Peer Review Report

Review Report on Revisiting transfer functions: learning about a lagged exposure–outcome association in time-series data.

Hints and Kinks, Int J Public Health

Reviewer: Antonio Gasparrini
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EVALUATION

Q 1 **Please describe the new method reported in this manuscript, and its purpose.**

The application of transfer functions in distributed lag model to investigate lagged associations.

Q 2 **Please highlight the limitations and advantages.**

Advantages: 1) no need to specify a lag length; 2) different shapes of lag structures available throught the selection of function parameters.
Limitations: 1) need to rely on traditional methods to select the parameters; 2) limited to linear associations; 3) no information on the comparative performance versus traditional methods.

Q 3 **Are there objective errors or fundamental flaws? If yes, please detail your concerns.**

No fundamental flaws.
The main issues are the misleading presentation of the methodology, already established in the literature of distributed lag models, as a novel application in this setting, and the overstated advantages if compared to traditional methods.

Q 4 **Check List**

Is the English language of sufficient quality?
Yes.

Is the quality of the figures and tables satisfactory?
Yes.

Does the reference list cover the relevant literature adequately and in an unbiased manner, including the primary manuscript(s) that describe the methodology?
No.

Are the quantitative or qualitative methods sufficiently explained and documented?
Yes.

Are the quantitative methods valid and correctly applied? (e.g. sample size, choice of test)
Yes.

Are the qualitative methods valid and correctly applied? (e.g. sample selection, method of data collection)
Yes.

Are the data underlying the study available in either the article, supplement, or deposited in a repository?
No.

Does the study adhere to ethical standards including ethics committee approval and consent procedure?

Yes.

Q 5 **Please provide your detailed review report to the editor and authors (including any comments on the Q4 Check List):**

• Transfer functions have been proposed for distributed lag models (DLMs) decades ago, and described as infinite DLMs. For instance, they are described on the Wikipedia page about DLMs: https://en.wikipedia.org/wiki/Distributed_lag#Infinite_distributed_lags . However, the manuscript presents such methodology as a novel application of transfer functions in this setting, which is misleading. The authors must appropriately describe the method as already established and refer to the existing literature.
• The authors stated that traditional DLMs based on spline or polynomial functions necessitate the correct specification of the lag length. This is not completely true. Actually, these models assume that the chosen length covers the period in which there are non-null associations. This means that the selection of a lag length shorter that the actual lag window will result in biases. Conversely, the extension of the lag length beyond the effect period will not lead to biases, but just to an increase in the uncertainty (see simulation results in https://doi.org/10.1097/ede.0000000000000533). In practical terms, this indicates that the users must select a length that is long enough to cover the relevant effect. I suggest the authors elaborate further on the description of limitations of traditional methods to appropriately illustrate the context.
• The specific transfer function presented here, the Koyck decay, requires the selection of the parameters p and q. Wrong selections of such parameters are likely to result in biases in the estimation of the lag structure. Surprisingly, the authors suggest that users can rely on traditional DLMs with spline or polynomials to identify the correct shape and therefore select the appropriate parameters of the transfer function. But, on the one hand, if these traditional methods are intrinsically flawed in the absence of knowledge of the actual lag period, this would likely result in errors. On the other hand, if traditional DLMs can appropriately describe the lag shape, what are the advantages of using more complex methods?
• If the user should rely on selection method to identify the appropriate values of the parameters p and q, supposedly the same can be done to identify the proper lag windows in traditional DLMs, for instance performing models with increasing lag periods until the results suggest that the relevant effect window is covered. Is this the case?
• DLMs have been years ago extended to distributed lag non-linear models (DLNMs) to relax the strong assumption of a linear exposure-response relationship. It is not clear if the transfer function methodology can be extended along the same lines. If not, this must be acknowledged as a major limitation.
• The authors include in the supplementary material the code to specify the transfer function, written in Stan language and executed by rStan program. However, this code is not enough to reproduce the results. I suggest the authors include a fully reproducible code, together with the data, so that the users can replicate the analysis.
• The authors should acknowledge that a comprehensive evaluation of the methodology and the comparison with alternative approaches would require a simulation study.

QUALITY ASSESSMENT

Q 6 **Rigor**

Q 7 **Method validated by effective results**

Q 8 **Applicability**

Q 9 **Significance to the field**

Q 10 **Interest to a general audience**

Q 11 **Quality of the writing**

REVISION LEVEL

Q 12 **What is the level of revision required based on your comments:**

Major revisions.