its

September 20, 2024

1 Interupted time series analysis (ITS) modelling with restricted cubic spline and cyclical trends.

[14]:
```
# Import neccesary libraries.
import pymc as pm
import pandas as pd
from utils import rcspline_eval, h, RR_hdi_calculator
from model import run_mod
import matplotlib.pyplot as plt
import numpy as np
import arviz as az
```

```
WARNING (pytensor.tensor.blas): Using NumPy C-API based implementation for BLAS
functions.
```

2 Overview

The following is a Bayesian workflow example of an ITS analysis based on Bernal, Cummins, Gasparrini, (2017) tutorial using data from Barone-Adesi et al . (2011) and some advanced modelling options inspired by similar analysis from chapter two of Frank Harrells' wonderful Regression Modeling Strategies textbook. Specifically, the use of restricted cubic splines (rcs) Stone & Koo (1985) and cyclic trends to capture nonlinearity and seasonality due to the timeseries nature of the data whilst estimating a causal effect using an ITS analysis methodology (Bhaskaran et al. 2013).

Causal models using ITS can be easily estimated using Python/PyMC. Prepackaged examples are available in the form provided CausalPy, one of PyMC's ever-developing extension packages (Abril-Pla et al., 2023). Currently, however, the model syntax is limited and focuses on using prediction-based methods (this is likely due to the design choice of CausalPy to also support Scikit-learn forms of the models) to determine and visualise the causal effects similar to those generated by the R-based CausalImpact package.

The design choices for ITS analysis applied within the CausalPy package are just as applicable to the following analysis (probably warranting a seperate example) and the models applied. However, as stated above, the following analysis provides a Bayesian version to the tutorial analysis presented by Bernal et al., and as such, the focus here is on the statistical estimation of a causal estimand, specifcally the risk ratio difference between pre and post-intervention.

2.1 Data description

The data anlaysed below is taken from Barone-Adesi et al. (2011). Their study used an ITS design to determine the causal effect of a nation wide regulation on smoking in Italy on the standardised rate of acute coronary heart event cases (ACE) with focus in this analyis being specifically for the Sicily region.

