Introduction to Interrupted Time Series

Part II. Analysis Options

Joint CAPS/TAPS Methodology Seminar

January 19, 2016

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ITS Analysis Examples: Outline

. Voluntary industry electronic media ad ban on newspaper tobacco ads
    Very simple ITS model
    Linear model with AR1 residuals

. Expanded midwifery/laborist model & cesarean rates
    Including a non-equivalent control group
    Linear model with AR1 residuals

. Enhanced access to language interpreters & hospital readmission rates
    Including a non-equivalent control group
    Example with poor signal-to-noise ratio

. Effect of hysterectomy on HRQoL
    Prospective cohort study
    LMM of patient-level out comes

. JointPoint Software (only a mention)

. Summary

Units of observation

Unit(s) of observation observed across time

a. A single unit observed longitudinally: a patient, a hospital, a county

b. Multiple units observed longitudinally: longitudinal cohort sample

c. Multiple cross sectional samples of individual units
   (with perhaps some individual units observed more than once)

You may choose to aggregate data to a higher level of abstraction, e.g.,

Single unit observed:

daily summaries $\rightarrow$ monthly summaries

Multiple units observed:

patient-level outcomes in real time $\rightarrow$ monthly summaries

ITS: Tobacco Ad Images in Argentinean Newspapers

Beginning in the late 1980s, the tobacco industry anticipated
increased anti-smoking pressure

In 1997, the tobacco industry created a ‘weak’ voluntary ad ban
Ads OK’d on radio and TV from 10PM to 8AM, only

In 2000, the tobacco industry withdrew all ads from radio and TV

Q: How did the 2000 radio and TV ban affect ads in the print media?

Tobacco advertising and press coverage of smoking and health in 10 years of Argentinean newspapers

Sandra Braun [a,*], Raul Mejia [a], Joaquín Barnoya [b], Steven E. Gregorich [c], Eliseo J. Pérez-Stable [c,d]

2011. *CVD Prevention & Control*, 6, 71-80.

