Use of High-dimensional Propensity Scores (hdPS) in a Japanese National Claims Database

Jocelyn R. Wang, MS[1], **Sahar Syed (Presenting author)[2]**, Elizabeth M. Garry, PhD, MPH[1]
[1]Science, Aetion, Boston, MA
[2]Science, Aetion, New York, NY

Background

- Many analytical study designs to mitigate confounding have been used including researcher-defined propensity score (PS) analyses and automated high-dimensional propensity score (hdPS) analyses to further control for residual confounding.
- Although there is much evidence demonstrating the utility of hdPS algorithms for confounding control in comparative effectiveness studies using RWD in the United States (US) and United Kingdom (UK), its performance using Japanese RWD remains unclear given differences in healthcare practice and data collection.

Objective

Evaluate the performance of hdPS to improve confounding control in a national claims-based Japanese RWD source using the known moderate protective effect of COX-2 inhibitor (Cox-2i) on severe gastrointestinal (GI) complications as an example.

Methods

Data. Japanese Medical Data Center (JMDC), Payer-Based Database 2007-2011.

Population.

- We Included patients with a new Cox-2 (exposure) or non-selective traditional NSAID (tNSAID) (referent) claim Jan2007-Dec2011.
- Patients were required to be continuously enrolled and have no evidence of either treatment during the 12-month baseline period prior to index treatment initiation (new-user washout).
- Patients were required to have no recorded history of any of the following conditions before the treatment index date: cancer other than non-melanoma skin cancer, chronic liver disease, Mallory–Weiss syndrome, coagulopathy, esophageal varices, chronic alcoholism, or bariatric or other surgery resulting in the gastrojejunal anastomosis.

Primary Outcome. Gastrointestinal (GI) complication was defined as at least one ICD-10 (Sub-classification) diagnosis claim for GI hemorrhage or peptic ulcers with a confirmed diagnosis flag. The outcome was measured over the follow-up period, which started on the treatment index date and ended upon the occurrence of the outcome, end of data, disenrollment, death, or a maximum of 180 days

Data Analyses.

- For PS and hdPS analyses, a set of covariates were prespecified using subject-matter knowledge only (i.e., selected *a priori*) including demographics (age, sex), calendar year of cohort entry, healthcare resource utilization, comorbidities, and medication use.
- We employed 1:1 nearest-neighbor PS-matching for initiating a COX-2i using 3 separate PS models: 1) all prespecified covariates; 2) prespecified age and sex demographics + hdPS-selected covariates, and 3) all prespecified covariates + hdPS-selected covariates. (**Table 1**)
- Candidate covariates for the hdPS model were autoselected from the following: 3-digit ICD-10 diagnosis codes, EphMRA ATC codes, and procedure category names.
- Covariate balance was evaluated using absolute standardized differences (ASD) between the treatment arms of prespecified covariates, defining imbalance as an ASD > 0.1.
- Data were analyzed using the Aetion Evidence Platform (AEP)®.

Results

- While 7 out of 19 covariates were imbalanced in the unmatched cohort, covariate balance was achieved for all covariates in all PS models, with ASDs for the hdPS models generally lower than the prespecified. (**Table 2**)
- The unmatched HR for COX-2i versus tNSAIDs initiators was 1.11 (0.84 - 1.45), and matched HRs were 0.87 (0.61 - 1.26), 1.02 (0.80 - 1.30), and 0.72 (0.50 - 1.02) for the prespecified, hdPS alone, and prespecified + hdPS models, respectively. (**Figure 1**)

Table 1. Description of confounding strategies

Model	Description
Model A	Unadjusted
Model B	PS-matched (all prespecified covariates)
Model C	hdPS-matched (prespecified age and sex demographics + hdPS-selected covariates)
Model D	hdPS-matched (all prespecified covariates + hdPS-selected covariates)

Table 2. Absolute standardized differences (ASD) for baseline characteristics pre and post-matching

Variable	Model A	Model B	Model C	Model D
Year of Cohort Entry Date	0.023	0.067	0.006	0.042
Age	0.372	0.021	0.009	0.008
Sex	0.127	0.008	0.010	0.020
Alcohol consumption	0.003	0.024	0.016	0.012
Smoking	0.059	0.015	0.002	0.022
BMI value	0.017	0.035	0.027	0.010
Any inpatient visit	0.005	0.000	0.037	0.031
Any outpatient visit	0.109	0.026	0.008	0.004
Any prescriptions	0.035	0.011	0.003	0.020
Congestive heart failure	0.012	0.022	0.025	0.034
Coronary artery disease	0.030	0.000	0.008	0.000
Essential Hypertension	0.080	0.038	0.016	0.021
Osteoarthritis	0.102	0.016	0.026	0.046
Peptic ulcer disease	0.038	0.018	0.011	0.022
Rheumatoid arthritis	0.099	0.022	0.023	0.049
Anticoagulants	0.003	0.007	0.003	0.029
Antiplatelets	0.040	0.005	0.028	0.000
Gastroprotective drugs	0.042	0.017	0.017	0.020
Oral steroids	0.007	0.000	0.023	0.030