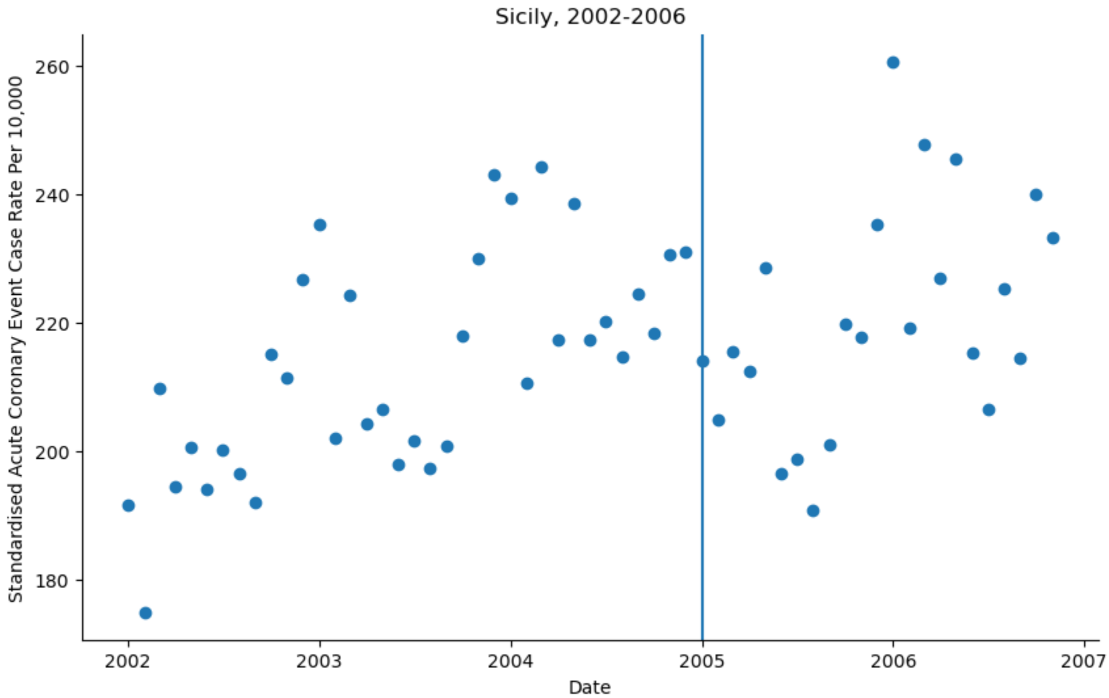
2.2 Import data

[15]:
```
# Load in data
df = pd.read_csv("https://raw.githubusercontent.com/HPCurtis/Datasets/main/
↪sicily.csv")

# Add datetiem for plotting.
df['date'] = pd.to_datetime(df[['year', 'month']].assign(day=1))

# Identify intervention date.
intervention_time = df.time[36]
intervention_date = df.date[36]
```

[34]:
```
df.head()
```

[34]:
```
   Unnamed: 0  year  month  aces  time  smokban       pop    stdpop  \
0           1  2002      1   728     1        0  364277.4  379875.3
1           2  2002      2   659     2        0  364277.4  376495.5
2           3  2002      3   791     3        0  364277.4  377040.8
3           4  2002      4   734     4        0  364277.4  377116.4
4           5  2002      5   757     5        0  364277.4  377383.4

         rate       date
0  191.641836 2002-01-01
1  175.035293 2002-02-01
2  209.791619 2002-03-01
3  194.634866 2002-04-01
4  200.591759 2002-05-01
```

[33]:
```
# Visualsie the ACE data.
_, ax = plt.subplots(figsize=(10, 6));
plt.scatter(x=df.date, y=df.rate);
plt.title("Sicily, 2002-2006")
plt.ylabel('Standardised Acute Coronary Event Case Rate Per 10,000');
plt.xlabel('Date');
plt.axvline(intervention_date);
ax.spines['top'].set_visible(False);
ax.spines['right'].set_visible(False);
plt.savefig('vis/ACE_scatter.png')
```



3 Model overviews

For the folwing analysesnin this tutorial two sepearate models that build on top of each other were fit to the data. Both models ufndm,etnally are a form of Poisson Regression that modelled the Rate of ACE using restricted cubic splines (RCS) and offset term. The difference bertween the two models is that the second model adds cyclical terms in the form of sin and cosine functions to model 12 month seasonality. The following models are espressed in mathmatical form that coincides closely with code implementation of PyMC model found in model.py other that split of the COS and SIN Terms

3.0.1 RCS Model

$$y \sim \text{Poisson}(\lambda) \tag{1}$$

$$\lambda = \exp\left(a + \text{offset}(z)\right) + f(x) \tag{2}$$

$$f(x) = \sum_{k=1}^{n} \beta_k \phi_k(x) \tag{3}$$

$$\alpha \sim \mathcal{N}(0, 10) \tag{4}$$

$$\beta_k \sim \mathcal{N}(0, 10) \tag{5}$$

3.0.2 RCS model with cyclic trend

$$
\begin{align}
y &\sim \text{Poisson}(\lambda) \tag{6}\\
\lambda &= \exp\left(a + \text{offset}(z)\right) + f(x) + \text{COS} + \text{SIN}) \tag{7}\\
f(x) &= \sum_{k=1}^{n} \beta_k \phi_k(x) \tag{8}\\
\text{COS} &= \sin\left(\frac{2\pi x}{12}\right) \tag{9}\\
\text{SIN} &= \cos\left(\frac{2\pi x}{12}\right) \tag{10}\\
\alpha &\sim \mathcal{N}(0, 10) \tag{11}\\
\beta_k &\sim \mathcal{N}(0, 10) \tag{12}\\
& \tag{13}
\end{align}
$$

3.0.3 Generate model design matrices

No basic implementations of functions to generate design matrices for restricted cubic splines or basic cyclical trends exist in Python (or at least I couldn't find them). Therefore, I implemented the necessary functionality within the utils.py file associated with this analysis project. The implemetations are based of Frank Harrells Hmisc R package

[18]:
```
# Impact component (level change here) is the column of design matrix that␣
↪estimates
# the parameter for the causal effect.
level_change = (df.time >= 37).astype(int)

# Generate design matrices for rcs model  and rcs with cyclical components
dm, knots = rcspline_eval(df.time, nk = 6)
dm_cyl = h(df.time, knots=knots)

# Add causal parameter column to each model matrix.
dm = np.column_stack((dm, level_change))
dm_cyl = np.column_stack((dm_cyl, level_change))

# Add offet to model matrix to deal with overdisperison.
offset = np.log(df['stdpop']).values
```

