Data-driven identification of adverse event reporting patterns for Japan in VigiBase and follow-up analysis in JADER

Office of Research Promotion
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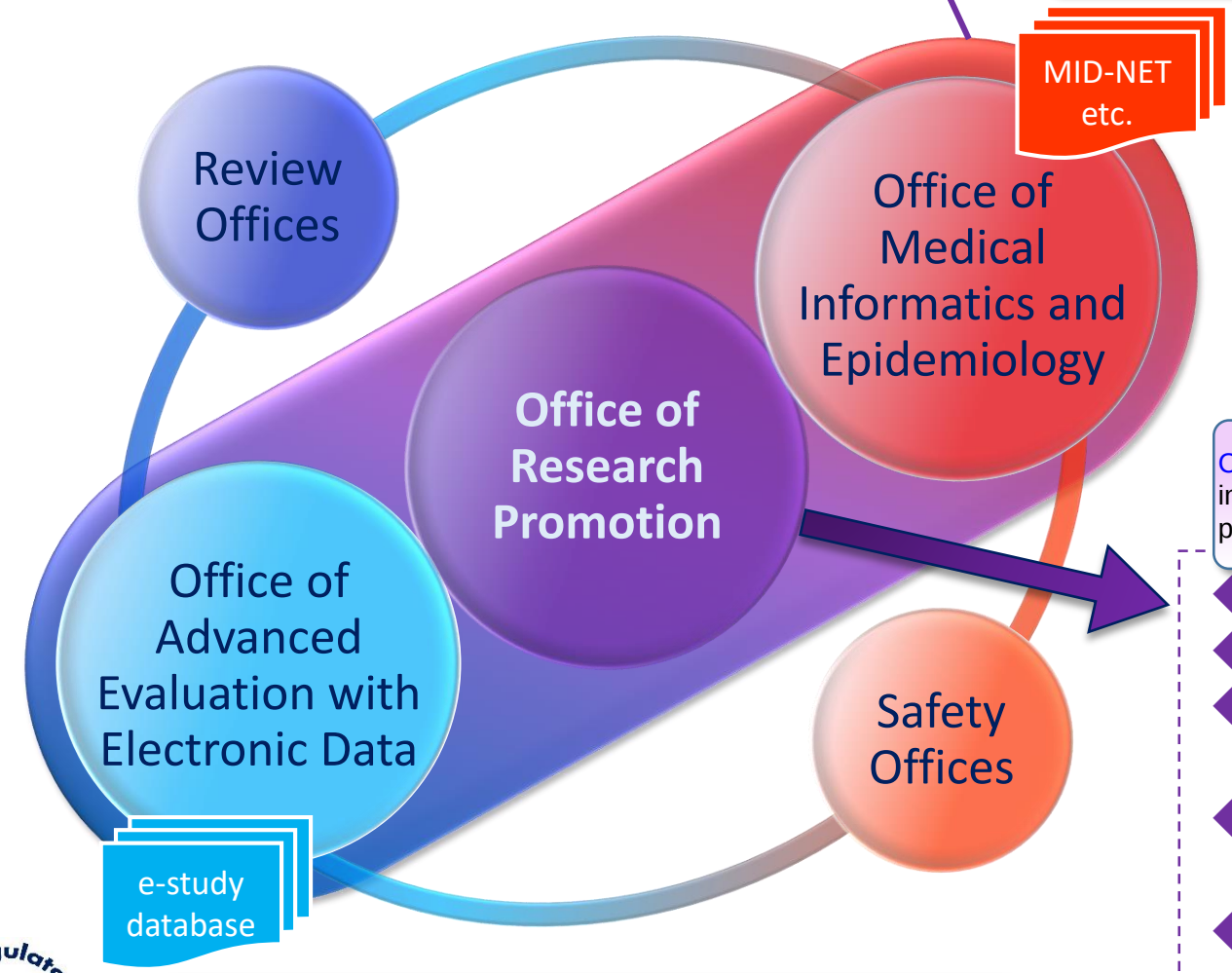
Disclaimer

The views and opinions expressed in this presentation are those of the speaker and are not necessarily those of the PMDA.
The speaker has no conflicts of interest to declare.

