Reviewer's report

Title: Association between unemployment rates and prescription drug utilization in the United States, 2007-2010

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Reviewer: Tim Bruckner

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Major Compulsory Revisions

The Authors use a strong dataset to address the important question of whether prescription drug sales move inversely with the unemployment rate. The Authors motivate their test with both epidemiologic and health care services literature, which allows for potentially positive or negative associations among unemployment and utilization. The Authors generally report modest positive associations between (within-state) unemployment rates and prescription sales.

I find the paper well-written and clear. The figures enhance the analytic interpretation, as does the important supplement on the random effects specification. I do have several questions regarding the a priori goals, analytic decisions, and presentation and interpretation of findings. Below I list them in order of importance.

1. Coherence between research objectives, choice of counterfactual population, and interpretation of results.

As stated in the last paragraph of the Introduction, the Authors state directional hypotheses about associations between unemployment rates and drug sales in certain therapeutic classes. In addition, they point out the benefit of having great data—the ability to explore/examine variation in therapeutics across states and times. Each of these exercises could warrant a separate (and much longer) paper, yet the Authors attempt to accomplish both in this short manuscript.

A straightforward econometric approach to the hypothesis, given the structure of their data (50 states x 34 months = 1700 state-month observations), would involve a panel fixed effects design, with both state (50-1) and month (34-1, or perhaps 12 calendar months-1) fixed effects. In addition to these controls, the Authors would then add their control variables (e.g., demographics), and then their independent variable of interest (unemployment rate, either in raw or in a de-trended, de-seasonalized form depending on their hypothesis). Then, diagnostics would ensure removal of autocorrelated errors if they were detected (which I presume is an important problem in drug sales that month fixed effects cannot necessarily remove).

The authors opt for a random effects model that in some sense partitions the variance from the model above into within- and across- state effects. However, I
am not clear whether counterfactual reasoning (for testing your hypothesis) would use the across-state effect. Are we to assume, for example, that (holding all the covariates constant) California and Arkansas are exchangeable in their prescription drug rates save for the difference in the level of their unemployment rate? I would welcome a clearer justification for their specific random effects model, and an explicit discussion of what confounders this random effects model does not rule out (e.g., autocorrelated errors, monthly [not seasonal] factors shared across all states that cause both predictably high unemployment rates [e.g., January layoffs after the holidays] and drug sales, etc.). This logic would help the reader assess the “fit” between their model and the hypothesis, as well as the ability of the model to rule out plausible rival explanations for their findings.

2. Interpretation of findings hinges on within-state results

"In addition to the absence of any strong effect of the recession on prescription utilization" -- this quote contrasts the large inverse association between atypicals and across-state unemployment rates, so I assume that the main findings involve within-state results. Again, the exposition of the across state (i.e., exploration?) and within-state (hypothesis test?) analyses could be clearer, if you wanted to retain the random-effects model.

3. Discussion is too brief and too general.

I understand the word count limitations, but after having read the paper I am left wanting more discussion on why you had specific a priori hypotheses of associations in some drug classes but not others, why the 16% effect of atypical antipsychotics with 1% change in unemployment rate might occur, whether changes in oral contraceptive use indicate potential changes in fertility behavior, or whether drug use even gauges true time-varying incidence of health conditions. I understand the limitations of ecological data in making individual inferences, but I would welcome a more precise discussion of at least a subset of the findings. What specific testable propositions for future inquiry arise from your research?

Minor essential revisions

• Typo- "and we the elderly accounted for only approximately one-quarter of the entire market of therapies examined."

• Please reference the source of BLS data (website or other)

• Inconsistent description of time frame, I count only 34 months-- "retail prescription drug use over a five-year period."

With discussion of IRR, this is a multiplicative, not additive, scale, so 1/.75 = 1.33, not 1.25, correct?

• How can 95% CIs in Table 2 be so precise with only 1,700 state-month observations?

• Appendix Table:
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'