[19]:
```
# Fit PyMC models stored in model.py run_mod function.
trace, model_rcs = run_mod(dm = dm, df=df, offset=offset)
trace_cyl, model_cyl = run_mod(dm = dm_cyl, df=df, offset = offset)
```

```
0%|          | 0/2000 [00:00<?, ?it/s]

0%|          | 0/2000 [00:00<?, ?it/s]

0%|          | 0/2000 [00:00<?, ?it/s]

0%|          | 0/2000 [00:00<?, ?it/s]
```

```
Output()
```

```
  0%|          | 0/2000 [00:00<?, ?it/s]

  0%|          | 0/2000 [00:00<?, ?it/s]

  0%|          | 0/2000 [00:00<?, ?it/s]

  0%|          | 0/2000 [00:00<?, ?it/s]
```

```
Output()
```

4 Posterior checks

[20]:
```
# Output MCMC summaries for model parameters rcs only model.
az.summary(trace , var_names=["alpha","beta"])
```

[20]:
```
          mean     sd  hdi_3%  hdi_97%  mcse_mean  mcse_sd  ess_bulk  \
alpha   -7.539  0.018  -7.572   -7.504      0.000    0.000    1565.0
beta[0]  0.057  0.022   0.015    0.098      0.001    0.001     892.0
beta[1] -0.177  0.086  -0.341   -0.018      0.003    0.002     860.0
beta[2]  0.255  0.152  -0.036    0.539      0.005    0.004     853.0
beta[3] -0.238  0.185  -0.579    0.108      0.006    0.004    1004.0
beta[4] -0.108  0.060  -0.218    0.007      0.001    0.001    1914.0

         ess_tail  r_hat
alpha      1812.0   1.00
beta[0]     864.0   1.00
beta[1]     818.0   1.00
beta[2]     884.0   1.00
beta[3]    1259.0   1.01
beta[4]    1965.0   1.00
```

[21]:
```
# Output MCMC summaries for model parameters rcs and sine cosine function model.
az.summary(trace_cyl , var_names=["alpha","beta"])
```

[21]:
```
          mean     sd  hdi_3%  hdi_97%  mcse_mean  mcse_sd  ess_bulk  \
alpha   -7.541  0.019  -7.576   -7.508      0.000    0.000    1665.0
beta[0]  0.054  0.022   0.012    0.094      0.001    0.001     953.0
beta[1] -0.165  0.086  -0.322   -0.009      0.003    0.002     917.0
beta[2]  0.233  0.152  -0.067    0.489      0.005    0.004     933.0
```

```
beta[3] -0.219  0.187  -0.568    0.130      0.005    0.004    1224.0
beta[4]  0.032  0.013   0.009    0.059      0.000    0.000    2949.0
beta[5]  0.037  0.013   0.012    0.059      0.000    0.000    3207.0
beta[6] -0.131  0.061  -0.251   -0.020      0.001    0.001    2890.0

         ess_tail  r_hat
alpha      2177.0    1.0
beta[0]    1537.0    1.0
beta[1]    1541.0    1.0
beta[2]    1626.0    1.0
beta[3]    2117.0    1.0
beta[4]    2629.0    1.0
beta[5]    2342.0    1.0
beta[6]    2515.0    1.0
```

[22]:

```
az.plot_rank(trace, var_names=["alpha","beta"], figsize=(20,20));
plt.savefig('vis/rank_rcs.png')
```

[23]:
```python
az.plot_rank(trace_cyl, var_names=["alpha", "beta"], figsize=(25,25));
plt.savefig('vis/rank_cyl.png')
```