Center for Regulatory Science

Utilization of EMR database for pharmaco-epidemiological analysis (PEpi-study, cross-product analysis for better benefit/risk assessment)
-Implemented in 2016

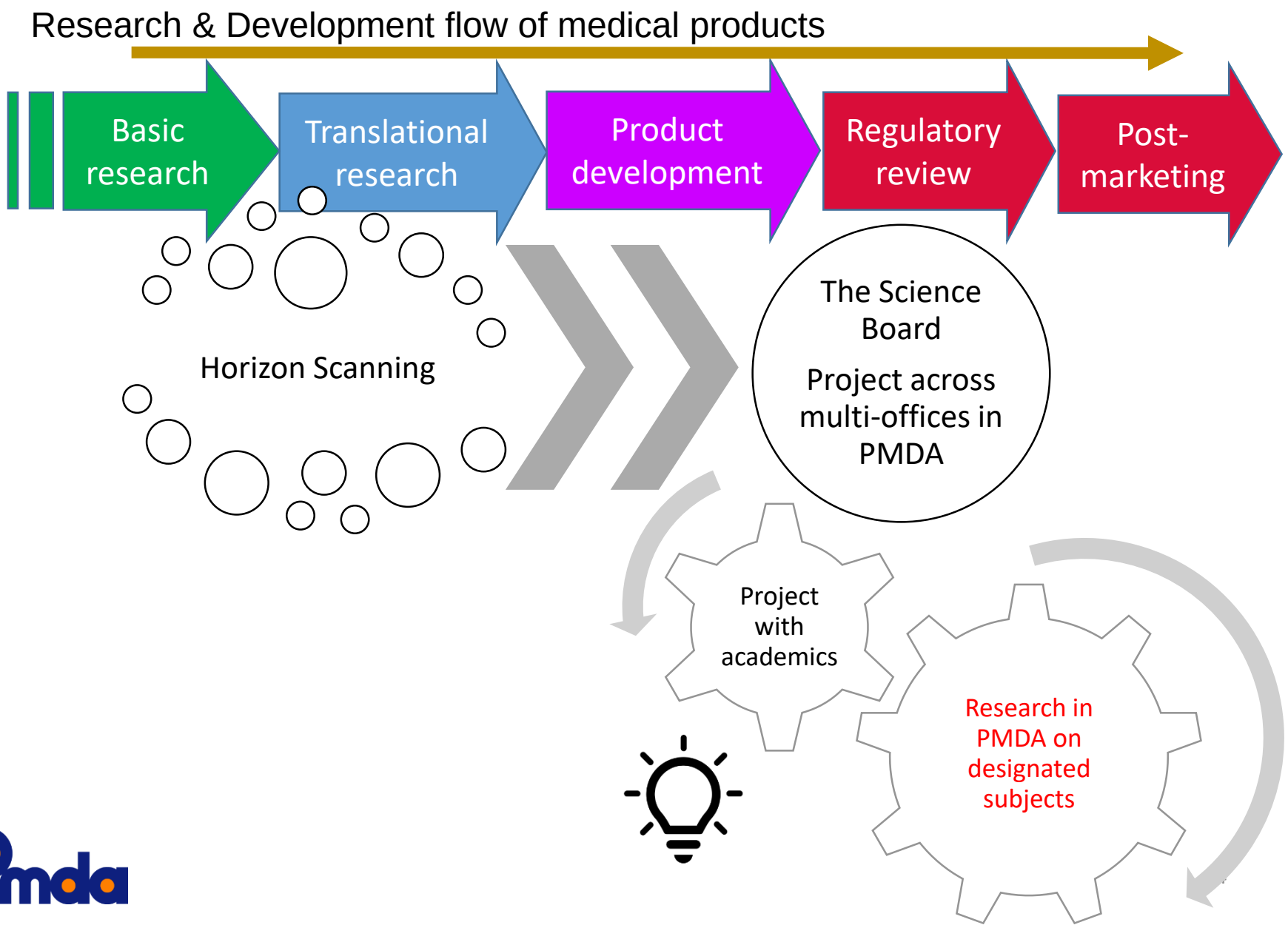


Coordination and project management in regulatory science research and publishing guidelines