Objective: Describe prevalence of tobacco-related images and articles

Design

. Observation period 1995-2004

. Industry self-imposed radio/TV ban in 2001

. 4 main national newspapers

. 4 sampled months per year March, June, August, November

ITS: Tobacco Ad Images in Argentinean Newspapers

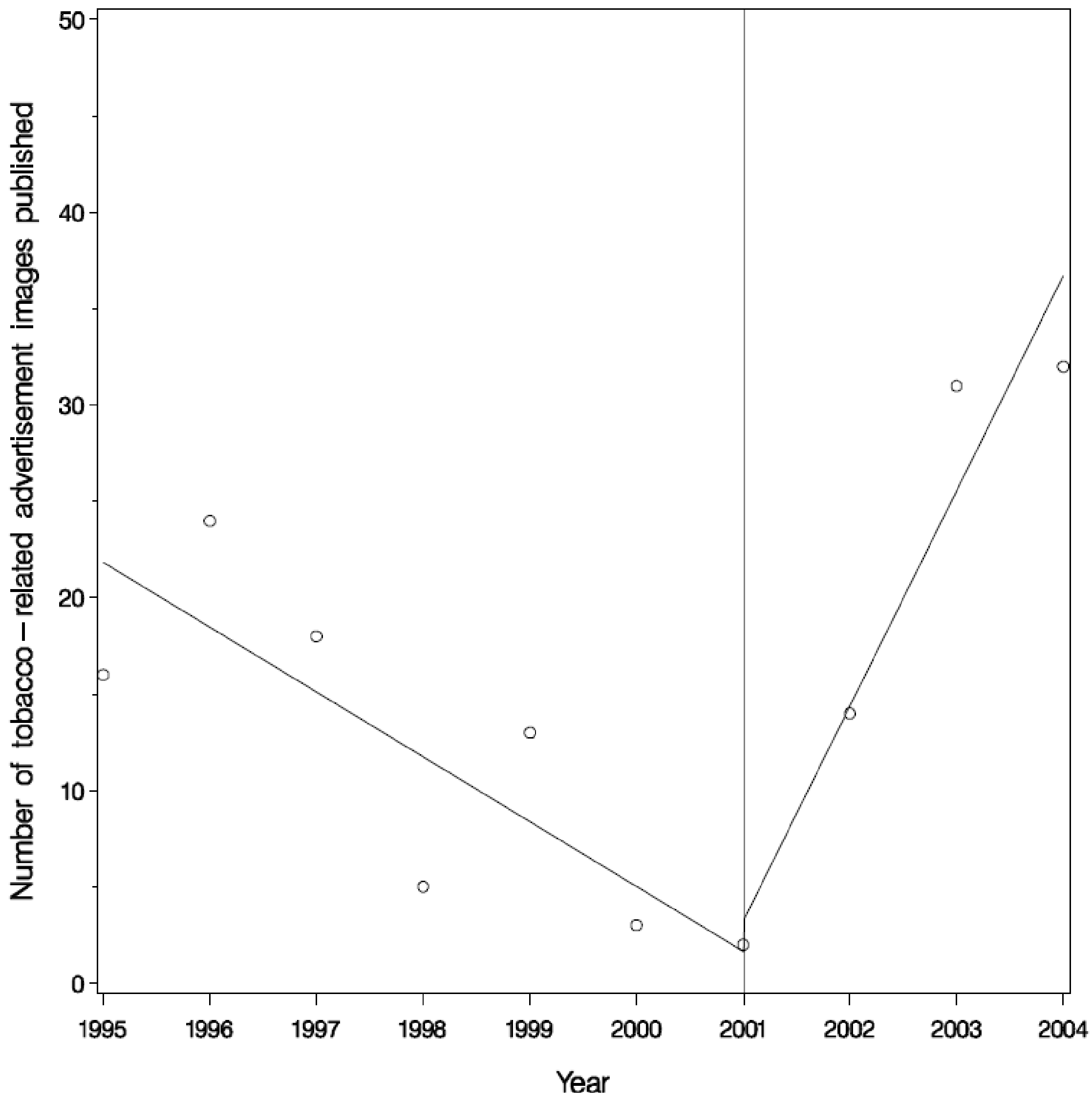
Basic Results

- *N*=4828 newspaper issues sampled
- *N*=1800 tobacco-related images or articles identified
  - *n*=360 articles
  - *n*=1283 non-advisement images
  - *n*=157 advertisement images

Data aggregation

- Data were aggregated up to calendar year
  - Aggregated across newspapers w/in each year
- This was done by primary authors, other options possible
- Sample size: *N*=10 calendar years (1995-2004)

ITS: Tobacco Ad Images in Argentinean Newspapers



ITS: Tobacco Ad Images in Argentinean Newspapers

Data

Year	Year_Rel	Ban	Ad_Images	Subj
1995	-6	0	16	1
1996	-5	0	24	1
1997	-4	0	18	1
1998	-3	0	5	1
1999	-2	0	13	1
2000	-1	0	3	1
2001	0	1	2	1
2002	+1	1	14	1
2003	+2	1	31	1
2004	+3	1	32	1

Code intervention onset as time=0

ITS: Tobacco Ad Images in Argentinean Newspapers

Analysis plan

. Preliminary analyses suggested that annual counts were reasonably symmetrically distributed

. Modeled via linear regression with AR1 residuals

```
proc mixed  data= Newspaper;
 class  Subj;
 model  Ad_Image  =  Year_Rel|Ban  /  s;
 estimate  'post-slope'  Year_Rel 1   Year_Rel*Ban 1;
 repeated  /  subject= Subj  type=AR(1);
run;
```

. Estimated intercept represents outcome level just prior to the ad ban

. Estimated effect of Ban represents ‘immediate effect’ of Ban

. Model estimates separate slopes for pre- and post- periods

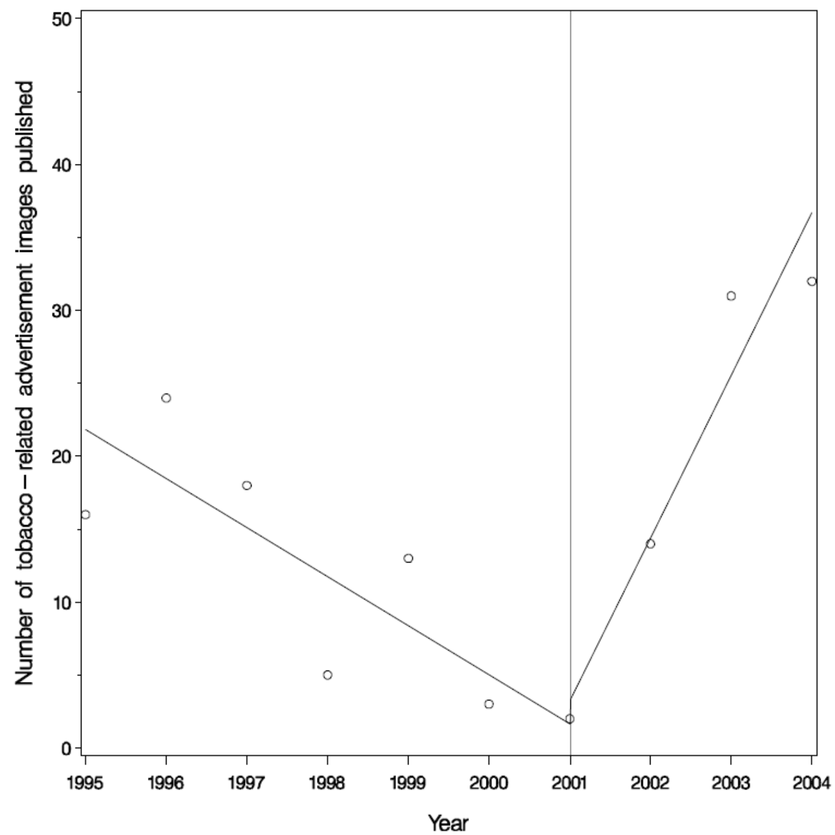
ITS: Tobacco Ad Images in Argentinean Newspapers

Modeling results

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	1.61	4.05	6	0.40	0.7055
Year_Rel	-3.37	1.06	6	-3.19	0.0188
Ban	1.63	5.85	6	0.28	0.7895
Rear_Rel*Ban	14.52	2.26	6	6.42	0.0007
post-slope	11.16	2.09	6	5.33	0.0018

