

# Data-driven identification of adverse event reporting patterns for Japan in the WHO global database

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## Background

Adverse event reporting patterns vary between countries, given differences in reporting culture, clinical practice and underlying patient populations. Japan collects over 50,000 domestic adverse event reports yearly and shares serious reports with VigiBase, the WHO global database of individual case safety reports. Understanding these reports in the global context could be helpful for regulators worldwide and aid hypothesis-generation for Japanese-specific vulnerabilities to adverse drug reactions.

## Objectives

To explore differences in the reporting of adverse events between Japan and other countries contributing to VigiBase.

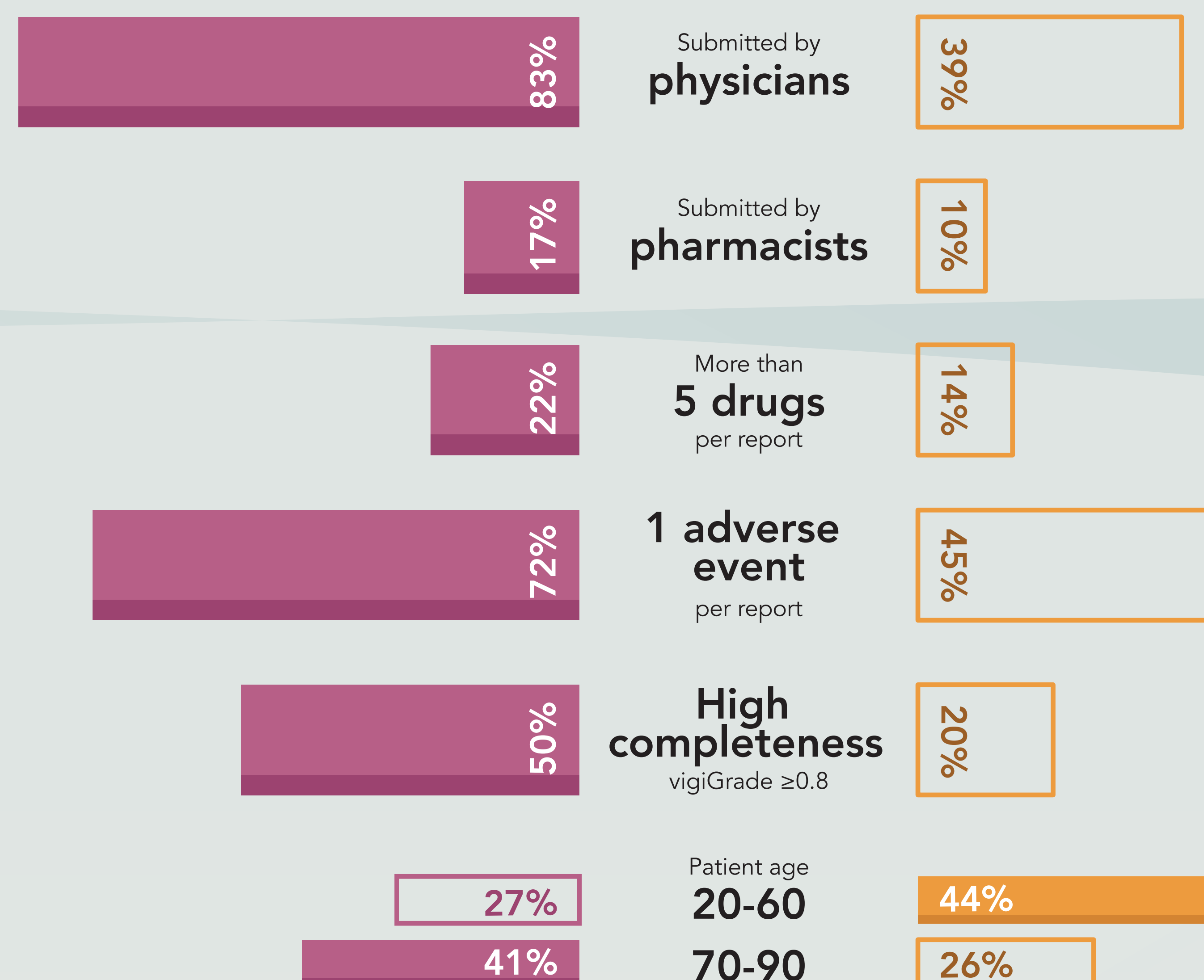
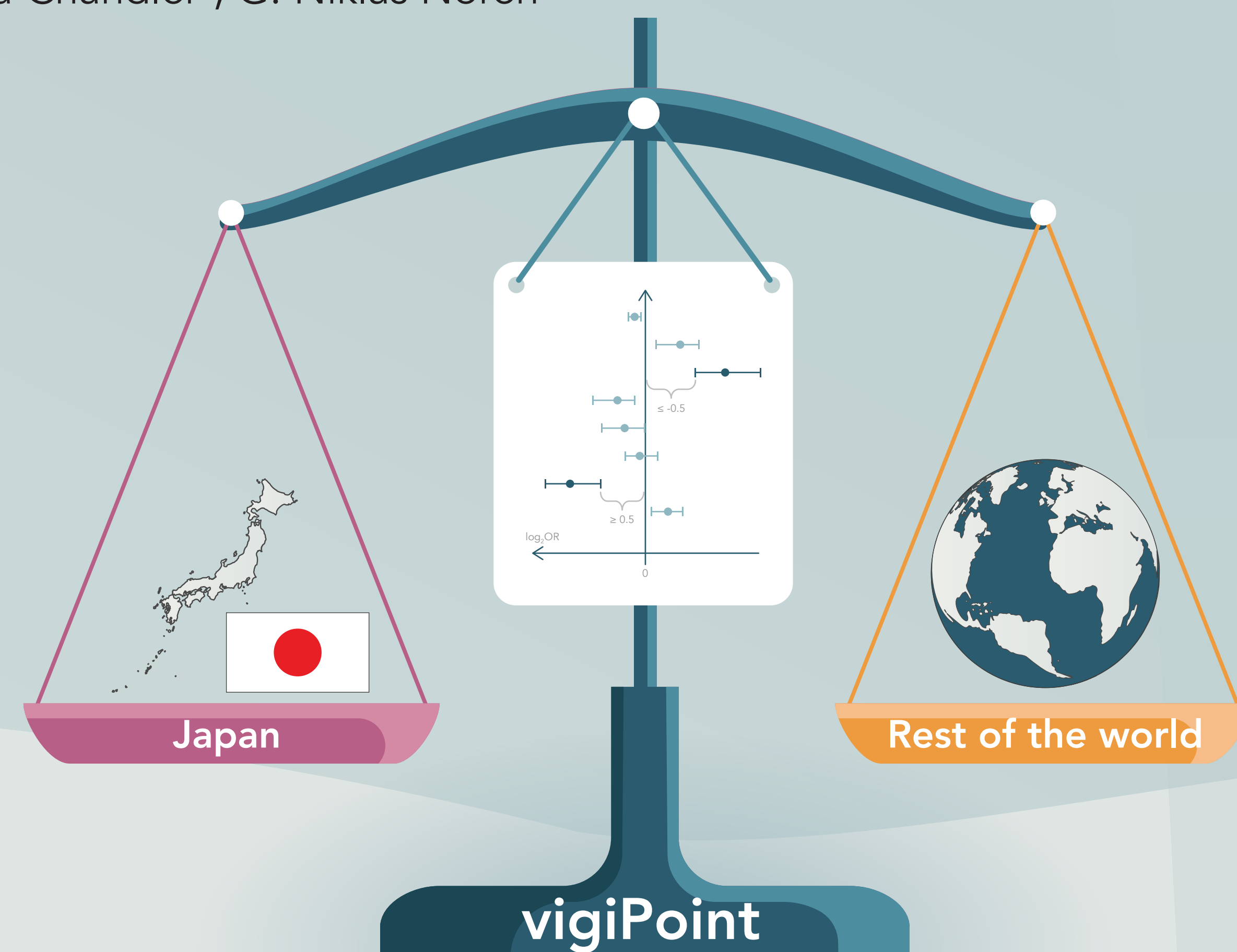
## Methods

