

TROY: Trials Replication through Observational study by Yonsei

PRESENTER: **Jaehyeong Cho**

INTRO

When it is difficult to generalize the results of RCTs, a retrospective study with well-controlled confounding factors through replication of the RCT design using observational data can be a complementary alternative.

When it is difficult to generalize the results of RCTs, a retrospective study with well-controlled confounding factors through replication of the RCT design using observational data can be a complementary alternative.

METHOD

1. The two common data model (CDM) databases used in this study are Yonsei University Healthcare System (YUHS) CDM database and Ajou University School of Medicine (AUSOM) CDM database.
2. The population of interest are as follows: 1) a group of patients that were as close as possible to the recruitment target of each pivotal RCT to be replicated (group 1), and 2) a group of all patients used by having an indication for the drug (group 2).
3. The 15 randomized clinical trials to be replicated in the TROY project are shown in Table 1.

Table 1. Replication list of pivotal randomized clinical trials considered in this study.

Study	Target drug (class)	Comparator drug (class)	Note
LEADER	Liraglutide (GLP-1)	DPP-4	Placebo-controlled RCT
DECLARE-TIMI 58	Dapagliflozin (SGLT-2)	DPP-4	Placebo-controlled RCT
EMPA-REG OUTCOME	Empagliflozin (SGLT-2)	DPP-4	Placebo-controlled RCT
CANVAS	Canagliflozin (SGLT-2)	DPP-4	Placebo-controlled RCT
CARMELINA	Linagliptin (DPP-4)	SU	Placebo-controlled RCT
TECOS	Sitagliptin (DPP-4)	SU	Placebo-controlled RCT
SAVOR-TIMI 53	Saxagliptin (DPP-4)	SU	Placebo-controlled RCT
CAROLINA	Linagliptin (DPP-4)	Glimepiride (SU)	
TRITON-TIMI 38	Prasugrel + Aspirin	Clopidogrel + Aspirin	
PLATO	Ticagrelor + Aspirin	Clopidogrel + Aspirin	
ROCKET AF	Rivaroxaban	Warfarin	
ARISTOTLE	Apixaban	Warfarin	
ENGAGE AF-TIMI 48	Edoxaban	Warfarin	
ORAL	Tofacitinib	TNF inhibitor	
STAR-RA	Tofacitinib	TNF inhibitor	

4. We compare outcomes between drugs (and classes) for each pivotal RCT emulated using the packages included in HADES (formally known as the OHDSI Methods Library).

This is ongoing research

We initiated the 'Trials Replication through Observational study by Yonsei (TROY)' project to generate large population-level evidence for 15 pivotal RCTs in the real world: Type 2 diabetes mellitus, atrial arrhythmia, acute coronary syndrome, and rheumatoid arthritis



Scan QR code link to GitHub repository

RESULTS

This is ongoing research. CohortDiagnostics was performed by replicating pivotal RCTs for three anticoagulants (ARTISTOTLE, ROCKET AF, and ENGAGE AF-TIMI 48), and the number of identified patients is presented in Table 2.

Table 2. Number of patients identified in the YUHS and AUSOM database.

Study	Target drug	Comparator drug	YUHS CDM (group 2)	AUSOM CDM (group 2)
Exposure				
ARISTOTLE	Apixaban	Warfarin	1,807(6,735) / 2,434(8,122)	135(487) / 195(961)
ROCKET AF	Rivaroxaban	Warfarin	463(2,763) / 1,864(6,355)	112(630) / 37(554)
ENGAGE AF-TIMI 48	Edoxaban	Warfarin	988(4,973) / 1,796(8,450)	252(1,186) / 170(995)
Outcome				
3P MACE	LEADER, EMPA-REG OUTCOME, CANVAS, CARMELINA, SAVOR-TIMI 53, CAROLINA, TRITON-TIMI 38, PLATO, ORAL		55,792	47,333
4P MACE	TECOS		73,573	75,205
HHF + CV death	DECLARE-TIMI 58		29,945	20,664
Stroke + systemic embolism	ROCKET AF, ARISTOTLE, ENGAGE AF-TIMI 48		45,996	34,382
Cancer	STAR-RA, ORAL		70,308	41,586
MI + Stroke	STAR-RA		51,146	42,277

