On The Use of Empirical Bayes for Comparative Interrupted Time Series with an Application to Mandatory Helmet Legislation

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1. Motivating Example
2. Interrupted Time Series
3. Empirical Bayes ITS
4. Results
5. Discussion
Mandatory bicycle helmet legislation in NSW

- Intervention directed at increasing helmet wearing among cyclists
  - Lower bicycle related head injuries
  - Not a panacea for all bicycle related injuries

- Applies to all age groups
- Went into effect in two stages
  - Adults (>16): 1 January 1991
  - Children: 1 July 1991
- Led to greater helmet wearing rates (~25% to ~80%)
- Associated with fewer bicycle related head injuries
Adult head injury hospitalisations in NSW

![Chart showing head injuries over months]

- Head Injuries
- Pre-law Average

Months:
- -18
- -12
- -6
- 0
- 6
- 12
- 18
Criticisms of MHL

- MHL is very controversial
- Leads to reductions in cycling?
  - Fewer cyclists → fewer bicycle related head injuries?
- Leads to increased risk to cyclists
  - Risk compensation, rotational injuries, safety in numbers?
- Has a negative health economics impact?
  - Quit cycling → no exercise → more obesity?
  - Morbidity/mortality from obesity outweighs safety benefit of helmets?
- Loss of freedom?
- Debate rages on after 20+ years
- The anti-helmet advocacy group Bicycle Helmet Research Foundation is the main proponent of these criticisms\(^1\)

\(^1\)www.cyclehelmets.org
Question 1
Is the drop in head injury associated solely, partly or not at all with the helmet law?

Question 2
Did the helmet law CAUSE the drop in head injury? (via increased helmet wearing)

Question 3
Did declines in cycling CAUSE the drop in head injury?
Causal Inference for Population-based Interventions

- Pre- and post-intervention periods are not randomised

⇒ **Causal inference is difficult**

- Relevant data is often missing
  - cycling exposure, risk of injury
- Routinely collected data is probably best option for assessment
  - hospitalisation data, census data, police data (traffic, criminal reports)
- A rigorous analysis is paramount
  - There are many examples where different analyses result in different conclusions

What is the **best** analytic method/framework?

- **Interrupted time series** is most common

2 Ramsay et al. (2003) "Interrupted time series designs in health technology assessment: Lessons learned from two systematic reviews of behavior change strategies."
Outline

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Interrupted Time Series (ITS)

- Type of quasi-experimental design
  - Participants are not randomised
- Estimates a time series before and after an intervention
  - Comparing single pre- and post-intervention effects can hide *history*
  - Multiple pre- and post-intervention observations avoids *regression to the mean*
- Important comparisons made between pre- and post-intervention time series
  - Change in level (immediate impact)
  - Change in slope (gradual impact)
**Interrupted time series (basic structural model)**

\[
y_t = \mu_t + \gamma_t + \sum_{j=1}^{k} \delta_j x_{jt} + \lambda w_t + \varepsilon_t
\]

\(\mu_t\) := trend
\(\gamma_t\) := seasonal component
\(x_{jt}\) := jth explanatory variable
\(\delta_j\) := coefficient for \(x_{jt}\)
\(\lambda\) := intervention effect
\(w_t\) := pre/post-law indicator
\(\varepsilon_t\) := irregular component
Effects are additive

- Outcome is comprised of

\[
\left( \begin{array}{c}
\text{basic pattern} \\
\text{cyclical effects} \\
\text{other effects} \\
\text{law effects} \\
\text{random noise}
\end{array} \right)
\]
Simple ITS

\[ \log(y_T) = \beta_0 + \beta_1 T + \beta_2 I + \beta_3 TI + u_T \]

where

- \( T \) := time
- \( I \) := \( \begin{cases} 0 & \text{pre-intervention} \\ 1 & \text{post-intervention} \end{cases} \)
- \( u_T \) := error process (time dependent?)

- Could also include cyclical effects or other (confounding) variables
- **Counterfactual** (or trajectory) is the estimated time series if the intervention had not occurred, for example

\[ \log(\hat{y}_T) = \hat{\beta}_0 + \hat{\beta}_1 T \]

- \( \beta_2 \) and \( \beta_3 \) are comparisons between the counterfactual and the post-intervention model
Change in Level

\[ \beta_2 \]

Intervention

counterfactual

Time
Change in Slope

Intervention

Time

\[ \beta_3 \]

counterfactual
Threat to Internal Validity

- Unmeasured confounding is a major weakness of ITS
- The use of a control/comparator time series is often recommended
  - Also affected by unmeasured confounding
  - Not subject to the intervention
  - Observations over the same time period
  - Could be a related observation from the same study unit
- Treatment and control are modelled simultaneously
  - Comparative interrupted time series (CITS)

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Comparative ITS

\[ \log(y_T) = \beta_0 + \beta_1 T + \beta_2 I + \beta_3 C + \beta_4 TI + \beta_5 TC + \beta_6 IC + \beta TIC_7 + u_T \]

where

\( C := \begin{cases} 1 & \text{primary time series} \\ 0 & \text{comparative time series} \end{cases} \)

\( u_T := \text{error process (time dependent?)} \)

- The comparison of the two times series is

\[ \log(y_T^P / y_T^C) = (\beta_3 + \beta_6 I) + (\beta_4 + \beta_7 I) T \]

- \( \beta_6 \) and \( \beta_7 \) are comparisons between the counterfactual and the post-intervention model \text{relative to the comparative time series}

- Assumes unmeasured confounding factors are identical for \( y_T^P \) and \( y_T^C \) and therefore cancel out
Question 4
How do we know whether a comparative time series has accounted for unmeasured confounding?

