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

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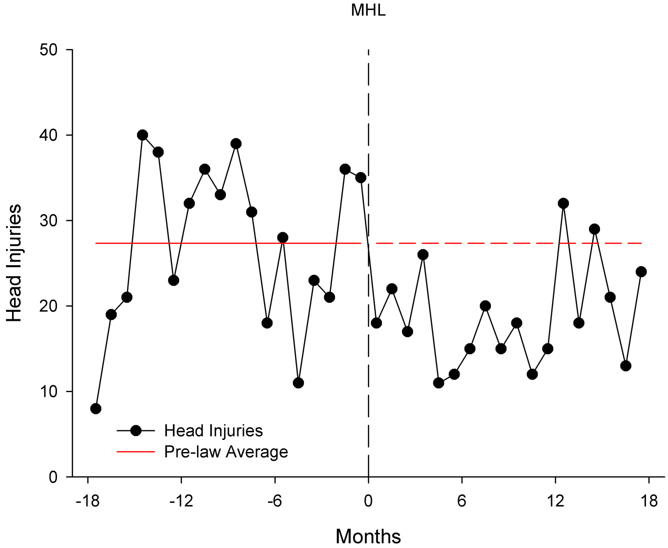
Outline

Mandatory bicycle helmet legislation in NSW

- Intervention directed at increasing helmet wearing among cyclists
  - $\rightarrow$ 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



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

BIG QUESTIONS

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

$\Rightarrow$**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[2]
- 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."

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1. Motivating Example
2. Interrupted Time Series
3. Empirical Bayes ITS
4. Results
5. Discussion

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)

Scary maths

Interrupted time series (basic structural model)

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

μ_t := trend
γ_t := seasonal component
x_{jt} := jth explanatory variable
δ_j := coefficient for x_{jt}
λ := intervention effect
w_t := pre/post-law indicator
ε_t := irregular component

Not so scary maths

Effects are additive

- Outcome is comprised of

$$\left(\begin{array}{c}\text{basic}\\\text{pattern}\end{array}\right)+\left(\begin{array}{c}\text{cyclical}\\\text{effects}\end{array}\right)+\left(\begin{array}{c}\text{other}\\\text{effects}\end{array}\right)+\left(\begin{array}{c}\text{law}\\\text{effects}\end{array}\right)+\left(\begin{array}{c}\text{random}\\\text{noise}\end{array}\right)$$

Simple ITS

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

where

$T :=$ time

$I := \begin{cases} 0 & \text{pre-intervention} \\ 1 & \text{post-intervention} \end{cases}$

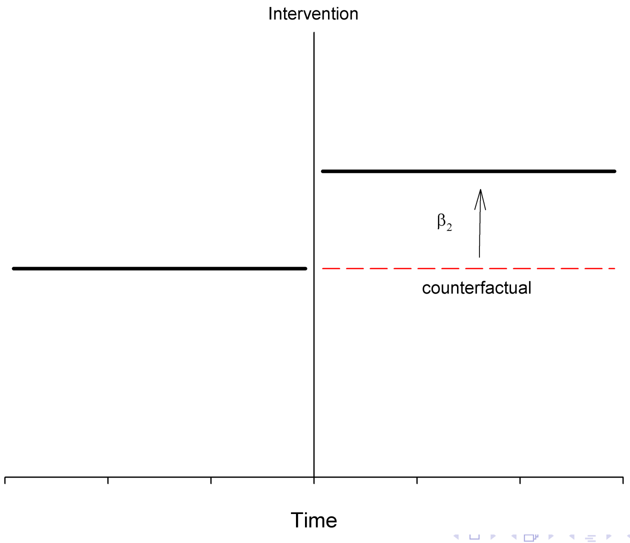
$u_T :=$ error process (time dependent?)