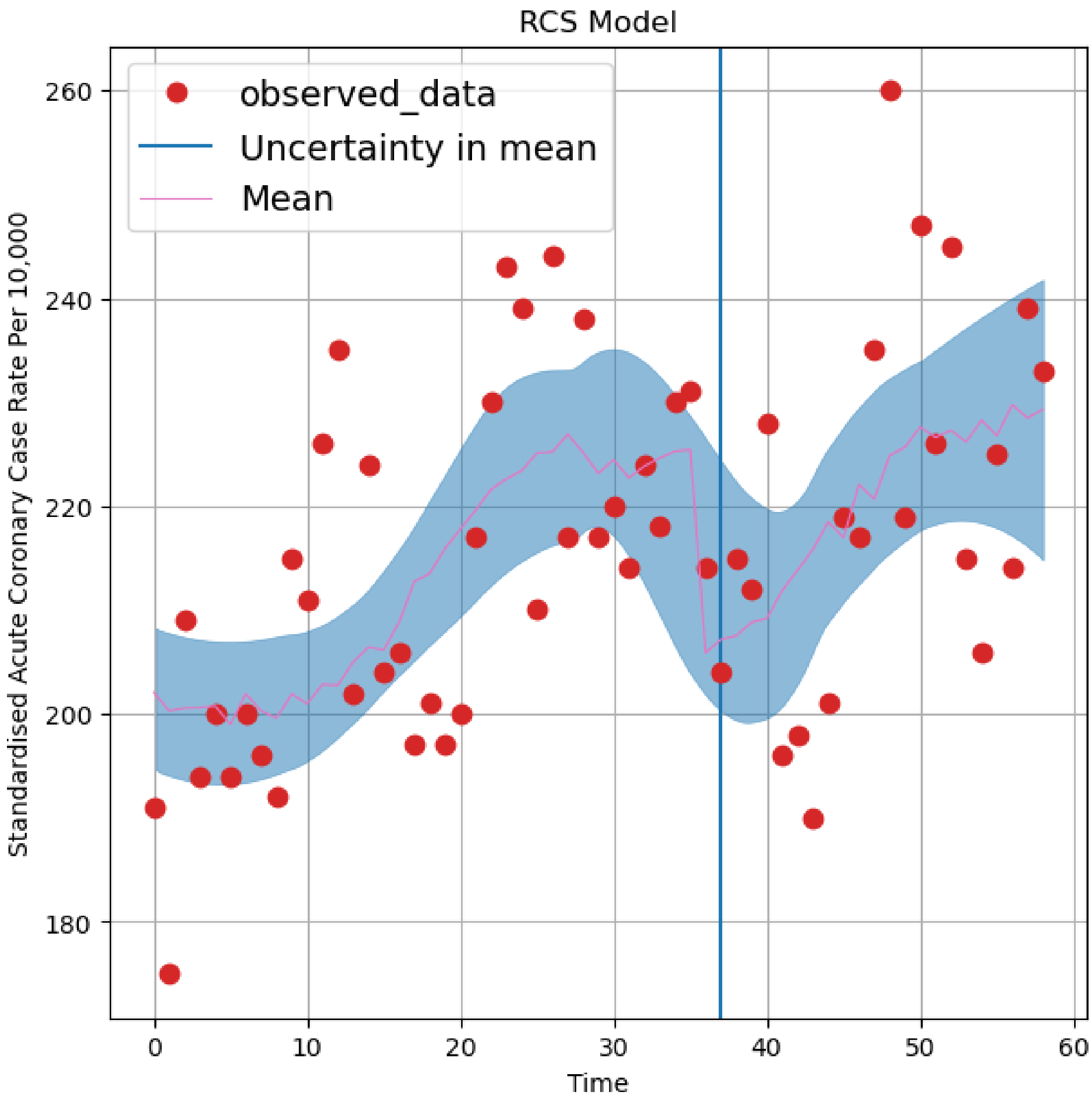
Summary for both models showed good effective sample size (ess) for bulk and tail ≥ 400 and rhat all at 1.0 which suggest the chains have converged Additionally, the rank plots show no issue or deformity in the chains away from uniformity (Vehtari et al. 2021).