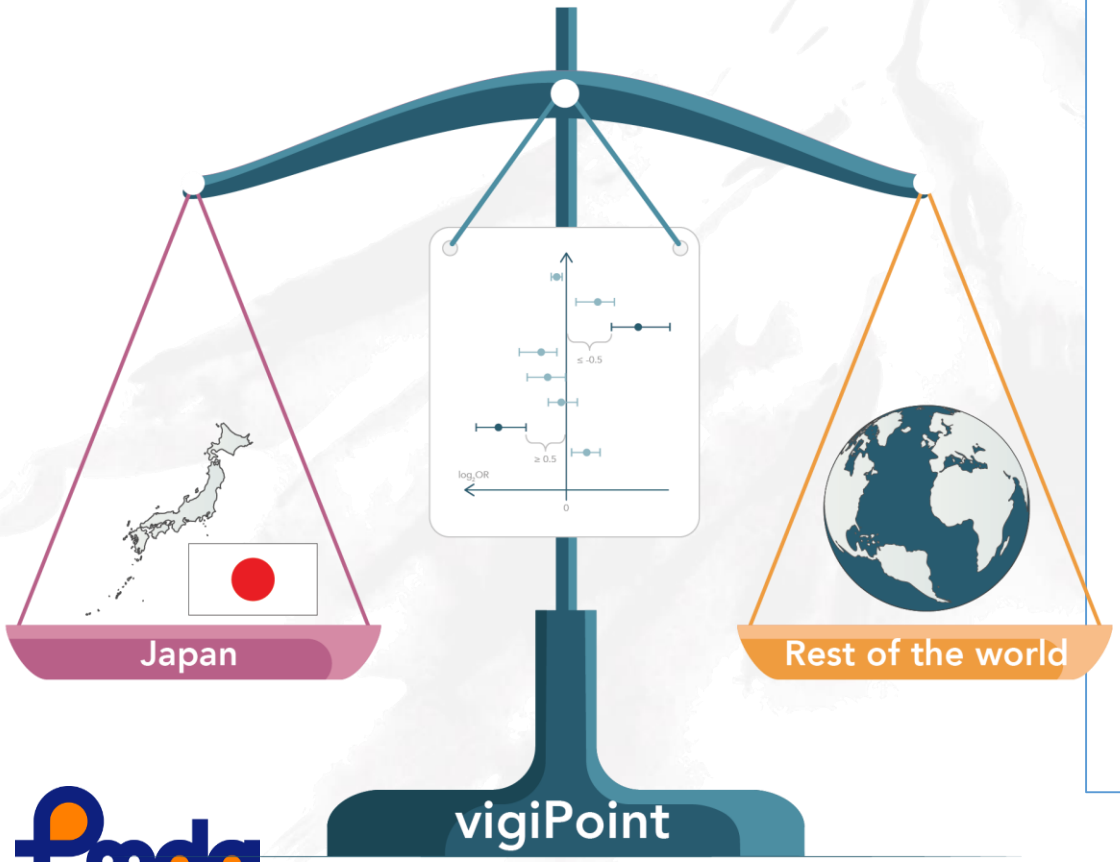
- Horizon Scanning
- The Science Board
- Collaborative projects across multi-officers
- Collaboration with academic organizations
- Research promotion and management

Utilization of clinical trial data on CDISC database (modeling & simulation, cross-product analysis for better benefit/risk assessment)
-CDISC data has been submitted by MAHs since October 2016

Regulatory Science Activities at PMDA



Key features of Japanese case reports



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ORIGINAL RESEARCH ARTICLE

Data-Driven Identification of Adverse Event Reporting Patterns for Japan in VigiBase, the WHO Global Database of Individual Case Safety Reports

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Abstract

Introduction Adverse event reporting patterns vary between countries, reflecting differences in reporting culture, clinical practice and underlying patient populations. Japan collects about 60,000 domestic adverse event reports yearly and shares serious reports with the World Health Organization (WHO) Programme for International Drug Monitoring in VigiBase, the WHO global database of individual case safety reports. Understanding these reports in the global context can be helpful for regulators worldwide and can aid hypothesis-generation for Japanese-specific vulnerabilities to adverse drug reactions.

Objective The objective of this study was to explore differences in the reporting of adverse events between Japan and other countries.

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 E2B format classified as serious and received in VigiBase between 2013 and 2018 with 2.5 million reports from the rest of the world (of which 51% are from the USA). Reporting patterns for which the 99% credibility interval of the 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 corresponding to 1% of the size of the Japanese data subset. As a sensitivity analysis, additional vigiPoint comparisons were performed between Japan and, in turn, Africa, the Americas, the Americas except the USA and Canada, Asia and Europe.

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 with a single adverse event (72% vs. 45%). More than half of the Japanese reports had a vigiGrade completeness score above 0.8 compared with about one in five from the rest of the world. There were more reports than expected for patients aged 70–89 years and fewer reports for adults aged 20–59 years. Adverse events reported more often in Japan included interstitial lung disease, abnormal hepatic function, decreased platelet count, decreased neutrophil count and drug eruption. Adverse events reported less often included death, fatigue, dyspnoea, pain and headache. Drugs reported more often in Japan included prednisolone, methotrexate and peginterferon alfa-2b. Drugs reported less often included rosiglitazone and adalimumab as well as blood substitutes and perfusion solutions. The findings were generally robust to the sensitivity analysis except for the less often reported drugs, many of which were rarely reported in most countries, except in the USA.