- 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

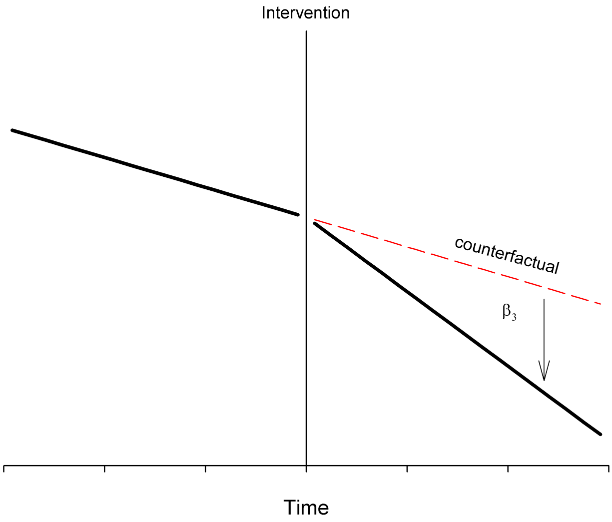
$$\log(\hat{y}_T) = \hat{\beta}_0 + \hat{\beta}_1 T$$

- β_2 and β_3 are comparisons between the counterfactual and the post-intervention model

Change in Level



Change in Slope



Threat to Internal Validity

- Unmeasured confounding is a major weakness of ITS
- The use of a control/comparator time series is often recommended[3]
  - 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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[3] Shadish, Cook & Campbell (2002) *Experimental and Quasi-experimental designs for generalized causal inference.*

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

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

$u_T :=$ error process (time dependent?)

- The comparison of the two times series is

$$\log(y_T^p / y_T^c) = (\beta_3 + \beta_6 I) + (\beta_4 + \beta_7 I)\, T$$

- β_6 and β_7 are comparisons between the counterfactual and the post-intervention model **relative to the comparative time series**
- Assumes unmeasured confounding factors are identical for y_T^p and y_T^c and therefore cancel out

How to Choose a Comparative Time Series?

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[4]
   - Only time varying component?
2. Walter et al. (2013) chose comparative time series based on highest within-time period correlation[5]
   - What if unmeasured confounders are not similar?

$$\phi = \frac{cov(\varepsilon_t^p, \varepsilon_t^c)}{\sqrt{var(\varepsilon_t^p) var(\varepsilon_t^c)}} \neq \frac{cov(\eta_t^p + \varepsilon_t^p, \eta_t^c + \varepsilon_t^c)}{\sqrt{var(\eta_t^p + \varepsilon_t^p) var(\eta_t^c + \varepsilon_t^c)}}$$

[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"

Outline

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

$$\Delta_T^p - \Delta_T^c = \log(y_T^p / y_T^c) - \log(\hat{y}_T^{EB-p} / \hat{y}_T^{EB-c})$$

- No **relative** intervention effect when $\bar{\Delta}_T^p - \bar{\Delta}_T^c = 0$
- 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

Comparator	Pre-law similarity $\hat{\beta}_5$ (SE)	Within-time correlation $\hat{\phi}$
Arm	-0.008 (0.015)	0.026
Leg	0.023 (0.021)	0.096
Head-Peds	-0.008 (0.020)	-0.063
Beer	**0.003 (0.015)**	**0.185**

- 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

Comparator	Intercept	Slope
Arm	-0.263 (0.138)	0.010 (0.013)
Leg	-0.263 (0.157)	-0.025 (0.015)
Head-Peds	-0.383 (0.190)	0.001 (0.018)
Beer	-0.494 (0.165)	0.010 (0.016)

- All slope estimates are statistically non-significant and "small"
- All intercept estimates are statistically significant (or nearly so)

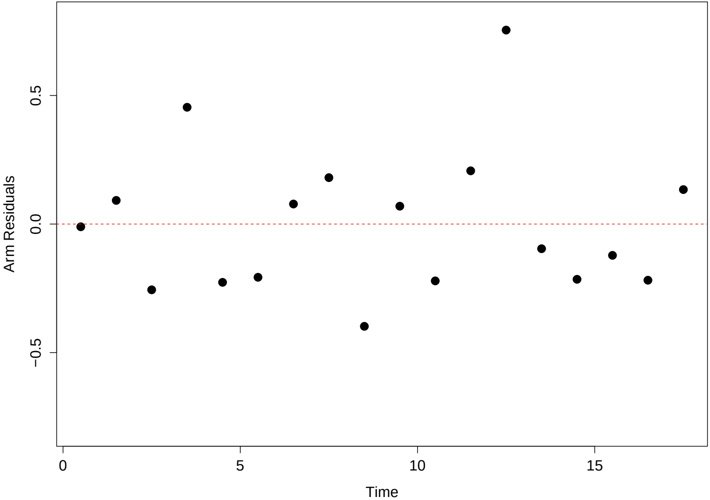
Empirical Bayes Criterion

- Head injuries had the greatest relative decline compared to Australian beer production