5 Model Fit

[27]:
```
_, ax = plt.subplots(figsize=(7, 7))
az.plot_lm(idata=trace, y="y", num_samples=500, axes=ax, kind_model="hdi",␣
 ↪y_model="lamda")
plt.ylabel("Standardised Acute Coronary Case Rate Per 10,000")
plt.xlabel("Time")
plt.title("RCS Model");
```

```
plt.axvline(intervention_time)
plt.savefig('vis/rcs_fit.png')
```

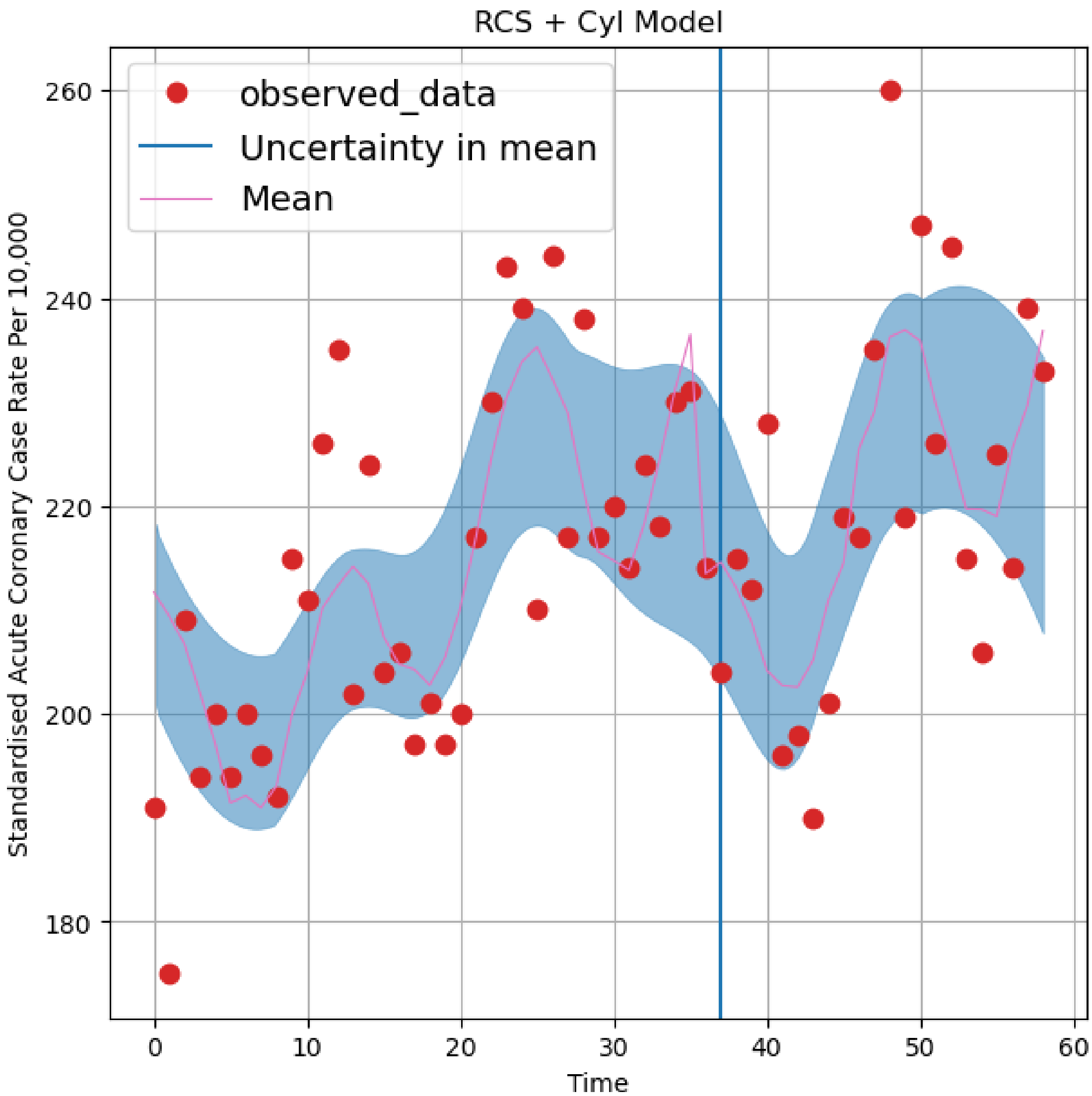
```
/home/harrison/anaconda3/envs/pymc_env/lib/python3.11/site-
packages/arviz/plots/lmplot.py:211: UserWarning: posterior_predictive not found
in idata
  warnings.warn("posterior_predictive not found in idata", UserWarning)
```