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

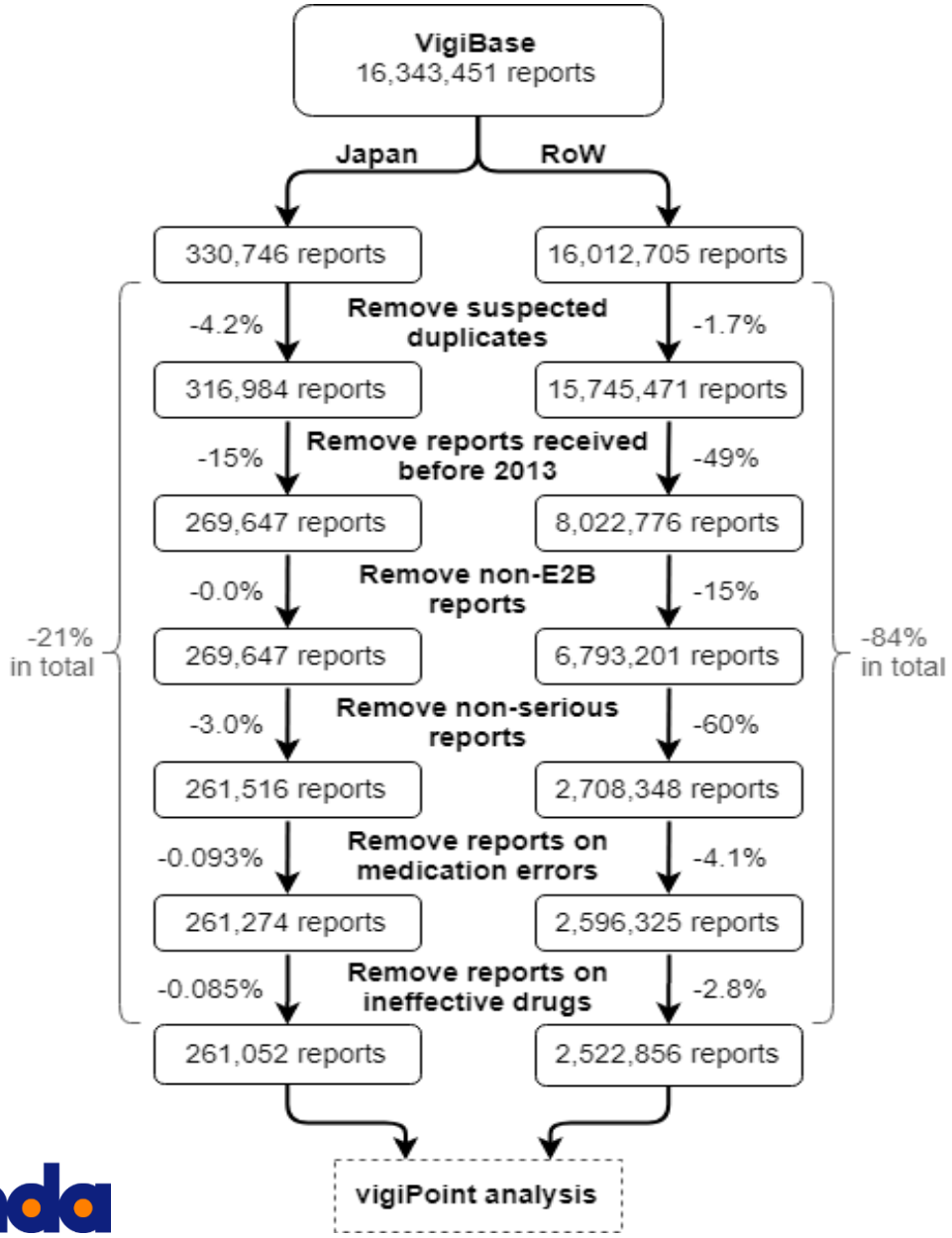
Electronic supplementary material The online version of this article (https://doi.org/10.1007/s40264-019-00861-y) contains supplementary material, which is available to authorized users.

Extended author information available on the last page of the article

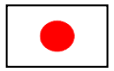
1 Background

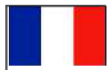
Japan joined the World Health Organization (WHO) Programme for International Drug Monitoring in 1972. At the time, it was one of only 14 member countries and the

Key features of Japanese case reports




1,286,362 (51%)


261,052 (9.4%)

