

Comparative Risk for Neuropsychiatric Events in Leukotriene Receptor Antagonists versus Inhaled Corticosteroids in Children with Asthma

PRESENTER: Subin Kim, Seng Chan You

INTRODUCTION

- Leukotriene receptor antagonists (LTRA) are widely prescribed in children with asthma.
- In 2020, the US FDA warned of the neuropsychiatric adverse drug reactions of LTRA; but the evidence from observational studies is still inconclusive.
- In previous studies, neuropsychiatric events (NPEs) are generally identified using the diagnostic codes.
- However, NPEs are often under-documented in structured EMR.
- Thus, to mitigate these limitations, we leveraged **structured EMR as well as unstructured clinical notes** to assess the risk of NPEs in LTRA compared to inhaled corticosteroids (ICS).

METHODS

Data Source

- We used the EMR database of the Severance Hospital, which contains information about more than 7 million patients in South Korea.
- Both structured EMR data converted to OMOP-CDM as well as the unstructured text of clinical notes were collected.

Study Population

- Patients aged 5-18 years who were first prescribed LTRA or ICS due to asthma were included in this study.

Outcomes

- The primary outcome was the **1-year risk of newly-developed NPEs** (composite of psychotic, mood, anxiety, sleep-related, cognitive, movement, and personality disorders indicated in the LTRA label).
- In **structured EMR**, NPEs were identified using **diagnostic codes**.
- To define NPEs using **narrative clinical notes**, we developed a **BERT-based model** to detect the occurrence of NPEs documented in the patients' clinical notes.

We identified neuropsychiatric events in unstructured EMR using deep-learning algorithms as well as in structured EMR

The risk of neuropsychiatric events among child asthma was not higher in LTRA compared with ICS

	LTRA		ICS		HR (95% CI)
	Patients	Events	Patients	Events	
1-year risk					
By diagnostic codes	2,486	37	2,167	45	0.62 (0.36 – 1.06)
By clinical notes	2,304	117	2,009	103	0.88 (0.64 – 1.20)

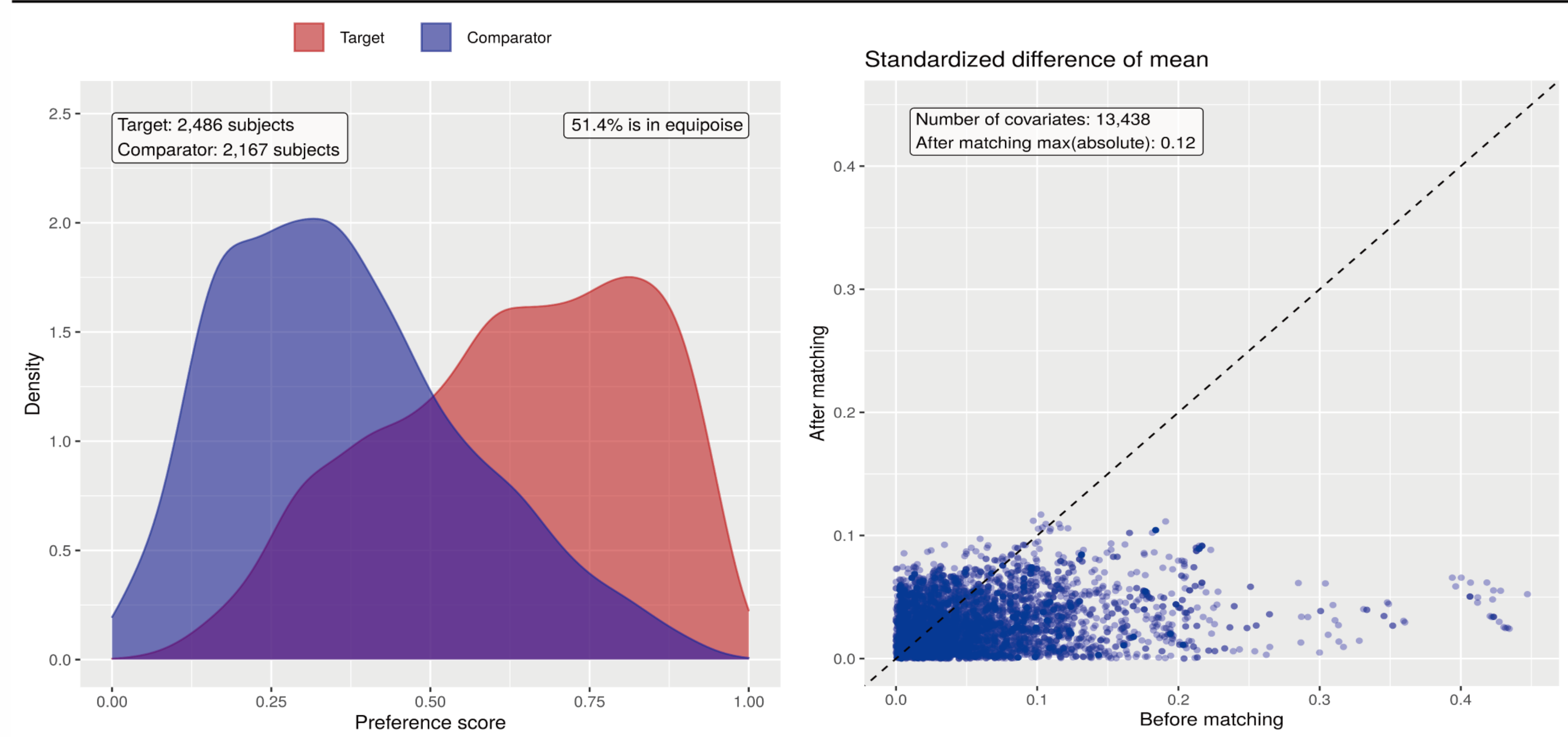


Figure 1. 1-year risk of neuropsychiatric events in LTRA compared with ICS, preference score distribution and covariate balance plot before and after PS stratification

