Evaluating the Comparative Self-Controlled Case Series Method
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BACKGROUND
• New user cohort design evaluates the risk of health outcomes in a treatment group relative to a comparator group; selection effects drive treatment assignment and are mitigated by propensity score methods using observed covariates.¹-⁴
• Self-controlled case series (SCCS) design evaluates the risk of health outcomes in cases only by comparing event rates in unexposed and exposed time; implicitly controls for fixed and unobserved covariates.¹-⁴
• The novel comparative self-controlled case series (CSCCS) combines advantages of new user cohort and SCCS designs; treatment and comparator groups balanced on observed covariates, estimate treatment and comparator effects in balanced groups while controlling for unobserved covariates.

OBJECTIVES
• Design a statistically efficient, low residual bias method for estimating treatment effect that controls for observed and unobserved covariates.
• Compare direction, magnitude, and precision of CSCSS effect estimates relative to those generated by new user cohort design.
• Evaluate CSCSS with model calibration and discriminative performance metrics.¹,⁴

METHODS
• Preliminary SCCS approach is demonstrated by comparing celecoxib and non-selective non-steroidal anti-inflammatory drugs (nsNSAIDs) for risk of myocardial infarction (MI) and gastrointestinal hemorrhage (GI bleed) in osteoarthritis patients.
• Method executed against Truven MarketScan Multi-State Medicaid (MDCD) and Truven MarketScan Medicare Supplemental Beneficiaries (MDCR).
• The SCCS design is extended to the treatment vs. comparator framework by executing parallel SCCS analyses on propensity score balanced incident new user cohorts; relative outcome risk is the ratio of rate ratios (RRR).⁵

RESULTS
• Many fewer patients needed for CSCSS than new user cohort design (Table 1) to achieve comparable or improved precision.
• average uncertainty of effect across all outcomes in CSCSS is 10.6% lower than new user cohort in MDCD; 5.6% lower in MDCR.

Table 1. Incident exposure and outcome counts for new user cohort and CSCSS designs comparing celecoxib vs. nsNSAIDs on MI and GI bleed

<table>
<thead>
<tr>
<th>DB</th>
<th>Design</th>
<th>Exposed, n</th>
<th>Celecoxib</th>
<th>nsNSAIDs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>MI, n(e)</td>
<td>GI, n(e)</td>
</tr>
<tr>
<td>MDCD</td>
<td>New User Cohort</td>
<td>13737</td>
<td>19(19)</td>
<td>32(32)</td>
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<tr>
<td></td>
<td>SCCS, Mi</td>
<td>260</td>
<td>260(40)</td>
<td>252(252)</td>
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<tr>
<td></td>
<td>SCCS, Gi</td>
<td>327</td>
<td>327(508)</td>
<td>297</td>
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<tr>
<td></td>
<td>MDCR</td>
<td>57547</td>
<td>115(115)</td>
<td>155(155)</td>
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<tr>
<td></td>
<td>SCCS, Mi</td>
<td>1435</td>
<td>1435(2655)</td>
<td>1460</td>
</tr>
<tr>
<td></td>
<td>SCCS, Gi</td>
<td>1853</td>
<td>1853(2999)</td>
<td>1744</td>
</tr>
</tbody>
</table>

*DB=database, SCCS=Self-controlled Case Series, CSCSS=Comparative Self-Controlled Case Series, nsNSAID=non-NSAID, GI=gastrintestinal bleed, MI=myocardial infarction, n(e)=patient count(event count).
• Inconsistent results between new user cohort and CSCSS designs for 3 of 4 test cases (MI and GI bleed in MDCD, MI in MDCR) (Table 2, Figure 1a, 2a).

CONCLUSION
• Preliminary results are inconclusive; unable to conclude that CSCSS effect estimates are comparable to those from new user cohort design.
• Execution across many drug-outcome pairs of known positive and negative signal across a database network necessary for full evaluation.
• Statistical efficient advantages for estimating comparative treatment effects on low-prevalence outcomes.

REFERENCES

CONFLICT OF INTEREST
• RR, NS, E, and PR are full-time employees of Janssen Research and Development, a unit of Johnson and Johnson. The work of this study was part of their employment. They hold pension rights from the company and own stock and stock options.