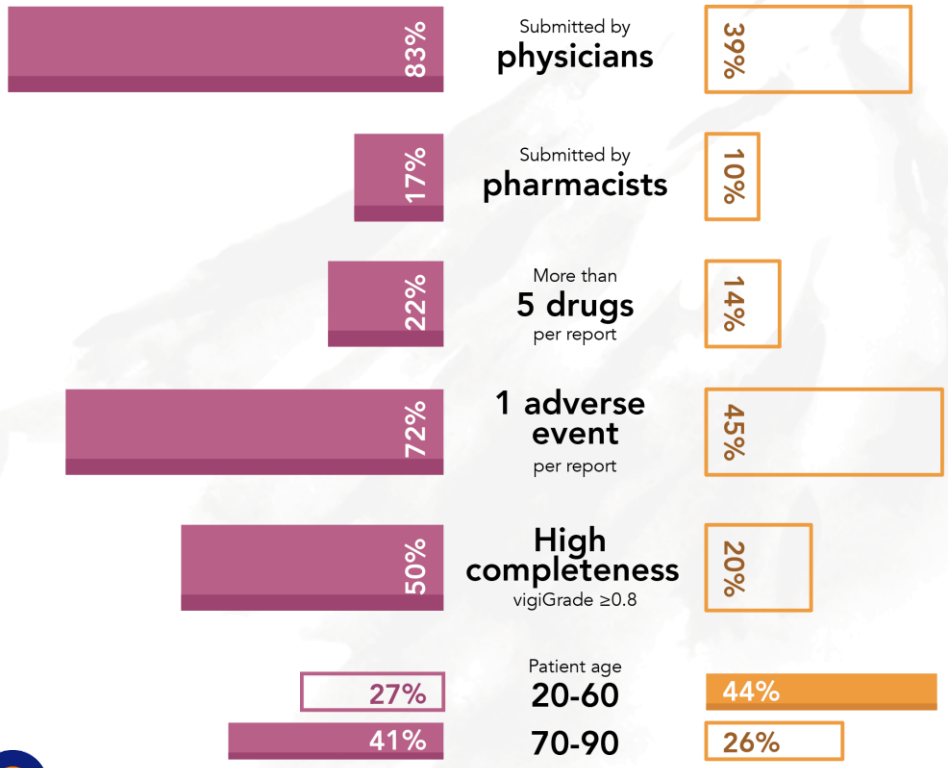

222,498 (8.8%)


152,577 (6.0%)

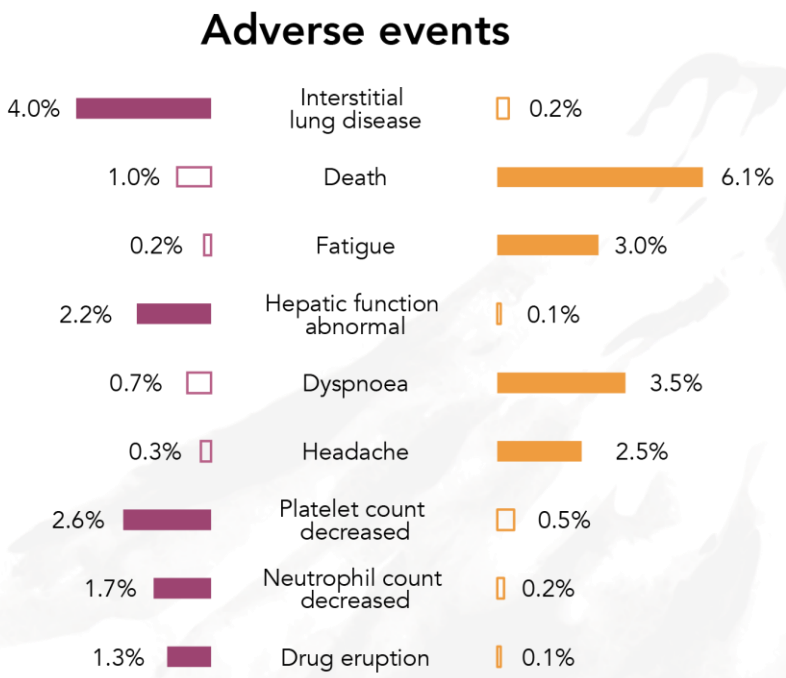

141,781 (5.6%)

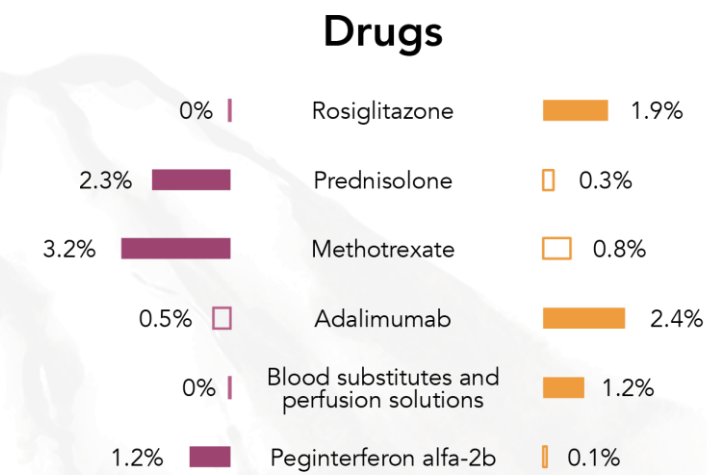

137,980 (5.5%)