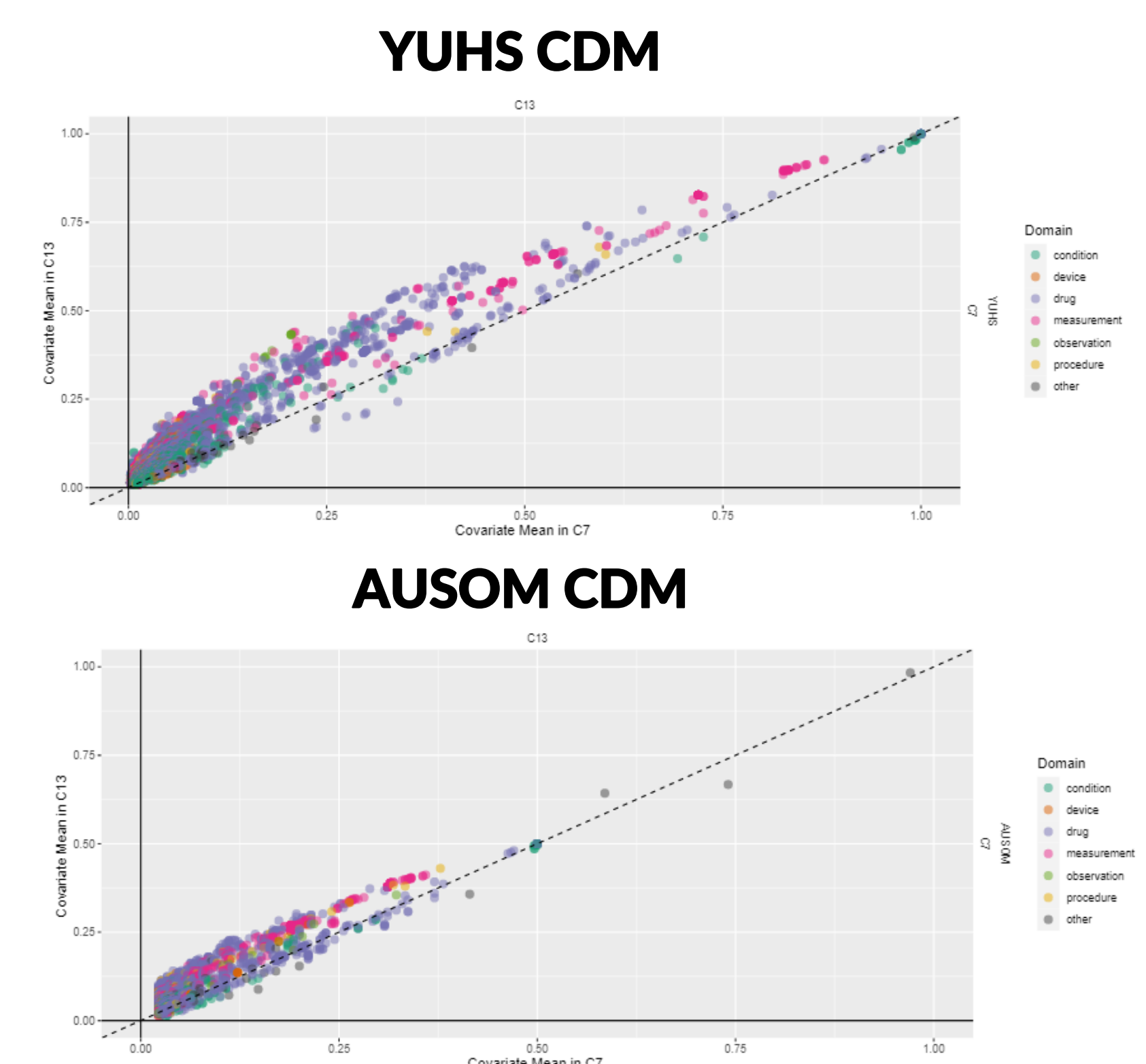


Figure 1 shows the comparison of patient characteristics between group 1 and group 2 for Apixaban.

Jaehyeong Cho^{1,2} (boyinai03@gmail.com), Chungsoo Kim³ (ted9219@ajou.ac.kr), Kyulee Jeon^{2,3} (kyulee.jeon@gmail.com), Ju-Young Shin⁴ (shin.jy@skku.edu), Rae Woong Park^{3,5} (veritas@ajou.ac.kr), Kyung Won Kim^{2,6} (kwkim@yuhs.ac), Seng Chan You^{1,2} (seng.chan.you@ohdsi.org)



¹Department of Biomedical Systems Informatics, Yonsei University College of Medicine, Seoul, Republic of Korea

²Institute for Innovation in Digital Healthcare, Yonsei University, Seoul, Republic of Korea

³Department of Biomedical Sciences, Ajou University School of Medicine, Suwon, Republic of Korea

⁴School of Pharmacy, Sungkyunkwan University, Suwon, Republic of Korea

⁵Department of Biomedical Informatics, Ajou University Graduate School of Medicine, Suwon, Republic of Korea

⁶Department of Pediatrics, Yonsei University College of Medicine, Seoul, Republic of Korea