Year	Year_Rel	Ban	Ad_Images
1995	-6	0	16
1996	-5	0	24
1997	-4	0	18
1998	-3	0	5
1999	-2	0	13
2000	-1	0	3
2001	0	1	2
2002	+1	1	14
2003	+2	1	31
2004	+3	1	32

AR(1) = -0.27



The Association of Expanded Access to a Collaborative Midwifery and Laborist Model With Cesarean Delivery Rates

Melissa G. Rosenstein, MD, MAS, Malini Nijagal, MD, Sanae Nakagawa, MS, Steven E. Gregorich, PhD, and Miriam Kuppermann, PhD, MPH

2015. *Obstetrics and Gynecology*, 126, 716-23.

Marin General Hospital

Publicly insured women

. Covered by Medi-Cal

. Prenatal care by nurse midwives in a public clinic

. Labor and delivery: Midwives with 24hr laborist back-up

Privately insured women

Prenatal care by private practice OB in group or solo practice setting

Labor & delivery

Prior to 2011: Private OB or covering partner

Beginning in 2011: Midwives with 24hr laborist back-up

Effect of Access to Midwifery on Cesarean Delivery Rates

Intervention group: Privately insured women

Change from private practice to NM/laborist labor & delivery model

Non-equivalent control group: Publicly insured women

Nurse midwife/laborist delivery model

Observation period

2005-2013: intervention onset in 2011 for privately insured

Primary outcomes

. CD rate: nulliparous, term, singleton, vertex pregnancies (NTSV)
N=3,560 from 2005 – 2013

. Vaginal birth rate among women w/ a prior cesarean delivery (VBAC)
N=1,324 from 2005 – 2013

Effect of Access to Midwifery on Cesarean Delivery Rates

Analysis Notes

We had access to patient-level outcomes

We aggregated up to annual rates (%)

Linear regression with AR1 residual correlation structure

The first author felt that reporting linear regression parameters representing expected changes in outcome prevalence (%) would be more accessible to readers

We could have modeled patient-level binary outcomes via GEE or GLMM
Or, we could have modeled aggregated outcomes as a binomial.
In those cases, we would have reported ORs versus linear reg. coeffs.

It would also be possible to model aggregated counts of CDs via, e.g., a negative binomial model, including an offset

With patient-level outcomes, you would not attempt to model AR1 resids.
You could cluster repeated deliveries within patients (VBAC outcome), if any parous women delivered more than once during the study

Figure 1: NTSV CD Rate Among Privately and Publicly Insured Women Before and After Expansion of Midwifery and Laborist Services

