Machine learning to predict safety signals using molecular similarity and disproportionate reporting rates

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Background

Disproportionality analysis, a way to quantify unexpectedness, is the standard approach in statistical signal detection. To improve signal detection, information can be leveraged from similar drugs. By using safety profiles of chemically similar drugs, the aim is to find signals earlier as chemical similarity gives additional support resulting in less case safety reports being required to detect signals. Furthermore, leveraging chemical similarity may propose a mechanism of action for the suspected adverse event.

Data

864 comparison drugs were chosen applying in- and exclusion criteria, such as molecular size, chemical information availability, and presence in VigiBase.

864 comparison drugs

317 test drugs are a subset with a label change

2177 adverse events

Methods

Chemical similarity between test and comparison drugs

Disproportionality of test drug and adverse event

Presence of the adverse event in the **label of the comparison drug**

Random forest machine learning model uses these features to make a prediction whether test drug and adverse event are a label change

Yes

No

Results

To find the best configuration of features, four experiments with different subsets of the features were performed.

	Methods	F1	Precision	Recall
Baseline: no random forest, only disproportionality feature over fixed threshold		0.41	**0.84**	0.26
Random forest with chemical similarity and comparator label information		0.66	0.66	0.68
Random forest with disproportionality feature		0.64	0.64	0.66
Random forest with all features		**0.74**	0.72	**0.76**

Conclusion

Best performances are achieved when chemical information and disproportionality are used together, showing that chemical information could support timely signal detection.

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