[28]:
```
_, ax = plt.subplots(figsize=(7, 7));
az.plot_lm(idata=trace_cyl, y="y", num_samples=500, axes=ax, kind_model="hdi",␣
  ↪y_model="lamda");
#plt.axvline(intervention_date);
plt.ylabel('Standardised Acute Coronary Case Rate Per 10,000');
```

```
plt.xlabel('Time');
plt.title("RCS + Cyl Model");
plt.axvline(intervention_time);
plt.savefig('vis/cyl_fit.png')
```

```
/home/harrison/anaconda3/envs/pymc_env/lib/python3.11/site-
packages/arviz/plots/lmplot.py:211: UserWarning: posterior_predictive not found
in idata
  warnings.warn("posterior_predictive not found in idata", UserWarning)
```



6 Posterior predictive checks

[13]:
```
# Using model objects  posterior preicitve simulations
with model_rcs:
    pm.sample_posterior_predictive(trace, extend_inferencedata=True,␣
 ↪random_seed=1)
with model_cyl:
    pm.sample_posterior_predictive(trace_cyl, extend_inferencedata=True,␣
 ↪random_seed=1)
```

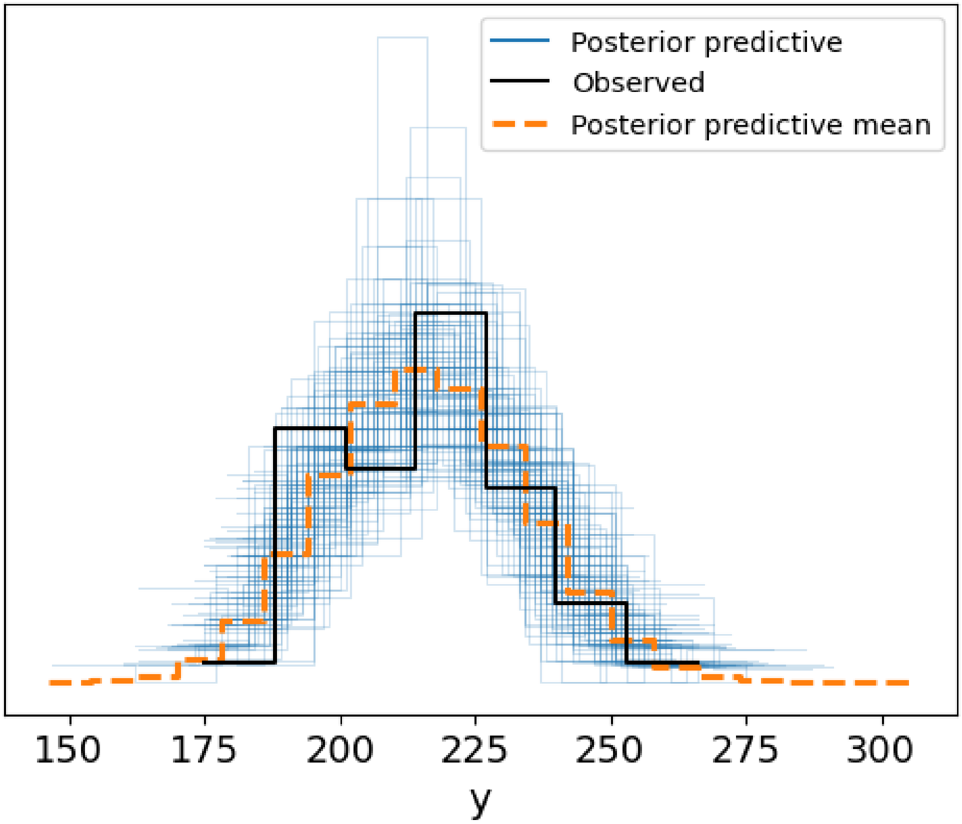
```
Sampling: [y]
```

```
Output()
```

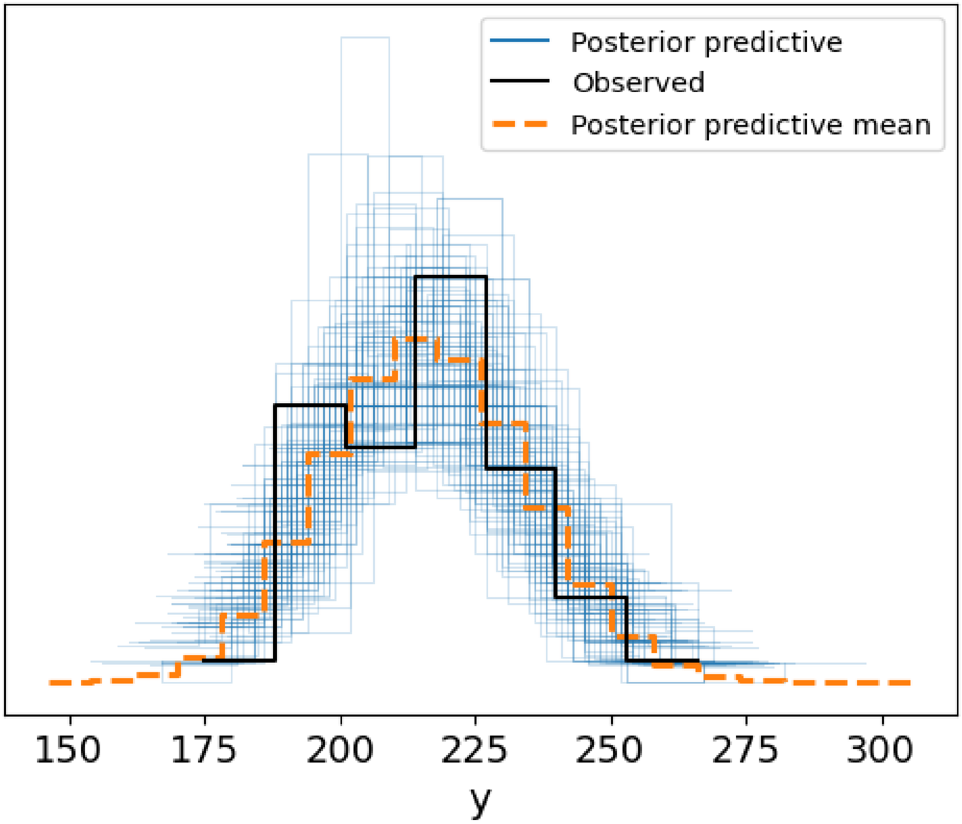
```
Sampling: [y]
```

```
Output()
```

[34]:
```