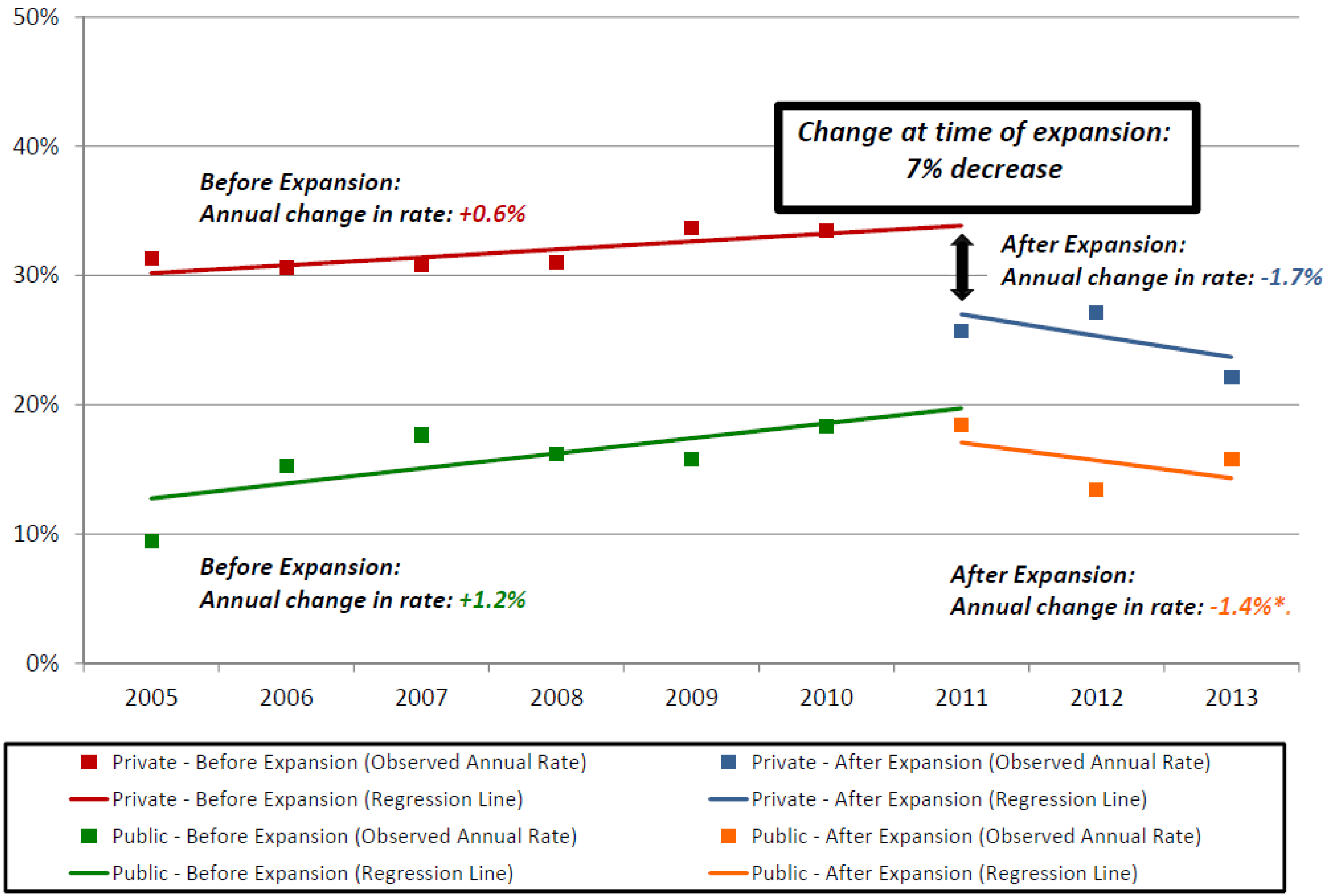
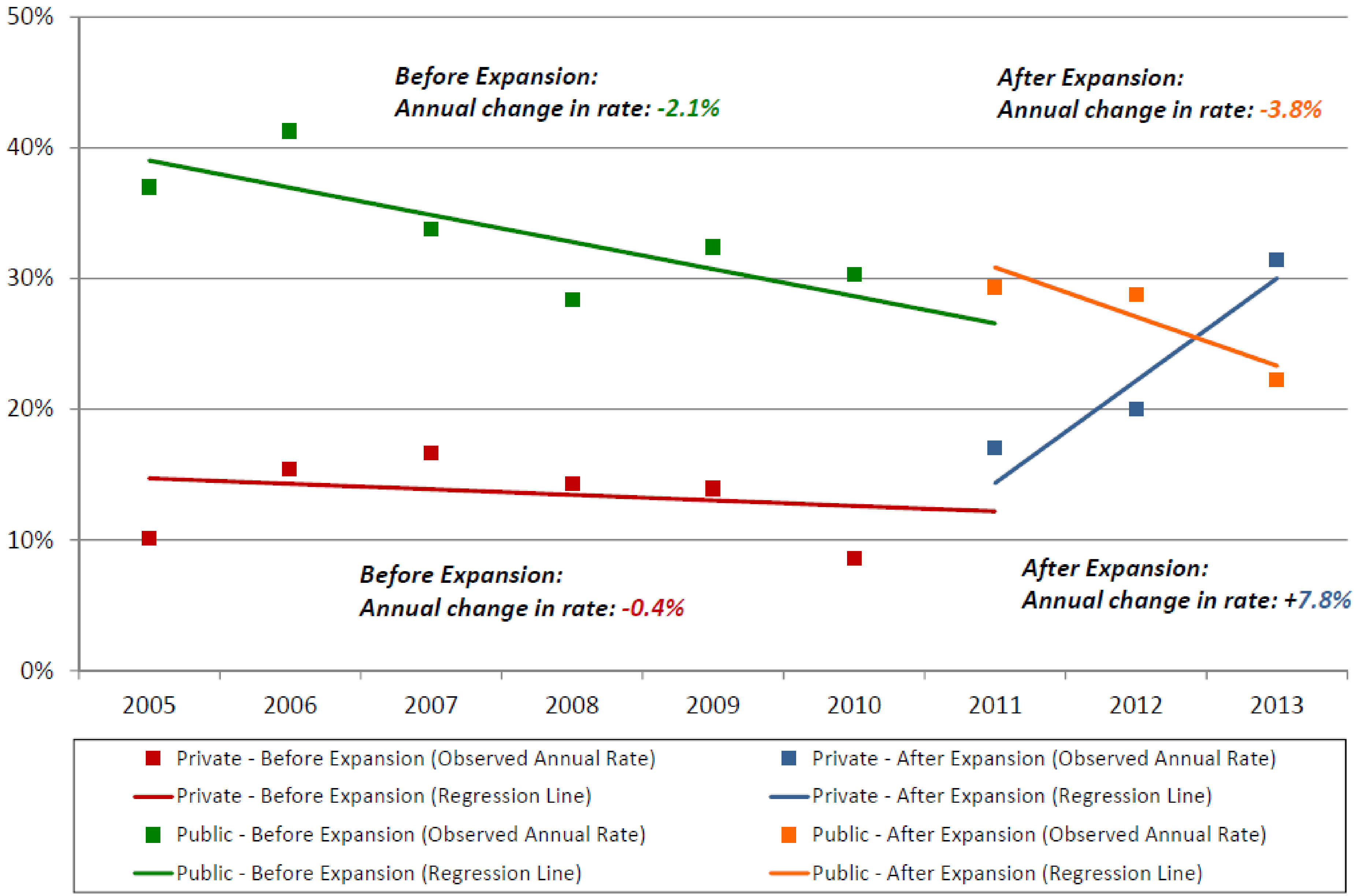


Figure 2: VBAC Rate Among Privately and Publicly Insured Women Before and After Expansion of Midwifery and Laborist Services



Easy Access to Professional Interpreters in the Hospital Decreases Readmission Rates for Limited English Proficient Patients

(submitted for publication). Leah S. Karliner, Eliseo J. Pérez-Stable, Steven E. Gregorich

Objective: Does increasing access to professional interpreters improve hospital outcomes among older LEP patients.

