Protocol for the comparison of Interrupted Time series analysis methods

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Version history

Amendment No.	Protocol version No.	Description of changes	Date of protocol
	Version 1	New document	

Aim and Objectives

The ***aim*** of this work it is compare interrupted time series (ITS) analysis methods using datasets from published studies in the healthcare setting.

The two ***objectives*** are

1. To compare the effect estimates, change in level and slope, their SEs, and p-values based on the ITS analysis method used.
2. To compare the performance of the ITS analysis methods.

Inclusion criteria of the data

Results from Hudson et al[1] were used to aid the decision of which of the 200 data sets should be included. Firstly, based on the median and interquartile range (IQR) of the number of time points across the whole time series, the datasets will be categorised into three groups:

1. Short time series. This is based on the lower limit of the IQR of 14 (or close to 14) data points
2. Medium time series. This is based on the median of 36 (or close to 36) data point
3. Long time series. This is based on the upper limit of the IQR of 48 (or close to 48) data points.

Secondly, these categories will them be further grouped based on whether autocorrelation was present or not and whether it was positive or negative using the median and IQR. For positive autocorrelation, the median was 0.58 with an IQR of (0.45, 0.67) and -0.68 (-0.70, -0.32) for negative autocorrelation. Of the datasets identified we will exclude those where seasonality was present, where the order of autocorrelation was greater than one and individual level data (e.g. data on multiple hospitals within the same study). Finally, as the datasets were identified from those included in Chapter 3, the datasets will be limited to: a minimum of two data points in the pre-intervention phase and one in the post-intervention phase, the evaluation of one intervention, outcomes that can be analysed on a continuous scale, and the pre-intervention phase of the data series is linear.

Analysis methods

Eighteen ITS analysis methods have been identified. Of these four do not meet the inclusion criteria of the data (extended logistic regression, pooled and stacked segmented regression and generalised estimating equations). A further five methods were also excluded as two grouped the pre- and/or post intervention phase data and therefore did not utilise all available

data points (before-and-after and generalised linear model segmented regression); one did not provide estimates comparable with other ITS analysis methods (AUC); one transformed the data on a different scale (differencing); and the nonparametric approach was based on large data sets (100-300 observations) which, according to previous work,[1, 2, 3] are not common in the healthcare setting. Therefore, nine ITS analysis methods will be evaluated:

- Simple segmented regression (OLS)
- Prais-Winsten segmented regression
- Double bootstrap segmented regression
- Full maximum likelihood segmented regression
- Restricted maximum likelihood segmented regression
- Newey-West standard error segmented regression
- Auto Regressive Integrated Moving Average (ARIMA)
- Bayesian segmented regression
- Cochrane-Orcutt segmented regression

ITS model

All analysis methods will fit the following segmented linear regression model:

$$Y_t = \beta_0 + \beta_1 T_t + \beta_2 X_t + \beta_3 (T_t - T_i) X_t + \epsilon_t$$

where

Y_t is the outcome at time *t*;

T_t is a continuous variable and is time at time *t* i.e. time since the start of the data series i.e. 1,2, …, *n* where *n* is the last time point;

X_t is an indicator for the intervention at time *t* and is a dummy variable coded 0 for the pre-intervention phase and 1 for the post-intervention phase;

T_i corresponds to the time point, *i*, when the intervention started;

ϵ_t is the error term at time *t*.

The model parameters are: β_0 estimate is the baseline level (or intercept) and is the outcome at T=0; β_1 estimate is the pre-intervention trend which corresponds to a unit increase (or decrease) in outcome pre-intervention; β_2 estimate is the change in level (or the change in

outcome) at T_i, the point of intervention; β_3 is the change in trend (or slope), the difference between the post-intervention trend and the pre-intervention trend (or slope). The post-intervention trend is the sum of $\beta_1 + \beta_3$, which is the unit increase (or decrease) post-intervention.

As the included datasets might be measured on different units, the effect estimates will be standardised by dividing by the standard error.

Comparison of ITS analysis methods

To compare the ITS analysis methods, comparisons were made on the change in level and change in slope. The effect estimates and SEs were compared based on percentage change while p-values were compared based on whether it was statistically significant at the 0.05 level (p-value < 0.05).

The Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC) were used to formally compare ITS analysis methods. To help interpretation Burnham et al[4] was used.

References

(1) Hudson J, Fielding S, Ramsay CR. Methodology and reporting characteristics of studies using interrupted time series design in healthcare. BMC Medical Research Methodology 2019;19(1):137.

(2) Turner SL, Karahalios A, Forbes AB, Taljaard M, Grimshaw JM, Cheng AC, et al. Design characteristics and statistical methods used in interrupted time series studies evaluating public health interventions: a review. J Clin Epidemiol 2020;122:1-11

(3) Jandoc R, Burden AM, Mamdani M, Lévesque LE, Cadarette SM. Interrupted time series analysis in drug utilization research is increasing: systematic review and recommendations. J Clin Epidemiol 2015;68(8):950-956.

(4) Burnham KP, Anderson DR. Multimodel Inference: Understanding AIC and BIC in Model Selection. Sociological Methods & Research 2004;33(2):261-304.