Interrupted Time Series presentation notes:

ITS Overview

- Often a need to retrospectively evaluate interventions which have already been implemented, often for political reasons, either without randomization or to a whole population and so without any control
- ITS Increasingly being used for the evaluation of public health interventions;
- it is particularly suited to interventions introduced at a population level over a clearly defined time period and that target population-level health outcomes

What is a ITS?

- A time series is a continuous sequence of observations on a population, taken repeatedly (normally at equal intervals) over time.
- In ITS, the time series is used to establish an underlying trend for an outcome of interest, which is ‘interrupted’ by an intervention at a known point in time.
- We model a hypothetical scenario in which the intervention had not taken place and where the trend continues unchanged (this ‘expected’ trend, in the absence of the intervention is referred to as the ‘counterfactual’)
- This counterfactual scenario provides a comparison for the evaluation of the impact of the intervention by examining any change between the counterfactual and the observed data in the post-intervention period

The figure shows the rate of ACE (Acute Cardiovascular Event) over time (following smoking ban). White background, pre-intervention period; grey background, post-intervention period; continuous line, pre-intervention trend; dashed line, counterfactual

In post-intervention period, most the data points are below the counterfactual – gives visual suggestion of a decrease in ACEs following the intervention.

ITS models can provide statistical evidence about whether this represents a real decrease.

- The analysis approach shares many properties of regression-based approaches
- However, there are a range of unique features of time series data that require additional methodological considerations.

When is an interrupted time series design appropriate?

Intervention:

- Most importantly…ITS works best when there is a clear moment in time in which the intervention is introduced. In some evaluations it may be difficult to define when the intervention began and to differentiate the effects of different components.
- does not necessarily require the intervention to be introduced overnight but the period of implementation should be well defined so that the pre- and post-intervention periods can be considered separately.
- The implementation of the example intervention was very clear with a ban on smoking in public places throughout Italy at the beginning of January 2005.

Outcomes:

- Can be count, continuous or binary
- Works best when short-term outcomes are used (ie. Those that are expected to change relatively quickly after an intervention is implemented) or those that have a clearly defined lag before impact (not too much variation)
- In the outcome in the example, the authors quote evidence that the acute effects of both active and passive smoking disappear quickly after the exposure is removed – so ACE admissions should decrease. Something like lung cancer would be less appropriate as the timing between intervention and outcome is much less clear and can be highly variable.

Available data:

- Sequential measures of the outcome should be available both before and after the intervention
- Due to the requirement for repeated measures, routine data is often used for ITS
- No straightforward guidelines for the number of timepoints, and there's a few reasons for this:

Power increases with the number of time points..Studies with few time points or with small expected effect sizes should be interpreted with caution as they may be underpowered…

but it is not always preferable to have more data points:

- Eg. where historical trends have changed substantially, as this would not provide an accurate depiction of the current underlying trends.
- It is therefore recommended that pre-intervention data are inspected visually.
- Power depends on various other factors including distribution of data points before and after the intervention, variability within the data, strength of effect, and the presence of confounding effects such as seasonality.

Choosing an appropriate model

- Important to hypothesize how the intervention would impact on the outcome if it were effective,
- a gradual change in the gradient of the trend,
- a change in the level or both,
- and whether the change will follow the intervention immediately or there will be a lag period before any effect is expected.

IMPORTANT that the impact model is decided a priori.

Relying on the outcome data to select the best impact model is discouraged as this increases the likelihood of an effect being detected due to random fluctuations or chance,

Regression methods

This regression model represents the impact model (c) where there is both a step change and a slope change.

Models (a) and (b) can easily be specified by excluding the terms $\beta_3 TX_t$ or $\beta_2 X_t$, respectively.

Example again

This uses count data and so a poisson regression model was used.

Other regression models can be used, eg. Linear regression for continuous outcomes.

Given that a level change model was hypothesized, the interaction term for the slope change is not required in the model.

This model suggests that there is very strong evidence of a reduction in ACEs following the smoking ban

with a decrease of 11% [relative risk (RR) 0.894; 95% confidence interval (CI) 0.864-0.925; $P < 0.001$)

Methodological considerations:

there are a number of distinctive issues with time series data that may need to be addressed in order to improve the robustness of the analysis.

Seasonality:

- Many diseases and other outcomes have a seasonal pattern
- this could bias the results, especially in the analysis of short series
- eg. If there are more winter months in the pre-intervention period and more summer in the post-intervention

- Autocorrelation is another problem. An assumption of standard regression models is that observations are independent. This assumption is often violated in time series data because consecutive observations tend to be more similar to one another than those that are further apart.
- autocorrelation should always be assessed by examining the plot of residuals

There are a number of ways to manage seasonality in time series analyses:

- Stratify the model by month (or other time period)
- Use more complex functions such as Fourier terms
- can link to further information on this if interested.

Time varying confounders:

- ITS generally unaffected by typical confounding variables which remain fairly constant, such as population age distribution or socioeconomic status, as these only change relatively slowly over time and are normally taken into account when modelling the underlying long-term trend.
- ITS can be affected by time-varying confounders that change more rapidly.
- Talked about seasonality (which is one example)
- Another example is diseases prone to outbreaks in response to weather events (Example figure)
- Other events that affected the outcome eg. Financial crisis, changes in diagnostic methods,
- Other interventions being introduced which affect the outcome of interest

Solutions:

- Where such time-varying confounders have been measured, they can be controlled for by including variables representing them in the regression model (similar to other regression analyses)
- Where time-varying confounders are either unmeasured or unknown, there are design adaptations available:
- Controlled ITS (with a control group that does not receive the intervention but undergoes all other changes taking place at the time.
- multiple baseline design, (intervention is introduced in different locations at different times)
- Introduce and then withdraw the intervention to establish whether withdrawal of the intervention leads to a reversal of the effect.