Key features of Japanese case reports



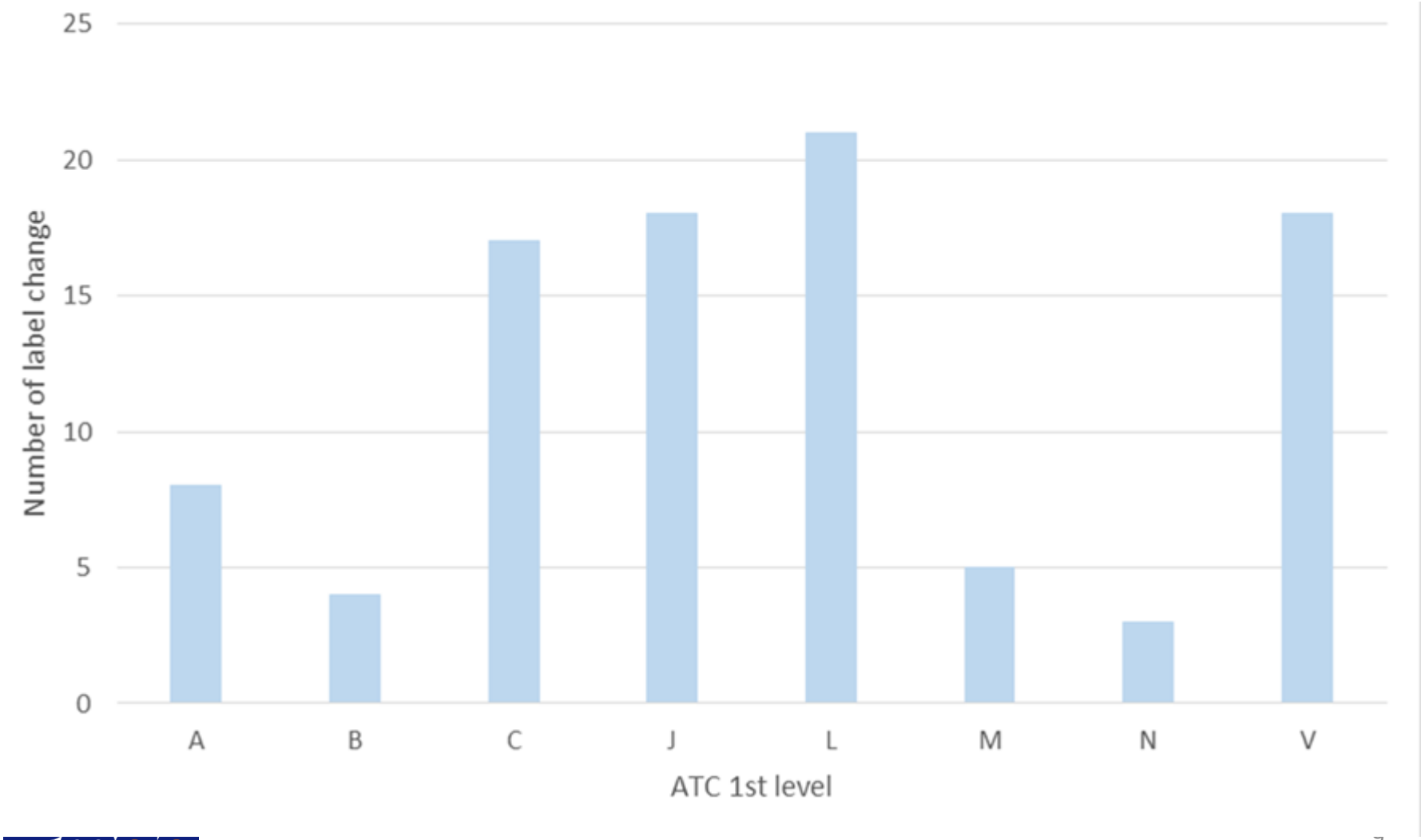
Key features of Japanese case reports





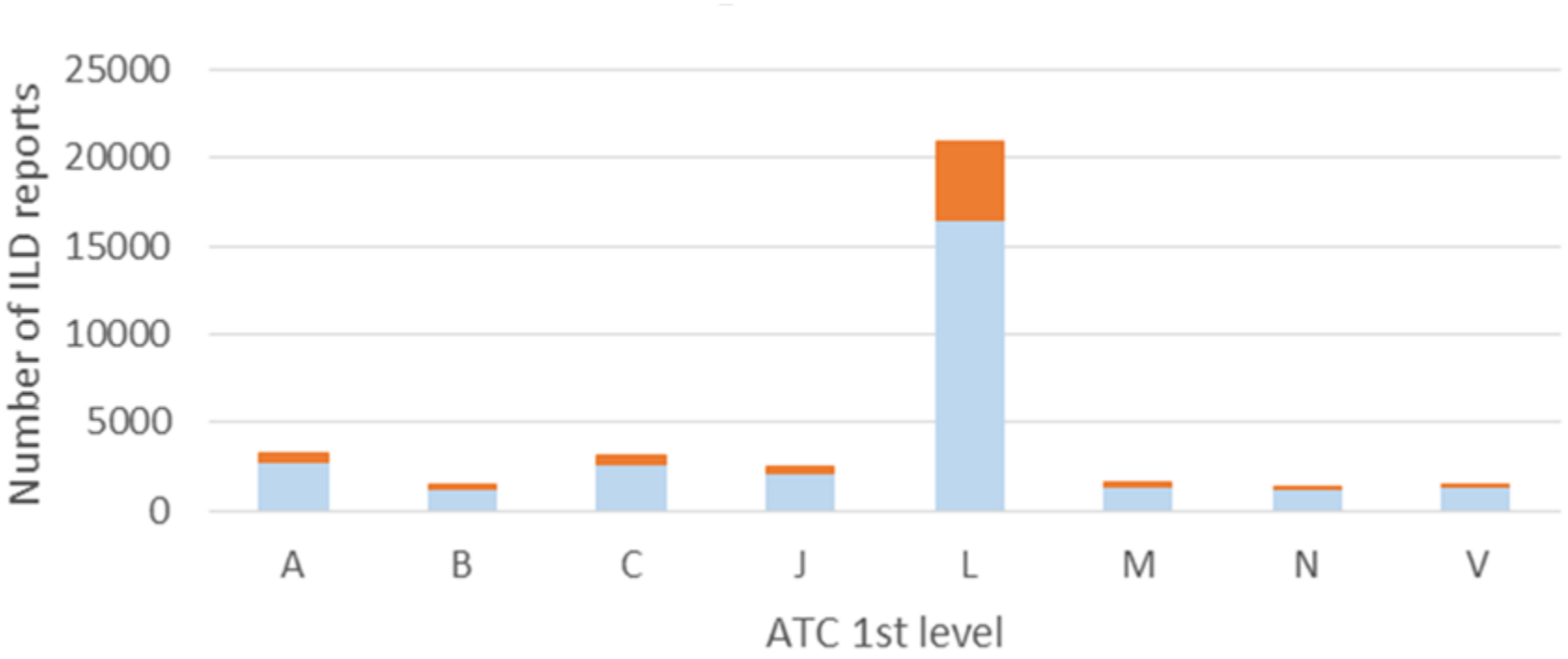
Analysis in JADER

Post-marketing safety label change for interstitial lung disease classified by suspected drugs ATC classification system level1