Intervention: Dual-handset interpreter telephone at hospital bedside.

Setting: Medicine floor of an academic medical center

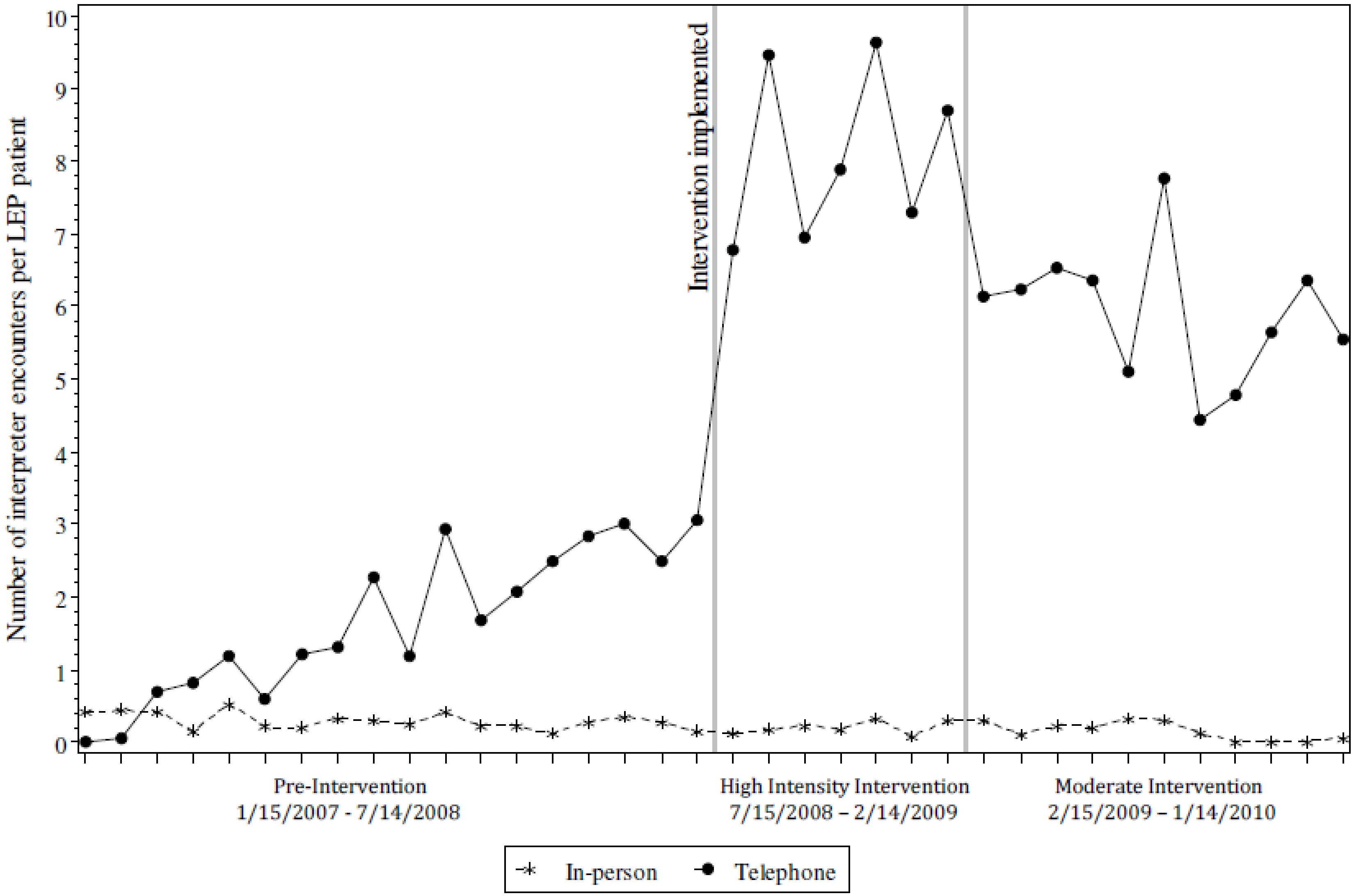
Participants: Patients ≥ 50 years discharged btwn Jan 2007 – Jan 2010
N=1,963 Limited English-proficiency (LEP) patients
N=6,114 English-proficient (EP) patients

Design: Natural experiment with varying intervention intensity.
Intended to be an ITS of intervention effectiveness for LEPs with a non-equivalent control group (EPs)

Main outcome: 30-day readmission to the hospital

Dual-handset 'bedside interpreter'

of interpreter encounters per LEP patient during 3 intervention periods



Dual-handset 'bedside interpreter' study

Intended as an ITS design with 3 intervention periods:

Pre-intervention, High-intensity intervention, Moderate intervention.