**vigiPoint** is a method for data-driven exploration in pharmacovigilance. It outlines data subsets, pinpoints key features and facilitates expert review, using odds ratios subjected to statistical shrinkage to distinguish one data subset from another. Here, we compared 260,000 Japanese reports in VigiBase to 2.5 million reports from the rest of the world (RoW; of which 51% from US). This included reports in E2B format classified as serious and received between 2013 and 2018. Reporting patterns for which the 99% credibility interval of a shrunk log-odds ratios were above 0.5 or below -0.5 were flagged as key features. The shrinkage was set to the **vigiPoint** default (1% of the Japanese data subset).

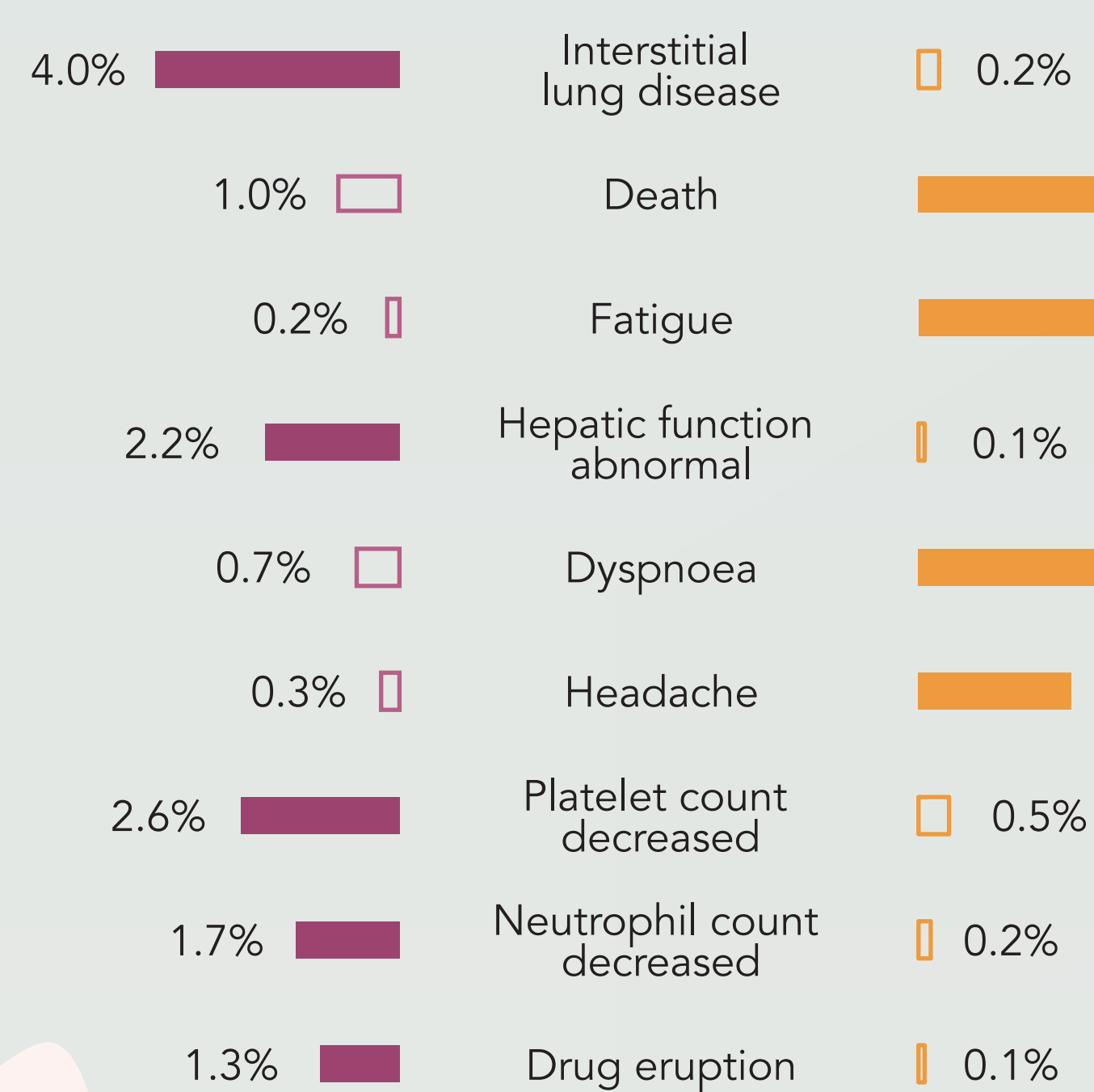
## Results

There were higher reporting rates in Japan from physicians (83% vs 39%) and pharmacists (17% vs 10%). It was also more common to see reports with more than five drugs per report (22% vs 14%) and reports with a single adverse event (72% vs 45%). More than half of the Japanese reports had a **vigiGrade** completeness score above 0.8 compared to about 1 in 5 in RoW. There were more reports than expected for patients aged 70-90 years and fewer reports for adults aged 20-60 years.

