**ONLINE APPENDIX 1: THE EQUATION OF THE COMPARATIVE INTERRUPTED TIME SERIES ANALYSIS AND THE CALCULATION OF PREDICTED VALUES**

We examined four outcomes in our study and we built a separate model for each outcome (4 outcomes) of a risk group (3 high-risk patient groups and their 3 counterparts). For a given outcome, our unit of analysis was a monthly measure which was derived by aggregating all of the transactions associated with a specific patient group in a given state during that month. For example, we aggregated all transactions that occurred in Dec 2011 from concomitant users who resided in Florida to obtain total opioid volume of concomitant users in Florida in Dec 2011; there is only one observation for each outcome in a month from a state for a given patient group. Given that we include both states in our model, we had 50 observations for each outcome (25 observation from the intervention state Florida and 25 observations from the comparison state Georgia).

**The equation of the model**

Outcome = intercept + β1\*month indicator + β2\*state indicator + β3\*period indicator + β4\*post-intervention month indicator + β5\*state indicator\*month indicator + β6\*state indicator\*period indicator + β7\*state indicator\*post-intervention month indicator

month indicator: a number representing which month this observation came from and ranging from 1 to 25.

state indicator: a binary indicator representing which state this observation came from (1: Florida / 0: Georgia).

period indicator: a binary indicator representing whether this observation came from the pre-policy period (1: No / 0: Yes).

post-intervention month indicator: a number representing which post-intervention month this observation came from and ranging from 0 to 13; all 12 observations coming from the pre-intervention period assigned to 0.

state indicator\*month indicator: the product of state indicator and month indicator

state indicator\*period indicator: the product of state indicator and period indicator

state indicator\*post-intervention month indicator: the product of state indicator and post-intervention month indicator

**Trend/Slope by state and period**

Using the equation above, I presented how the comparative change in trend was calculated.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pre-Intervention | Post-Intervention | Difference between periods |
| Florida | β1 + β5 | β1 + β4 + β5 + β7 | β4 + β7 |
| Georgia | β1 | β1 + β4 | β4 |
| Difference between states | β5 | β5 + β7 | β7 |

In Florida in the pre-intervention period, an outcome variable would increase by “β1 + β5” per month; in the post-intervention period, an outcome variable would increase by “β1 + β4 + β5 + β7” per month. The difference in slope between the pre- and post-intervention in Florida is “β4 + β7”.

In Georgia in the pre-intervention period, an outcome variable would increase by “β1” per month; in the post-intervention period, an outcome variable would increase by “β1 + β4” per month. The difference in slope between the pre- and post-intervention in Georgia is “β4”.

The difference between the difference in Florida and the difference in Georgia is “β7”, the main outcome in your study and reported under “comparative change in trend” in table 2.

**Predicted Values**

Predicted values were calculated under the assumption that the intervention was not implemented. If the intervention was not implemented, we would not expect to observe a comparative change in either level (β6) or slope (β7). Therefore, using the coefficients derived from the previous equation, the predicted value would be:

Predicted Outcome = intercept + β1\*month indicator + β2\*state indicator + β3\*period indicator + β4\*post-intervention month indicator + β5\*state indicator\*month indicator.