Patient-level data were available

We explored time trends of…

. Patient-level outcomes in continuous time
. Patient outcomes aggregated to calendar months (55 LEP; 170 EP)
. Patient outcomes aggregated to calendar quarter (164 LEP; 510 EP)

Any trend signals within intervention periods were swamped by noise

Eventually, we gave up on modeling trends within intervention periods

We modeled patient-level data and estimated readmission probabilities

within the 3 intervention periods and
whether the intervention effect was modified by language group
(a 2-way ANCOVA model)

Dual-handset 'bedside interpreter' study

Results: 30-day readmission rates from N=7389 discharges

	Pre-Intervention	High Intensity Intervention	Moderate Intensity Intervention
LEP	17.8% (n=938)	13.4% (n=365)	20.3% (n=493)
EP	16.7% (n=2931)	19.7% (n=1209)	17.6% (n=1453)

Effect of hysterectomy on HRQoL

Contributions of Hysterectomy and Uterus-Preserving Surgery to Health-Related Quality of Life

Miriam Kuppermann, PhD, MPH, Lee A. Learman, MD, PhD, Michael Schembri, BS, Steven E. Gregorich, PhD, Rebecca A. Jackson, MD, Alison Jacoby, MD, James Lewis, MD, and A. Eugene Washington, MD, MSC

2013. *Obstetrics & Gynecology*, 122, 15-25

Prospective cohort study: *N* = 1503 women, up to 8 years FU

. Pre menopausal women: aged 31-54 (mean = 42.5) at baseline

. Sought care in the previous year for
pelvic pain, abnormal uterine bleeding, and/or fibroids

. No cancer of the reproductive tract, intact uterus

. English or Spanish speakers

Effect of hysterectomy on HRQoL

Pre- and post-surgical HRQOL observations

. *n*=205 women had a hysterectomy sometime during the study

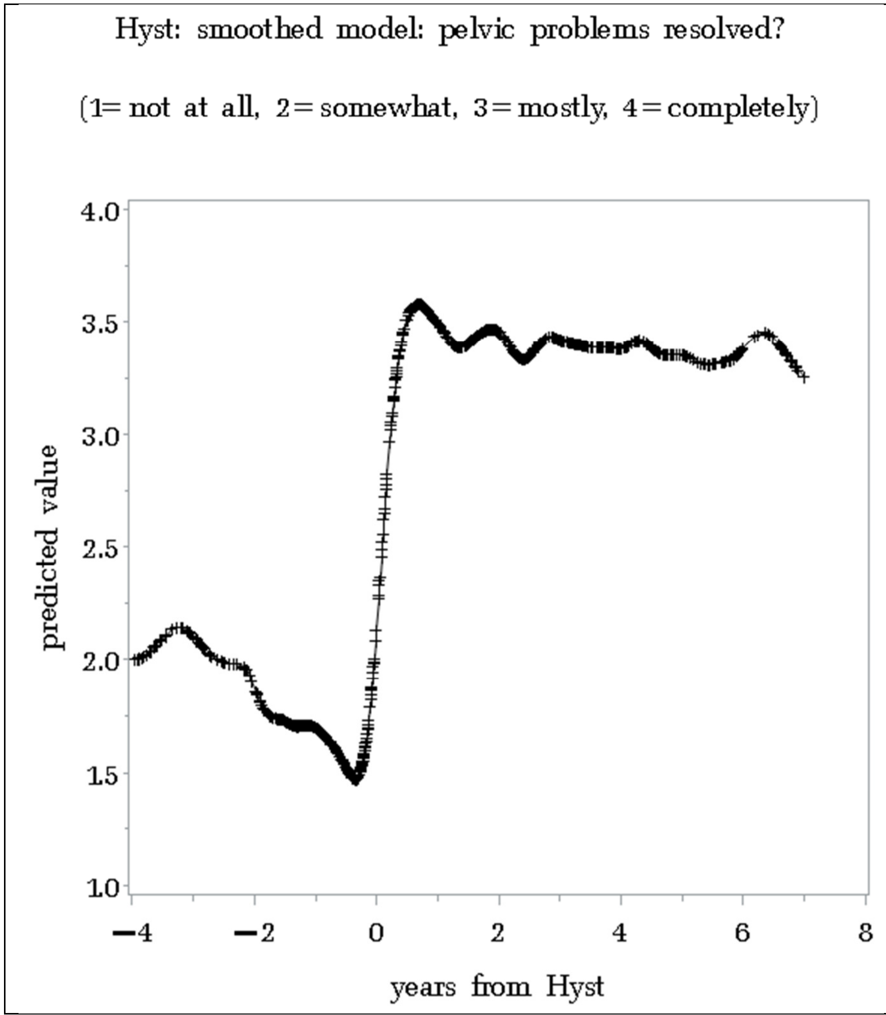
.Observation times were centered around the time of surgical intervention
Ranged from -8 to +8 years, but we restricted to -4 through +7

Main HRQoL outcome

. *P*erceived resolution of pelvic problems (PRPP)
(1=not at all, 2=somewhat, 3=mostly, 4=completely)