# Plot posterior predictive check plot.
az.plot_ppc(trace, num_pp_samples=100);
plt.savefig('vis/PPC_rcs.png')
```



[33]:
```
# Plot posterior predictive check.
az.plot_ppc(trace, num_pp_samples=100);
plt.savefig('vis/PPC_cyl.png')
```



Both models showed a good fit to the data with no major discrepancies between the posterior predictive distributions and the observed data.

6.1 Causal Inference estimates

[19]:
```
# Calculate Risk Ratio highest density interval (default 95%) for the impact␣
↪component of the ITS model.
hdi_rcs_lower, hdi_rcs_higher = RR_hdi_calculator(trace=trace.posterior.beta[:,:
↪,4])
hdi_cyl_lower, hdi_cyl_higher = RR_hdi_calculator(trace=trace_cyl.posterior.
↪beta[:,:,6])

# Risk ratio show decrease for relative risk after intervention of smoking␣
↪policy in both models
print("Risk Ratio for the RCS model", round(np.exp(trace.posterior.beta[:,:,4].
↪mean().values), 2), "\u00B1", f"CrI[{hdi_rcs_higher},{hdi_rcs_lower}]")
print("Risk Ratio for the RCS with cyclic trend (seasonality) model", round(np.
↪exp(trace_cyl.posterior.beta[:,:,6].mean().values), 2), "\u00B1",␣
↪f"CrI[{hdi_cyl_higher},{hdi_cyl_lower}]")
```

