Using Drug Package Insert Data to Identify Statin-related Prescribing Cascades: An Evaluation of Findings from Side Effect Resource (SIDER) and Commercial Claims Data

Priyanka J. Kulkarni, Earl J. Morris, Marta Walsh, Stephan Schmidt, Carl J. Pepine, Scott M. Vouri, Steven M. Smith
University of Florida College of Pharmacy, Gainesville, FL

UF Center for Integrative Cardiovascular and Metabolic Disease
UNIVERSITY of FLORIDA

EPH2

Introduction

- Statin-induced adverse events (AEs) may prompt additional pharmacotherapy resulting in prescribing cascades (PCs)
- We previously performed untargeted prescribing cascade signal detection using high throughput sequence symmetry analysis (HTSSA), identifying 160 statin-related PC signals (57 plausibly true PCs after expert review)
- However, HTSSA is computationally complex, and false positive signals are common
- Herein, we evaluated whether a targeted approach – informed by the Side Effect Resource (SIDER), a public database containing pharmaceutical package inserts data – captures similar findings more efficiently

Methods

- The SIDER database contains medication names, classified by Anatomical Therapeutic Chemical level 4 (ATC_4) codes, as well as AEs and indications of medications classified by Medical Dictionary for Regulatory Activities (MeDRA) codes, all collated from publicly available drug labelling
- We identified all MedDRA codes representing statin-related AEs from SIDER; for each MedDRA code, we identified all ATC_4 codes for which the MedDRA code was an indication (see **Figure 1** for an example)
- MeDRA codes were then dropped, leaving 'statin—other medication class' potential prescribing cascade signals.
- These signals were compared to empirically-derived signals from claims-based HTSSA (gold standard) to calculate sensitivity and specificity for SIDER signal detection

Conclusion

- SIDER predicted plausibly true statin-related PCs that were empirically identified (and expert-reviewed) from HTSSA, with low specificity (31.5%) but high sensitivity (80.7%)
- However, 18% (n=79) of predicted signals were clinically implausible PCs or likely attributable to disease progression or therapeutic escalation
- Although SIDER proved to be useful in identifying statin-related prescribing cascade signals, it is unlikely to be suitable as an efficient stand-alone tool due to its low specificity and clinically implausible signals

Table 1: Signal comparison between HTSSA and SIDER

		Claims-Based HTSSA (Gold standard)	
		Positive Signal	No Signal
SIDER	Positive Signal	125	251
	No Signal	35	128

Table 2: Comparison between plausible prescribing cascades detected by HTSSA and SIDER

		Claims-Based HTSSA (Gold standard)	
		Positive Signal	No Signal
SIDER	Positive Signal	46	330
	No Signal	11	152

Figure 1: Example of SIDER linkage to identify statin-related prescribing cascade signals

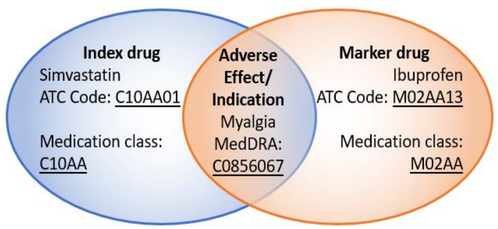
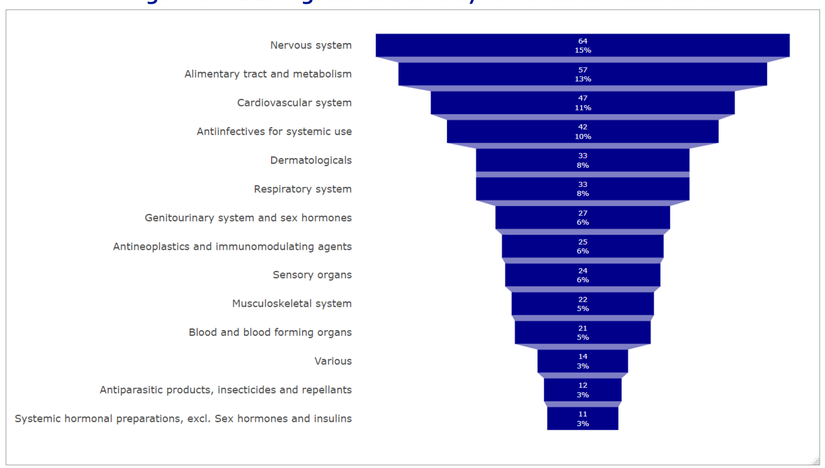


Figure 2: SIDER signals classified by ATC 1 marker class levels



Results

- We detected 432 potential signals using SIDER, compared to 160 empirically-identified signals using HTSSA screening, with a sensitivity of 78.1% (125 of 160 positive signals) and specificity of 33.8% (128 of 379 non-signals)
- To assess predictive ability of SIDER, signals were screened to capture the 57 plausibly true PCs which were empirically derived from HTSSA and reviewed by clinical experts
- Of these, 46 were predicted using SIDER with a sensitivity of 80.7% and specificity of 31.5%
- Conversely, SIDER predicted 79 signals that represented therapeutic escalation, disease progression or clinically implausible prescribing cascades for statins

Limitations and Discussion

- SIDER was last updated in 2015 and, thus, does not capture newer drug classes, recently discovered AEs, or recently-approved indications, reducing its ongoing utility in detecting prescribing cascade signals
- Our overall findings suggest that when combined with clinical expert review, medication package inserts could potentially prove to be a valuable resource to identify statin-related PCs if they are collated using ATC and MeDRA codes
- More updated data resources like U.S. FDALabel could prove to be a useful alternative but require further processing (e.g., with natural language processing) for use in cases such as this

Disclosures and Acknowledgements
This work was funded by the UF COP PROSPER program (Vouri/Smith MPIs)

Contact: priyanka.kulkarn@ufl.edu