Effect of hysterectomy on HRQoL

A smoothing spline model to explore the average trajectory




```
proc glimmix data=  Mydata;
  model  Dv =  Time;
  random  Time /
    subject=intercept type=rsmooth;
  output out= Smooth  pred= Dv_hat;
run;
```

Effect of hysterectomy on HRQoL

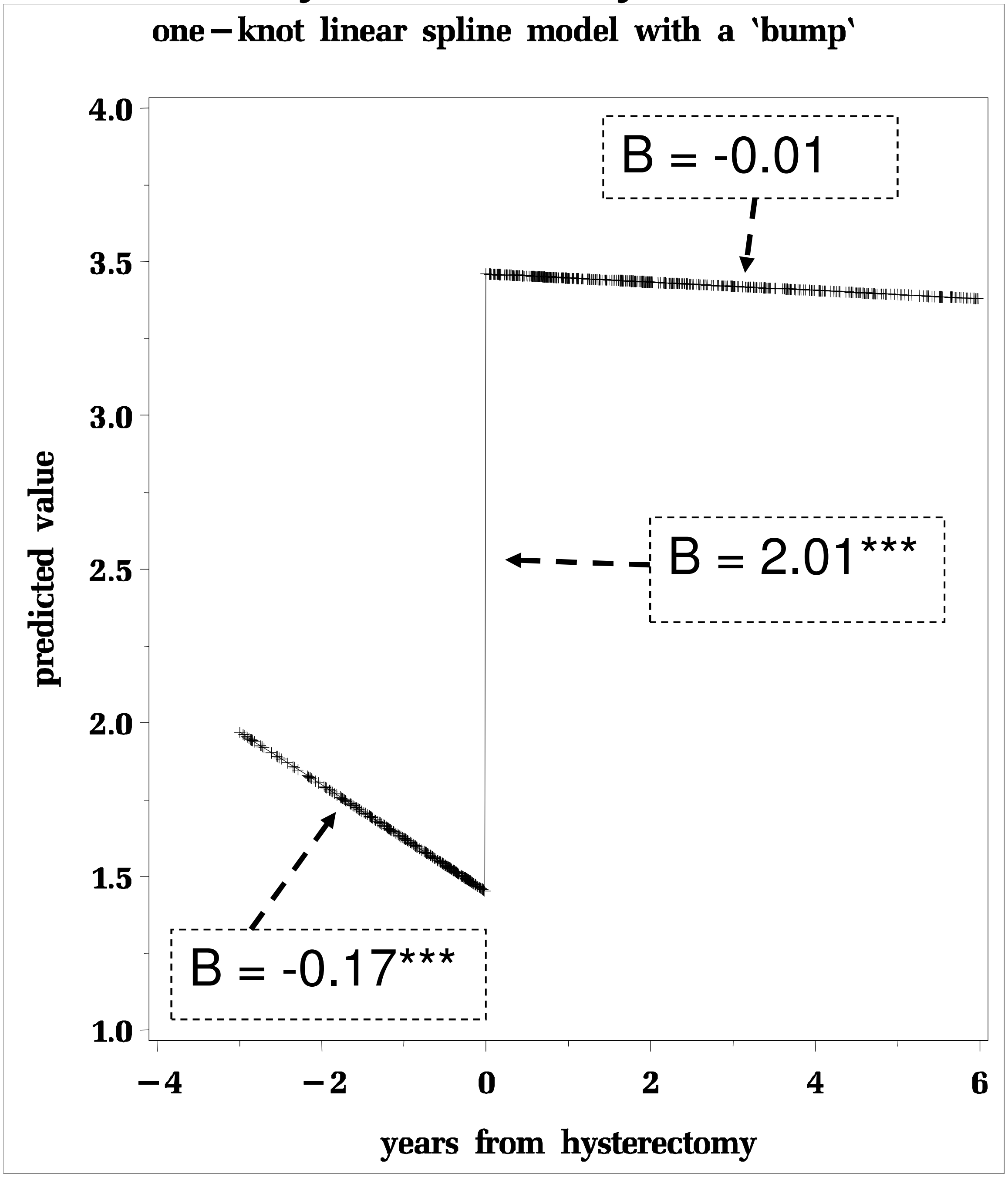
Based upon the smoothing spline model, a segmented linear regression model w/ a 'bump' at time of surgery seemed to represent the data well

```
proc mixed  method=reml  data= Mydata;
  class Id  _Surg_;
  model Dv =  Surg  Time(_Surg_)  /s  outpm= Dv_hat;
  random intercept  Surg  /  subject= Id  type=un;
run;
```

where, Surg = 0 prior to surgery and =1 following surgery;
Surg is identical to Surg, but is defined as a CLASS variable.

Initially, I fit random effects for pre- and post-surgery trajectories.
Those effects were non-significant and were dropped from the model.
Final model included random effects for intercepts & surgery 'bump.'