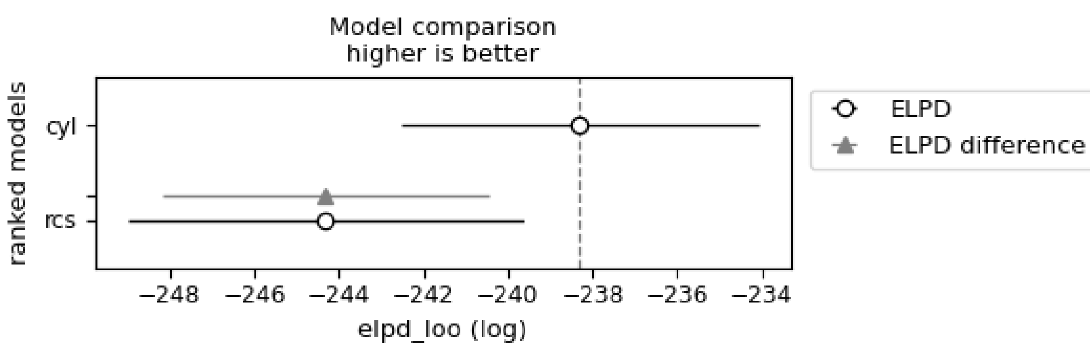
```
Risk Ratio for the RCS model 0.9 ± CrI[1.0,0.79]
```

```
Risk Ratio for the RCS with cyclic trend (seasonality) model 0.88 ±
CrI[0.98,0.78]
```

7 Model comparison

In Chapter 2 of Regression Modelling Strategies, the model comparison was conducted using the Akaike information crtierion (AIC). However, in the strictest sense, model comparison metrics should have little impact on which models are used when applying causal inference methods, as the models should be theoretically informed in terms of the estimand and the resulting estimates. However, this example does provide an option to show the superiority of model comparison methods within the Bayesian workflow/framework. Just keep in mind that such methods are designed for selecting the best model in terms of prediction and not causal inference McElreath (2020). Luckily, with this example and the models applied, the causal estimates are essentially the same as shown above, so there is less concern here about the distinction.

[28]:
```python
# Use arviz loo comparion methods using log-likelihoods calculated in the␣
 ↪run_mod() call.
df_comp_loo = az.compare({"rcs": trace, "cyl": trace_cyl})
az.plot_compare(df_comp_loo, insample_dev=False);
plt.tight_layout();
plt.savefig('vis/loo_comparison_plot.png');
```



The LOO-CV assessment above shows similar results to the AIC results found by Harrell see. However, our Bayesian models provide a much more useful picture in terms of model comparison, as uncertainty estimates naturally arise from the estimated posteriors. This is useful because, although the cyclical model was found to be superior for prediction by Harrell's AIC analysis, this is only in terms of a point estimate. In contrast, the Bayesian LOO-CV analysis provides uncertainty estimates, and as the figure above shows, there is a lot of overlap between the models. Therefore, we cannot conclude that the cyclical model is better for prediction than the simpler RCS model.

8 References

Abril-Pla, O., Andreani, V., Carroll, C., Dong, L., Fonnesbeck, C. J., Kochurov, M., ... & Zinkov, R. (2023). PyMC: a modern, and comprehensive probabilistic programming framework in Python. PeerJ Computer Science, 9, e1516.

Barone-Adesi, F., Gasparrini, A., Vizzini, L., Merletti, F., & Richiardi, L. (2011). Effects of Italian smoking regulation on rates of hospital admission for acute coronary events: a country-wide study. PloS one, 6(3), e17419.

Bernal, J. L., Cummins, S., & Gasparrini, A. (2017). Interrupted time series regression for the evaluation of public health interventions: a tutorial. International journal of epidemiology, 46(1), 348-355.

Bhaskaran, K., Gasparrini, A., Hajat, S., Smeeth, L., & Armstrong, B. (2013). Time series regression studies in environmental epidemiology. International journal of epidemiology, 42(4), 1187-1195.

Brodersen, K. H., Hauser, A., & Hauser, M. A. (2017). Package CausalImpact. Google LLC: Mountain View, CA, USA.

Lundberg, I., Johnson, R., & Stewart, B. M. (2021). What is your estimand? Defining the target quantity connects statistical evidence to theory. American Sociological Review, 86(3), 532-565.

McElreath R. Statistical Rethinking. 2nd Edition. London (UK): Routledge; 2020.

Stone, C. J., & Koo, C. Y. (1985). Additive splines in statistics. Proceedings of the Statistical Computing Section ASA, 45–48.

Vehtari, A., Gelman, A., Simpson, D., Carpenter, B., & Bürkner, P. C. (2021). Rank-normalization, folding, and localization: An improved Rˆ for assessing convergence of MCMC (with discussion). Bayesian analysis, 16(2), 667-718.

9 Web resources

https://hbiostat.org/rmsc/

https://github.com/harrelfe/Hmisc