Question 5
Given multiple comparators, how do you choose the best one?
How to Choose a Comparative Time Series?

1. Linden and Adams (2011) recommend choosing a comparative time series that is *similar* to the primary time series *before* the intervention. Only time varying component?

2. Walter et al. (2013) chose comparative time series based on highest within-time period correlation. What if unmeasured confounders are not similar?

\[
\phi = \frac{\text{cov}(\varepsilon_p, \varepsilon_c)}{\sqrt{\text{var}(\varepsilon_p) \text{var}(\varepsilon_c)}} 
eq \frac{\text{cov}(\eta_p + \varepsilon_p, \eta_c + \varepsilon_c)}{\sqrt{\text{var}(\eta_p + \varepsilon_p) \text{var}(\eta_c + \varepsilon_c)}}
\]

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4. Linden & Adams (2011) "Applying a propensity score-based weighting model to interrupted time series data: improving causal inference in programme evaluation"

5. Walter, Olivier, Churches & Grzebieta (2013) "The impact of compulsory helmet legislation on cyclist head injuries in New South Wales, Australia: A response"
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Empirical Bayes ITS

- Basic idea:
  1. Pre-intervention data is used to estimate a prior model
  2. This model is extrapolated over the post-intervention period (i.e., counterfactual)
  3. Post-intervention observations are analysed relative to the counterfactual (posterior)

- Pre-intervention model

\[
E \left( \log(y_{T}^{EB}) \right) = \alpha_0 + \alpha_1 T + \alpha_2 C + \alpha_3 TC, \quad T < 0
\]

- Counterfactual residuals

\[
\Delta_T = \log(y_T) - \log(\hat{y}_T^{EB}), \quad T > 0
\]

- No intervention effect when \( \bar{\Delta}_T = 0 \)
- Residuals will have systematic pattern if unmeasured confounders are not similar
Comparative Empirical Bayes ITS

- Including a comparative time series

  \[ \Delta^p_T - \Delta^c_T = \log(y^p_T / y^c_T) - \log(\hat{y}^{EB-p}_T / \hat{y}^{EB-c}_T) \]

- No \textit{relative} intervention effect when \( \bar{\Delta}^p_T - \bar{\Delta}^c_T = 0 \)

- Residuals will have systematic pattern if unmeasured confounders are not similar
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NSW Data

- Hospital presentations from 1 July 1989 to 30 June 1992
- Cases identified from ICD-9-CM
- Primary outcome: bicycle-related head injury hospitalisations
- Possible comparators
  - Bicycle-related arm injury hospitalisations (no head injury)
  - Bicycle-related leg injury hospitalisations (no head injury)
  - Pedestrian-related head injury hospitalisations
  - Australian beer production (sensitivity analysis?)
1st and 2nd Criteria

- Results from CITS models for each comparator

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Pre-law similarity $\hat{\beta}_5$ (SE)</th>
<th>Within-time correlation $\hat{\phi}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm</td>
<td>-0.008 (0.015)</td>
<td>0.026</td>
</tr>
<tr>
<td>Leg</td>
<td>0.023 (0.021)</td>
<td>0.096</td>
</tr>
<tr>
<td>Head-Peds</td>
<td>-0.008 (0.020)</td>
<td>-0.063</td>
</tr>
<tr>
<td>Beer</td>
<td><strong>0.003 (0.015)</strong></td>
<td><strong>0.185</strong></td>
</tr>
</tbody>
</table>

- Australian beer production is the “best” comparator using these criteria
Empirical Bayes Criterion

- Models were fit to pre-intervention data using each potential comparator.
- Linear models fit to counterfactual residuals.

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Intercept</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm</td>
<td>-0.263 (0.138)</td>
<td>0.010 (0.013)</td>
</tr>
<tr>
<td>Leg</td>
<td>-0.263 (0.157)</td>
<td>-0.025 (0.015)</td>
</tr>
<tr>
<td>Head-Peds</td>
<td>-0.383 (0.190)</td>
<td>0.001 (0.018)</td>
</tr>
<tr>
<td>Beer</td>
<td>-0.494 (0.165)</td>
<td>0.010 (0.016)</td>
</tr>
</tbody>
</table>

- All slope estimates are statistically non-significant and “small”.
- All intercept estimates are statistically significant (or nearly so).
Head injuries had the greatest relative decline compared to Australian beer production

$$\exp(-0.494) - 1 = -39\%$$

Is Australian beer production the “best” comparator to cycling head injury hospitalisations?

Residual analysis suggests cycling arm injuries are affected by similar unmeasured confounding
Arm Residuals

![Graph showing arm residuals over time](image-url)
Leg Residuals
Beer Residuals

J Olivier et al. (UNSW)

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Which Comparator is Best?

- Linden and Adams criterion
  - All do not differ significantly in pre-law period (Beer production better than others)

- Walter et al. criterion
  - Beer production exhibits largest within-month correlation

- Empirical Bayes (residual analysis) criterion
  - Arm injury residuals appear random
  - Systematic pattern for others → invalid statistical inference?

- Estimated intervention effect is smallest relative to arm injuries
  - Most conservative estimate
Causal inference for population-based interventions is difficult

Interrupted time series is likely the best analytic approach
  - Threats to internal validity (due to lack of randomisation)

The use of a comparative time series is promising
  - An analytic framework for choosing “best” comparator is needed
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Questions?