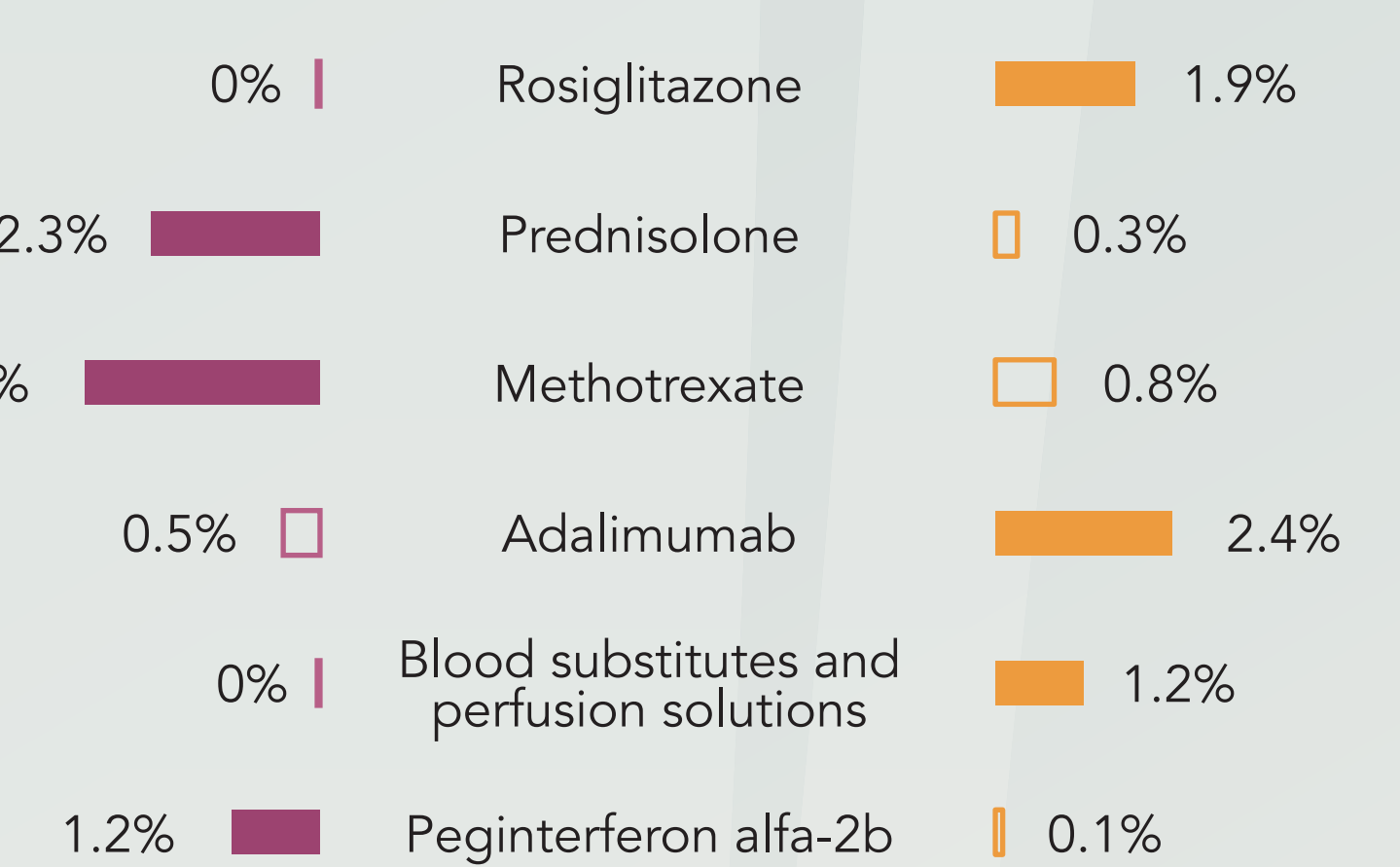
Adverse events reported more often in Japan included interstitial lung disease, hepatic function abnormal, platelet count decreased, neutrophil count decreased and drug eruption. Adverse events reported less often included death, fatigue, dyspnoea, fatigue and headache. Drugs reported more often in Japan included prednisolone, methotrexate and peginterferon alfa-2b. Drugs reported less often included rosiglitazone, adalimumab as well as blood substitutes and perfusion solutions.



## Adverse events



## Drugs



## Conclusions

Analysis of Japanese adverse events reports in global context has revealed key features that may reflect possible pharmaco-ethnic vulnerabilities in the Japanese, as well as differences in adverse events reporting and clinical practice. This knowledge is essential in the global collaboration of signal detection afforded by the WHO Programme for International Drug Monitoring.