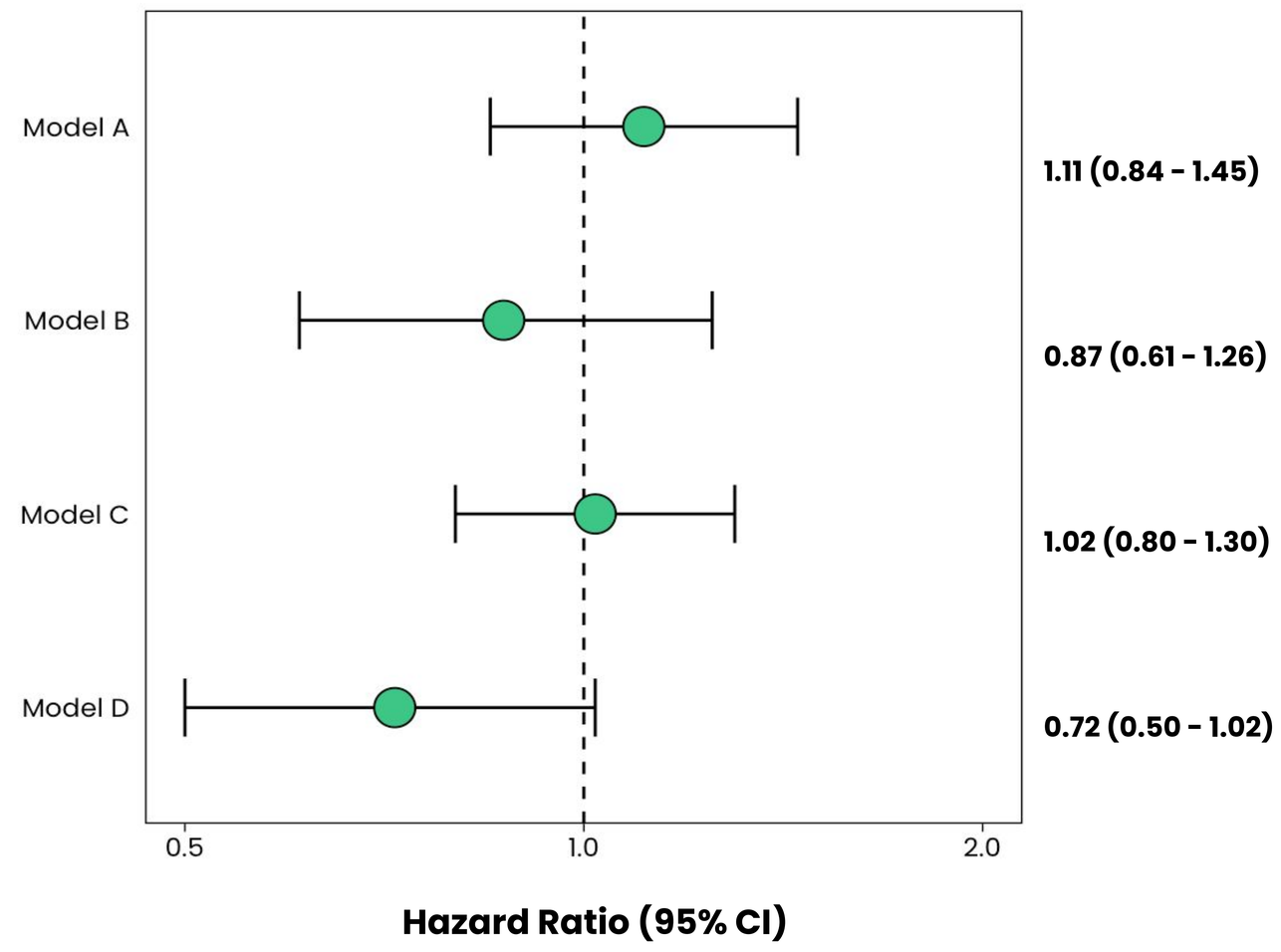

Figure 1. Effect estimates [HR (95%CI)] using various confounding adjustment strategies

Conclusions

Compared to the model with prespecified covariates alone, the addition of hdPS achieved greater balance and yielded an estimate closest to the expected effect for COX-2 inhibitors versus tNSAIDs, demonstrating its utility in Japanese RWD.

Disclosure

This project was unfunded. All authors are full-time employees of Aetion Inc. and hold stock options or equity in Aetion.