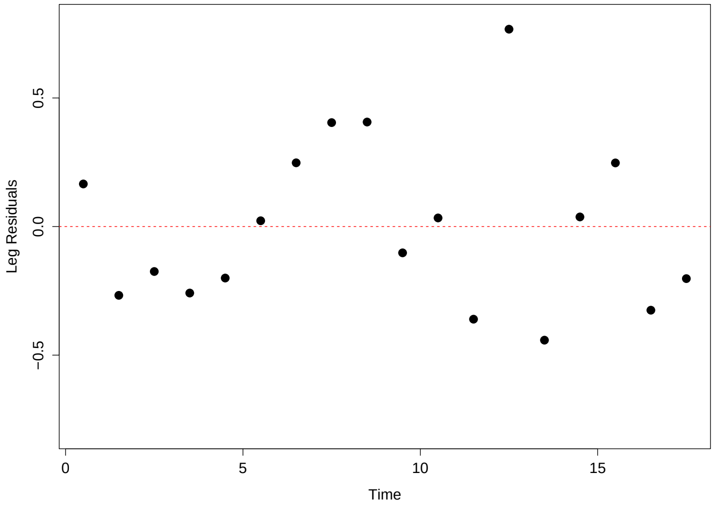
$$\exp\left(-\mathbf{0.494}\right) - \mathbf{1} = -\mathbf{39}\%$$

- Is Australian beer production the "best" comparator to cycling head injury hospitalisations?
- Residual analysis suggests cycling arm injuries are affected by similar unmeasured confounding

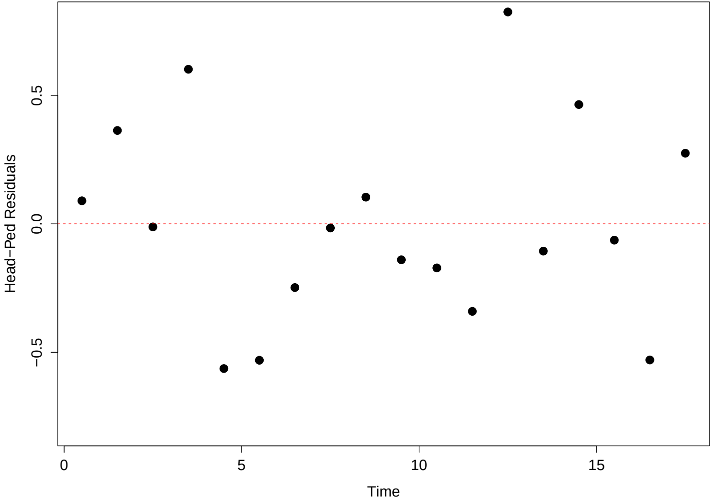
Arm Residuals



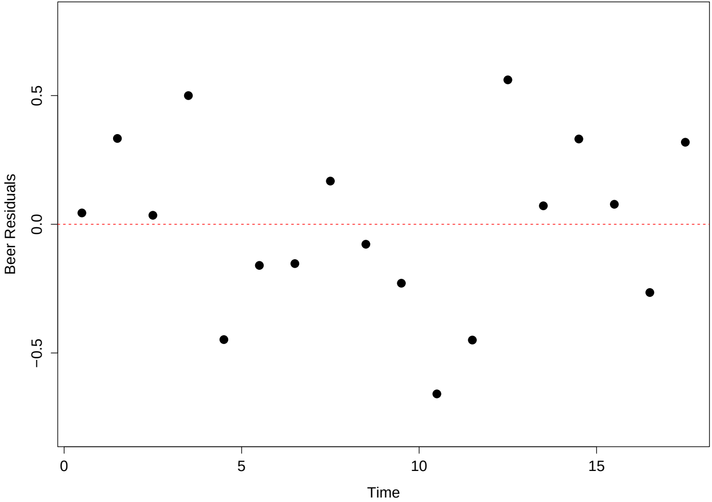
Leg Residuals



Pedestrian-Head Residuals



Beer Residuals



Outline

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 $\longrightarrow$ invalid statistical inference?
- Estimated intervention effect is smallest relative to arm injuries
  - Most conservative estimate

Discussion

- 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?