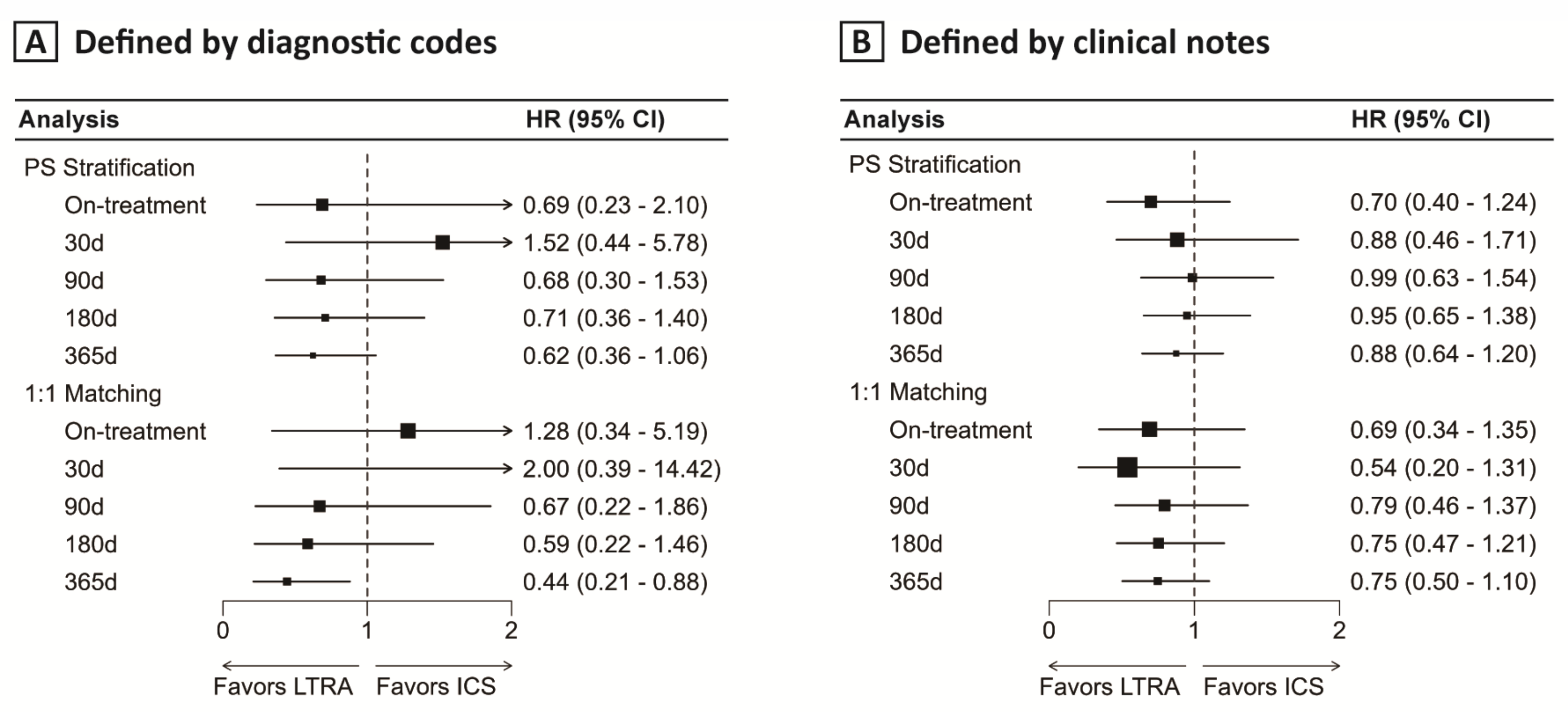


Figure 2. Sensitivity analyses for risk of neuropsychiatric events associated with LTRA and ICS

Statistical Analysis

- We used Cox proportional hazard regression models to estimate the association of exposure with outcomes after the propensity score (PS) stratification.

Sensitivity Analyses

- Sensitivity analyses were conducted using different definitions of the time-at-risk window, and the statistical analysis.
- We set 4 more time-at-risk windows and 1 additional PS adjustment.

RESULTS

- A total of 2,486 users of LTRA and 2,167 users of ICS were included.
- The preference score distribution of study drugs and covariate balance plot before and after propensity score stratification were shown in Figure 1.
- 82 NPEs were identified using diagnostics codes, whereas the deep-learning model captured 220 events using narrative clinical notes.
- Across various risk windows, statistical analyses, and outcome definitions, the risk of NPEs in LTRA was not higher than ICS (Figure 2).

CONCLUSION

- Among children with asthma, the risk of NPEs was not increased in LTRA compared with ICS.
- This finding was consistent across sensitivity analyses.

FUNDING

- This research was supported by a grant (22213MFDS486) from Ministry of Food and Drug Safety in 2022.

Subin Kim^{1,2}, Chang Hoon Han³, Jaehyeong Cho^{1,2}, Kyung Won Kim^{2,3}, Seng Chan You^{1,2}

¹Dept. of Biomedical Systems Informatics, Yonsei University College of Medicine, Seoul, Korea
²Institute for Innovation in Digital Health Care, Yonsei University
³Dept. of Pediatrics, Yonsei University College of Medicine, Seoul, Korea