Effect of hysterectomy on HRQoL



Component	Est.
VAR(int)	0.25
VAR(bump)	0.59
COV(i,b)	-0.26
(r =	-0.69)
VAR(res)	0.35

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post- v pre-HYST slopes,

$\Delta = 0.16$**

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intercept = 1.45

JointPoint Trend Analysis Software

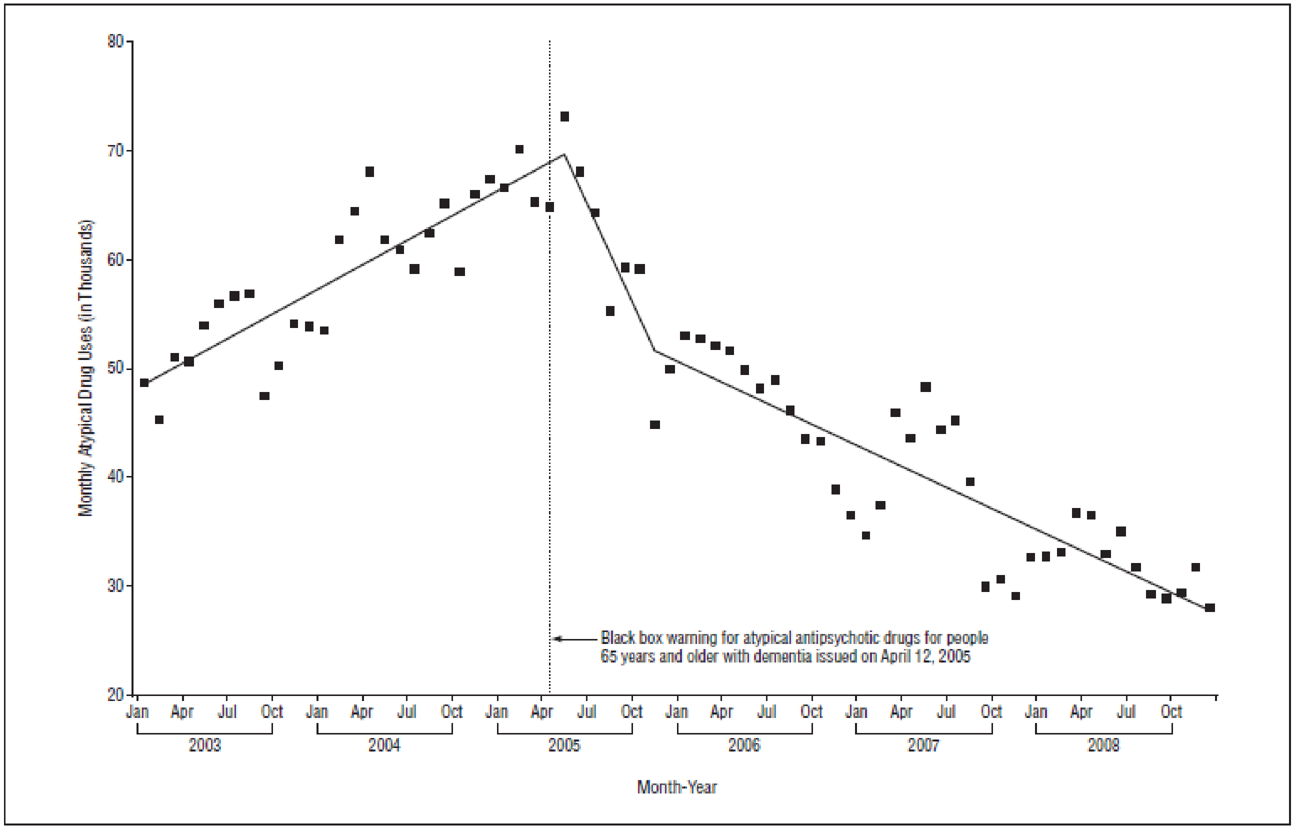

Figure 2. Joinpoint Regression Program analysis for atypical antipsychotics use among elderly patients with dementia. The data points represent patients 65 years and older with dementia (smoothed 6-month averages); the solid line, fitted joinpoint time series.

2010. Dorsey, RE et al. *Arch Intern Med*, 170, 96–103

. Program can automatically select number and location of 'knots'
. 'Bumps' (disjoint knots) not allowed (?)
. Linear (or log-linear) models, only; AR residuals OK

Download from http://surveillance.cancer.gov/joinpoint/

Summary

Impact of unit of analysis on modeling options

With one observation per time point

- Linear models with AR1 residuals
- Other GLMs possible, e.g., logistic or count outcome models

With multiple observations per time point

- . Linear or logistic models can be fit
- . Account for repeated observations of the same unit: GEE/GLMM
- . Account for clustering of observations, if any

Covariates at same level of abstraction as outcomes (or higher)

- If you aggregate outcome data, you'll also aggregate covariates
- When modeling patient-level or monthly aggregate outcome,
  consider including a covariate indicating calendar month
  (or quarter, if outcomes aggregated to that level)

Summary

Impact of unit of analysis on modeling options

. When aggregating multi-unit data with binary outcomes
you have choices regarding how to define the outcome

. mean response (proportion)

. median

. binomial or count outcome with denominator as ‘offset’

Other thoughts

. When modeling aggregated outcomes,

Center time variable: time=0 when intervention is first implemented

Intervention indicator = 0 prior to intervention; =1 during intervention

Grand-mean center covariates

This allows for most straightforward interpretation of parameters

With a few small tweaks, models that you are already familiar with
can useful for analysis of data from ITS designs with short series

END