original paper.