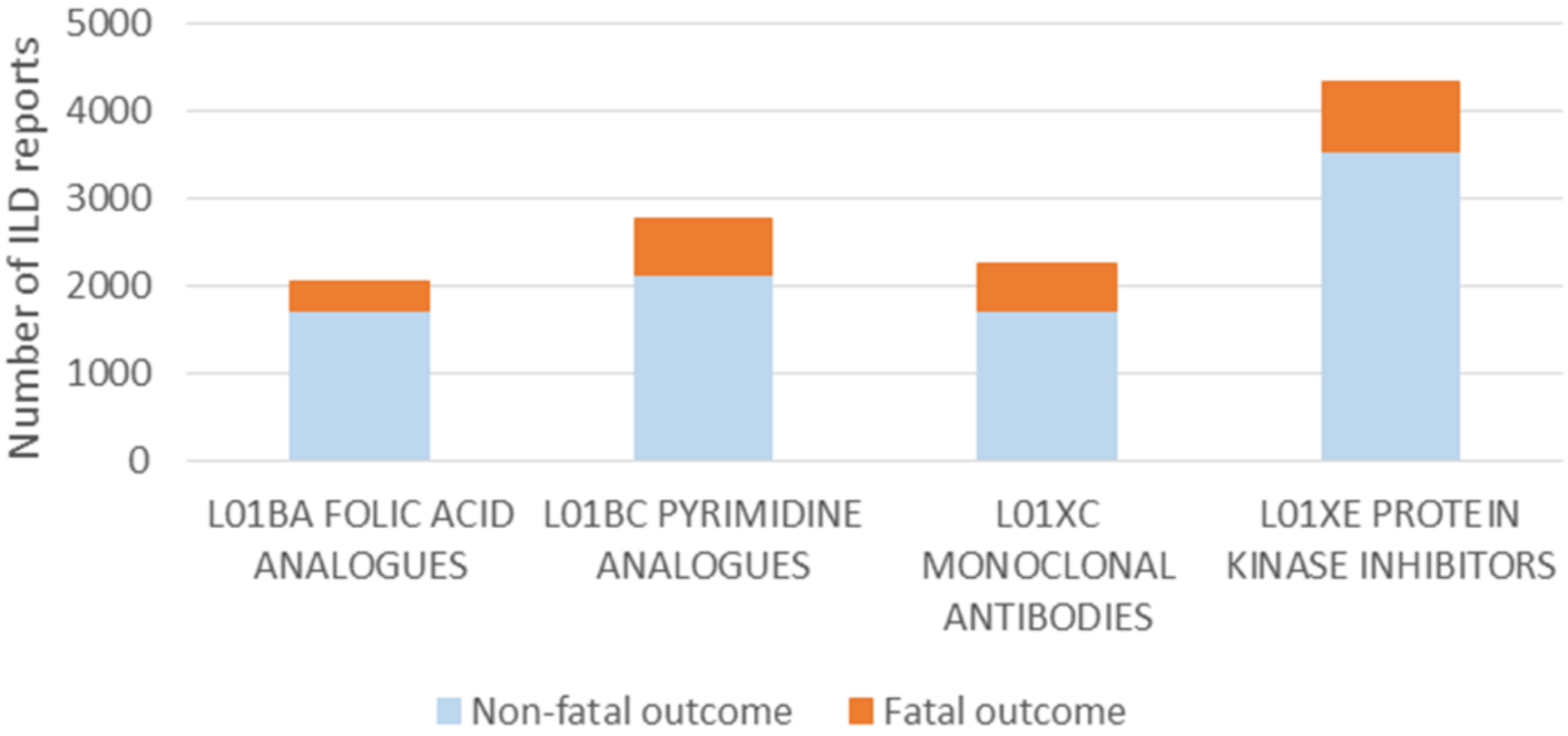
Analysis in JADER

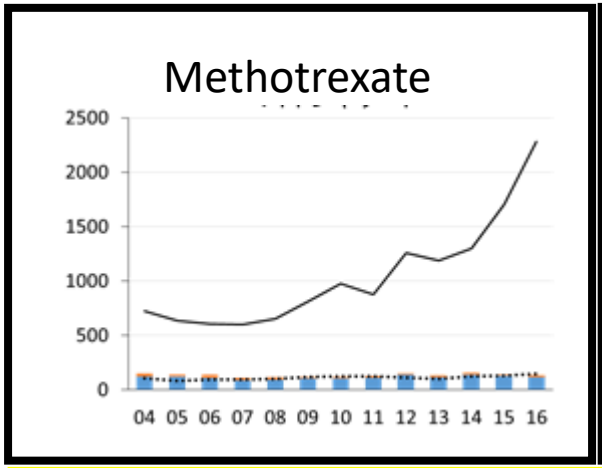
Interstitial lung disease reports in the drug classes

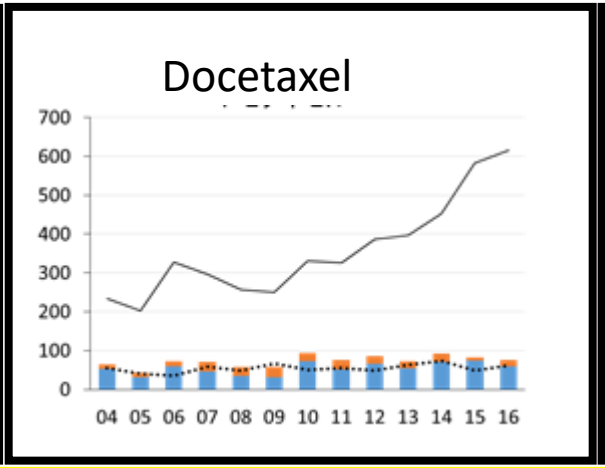


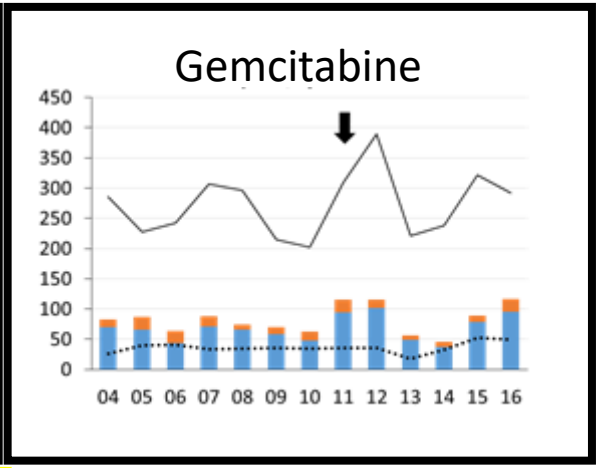
Analysis in JADER

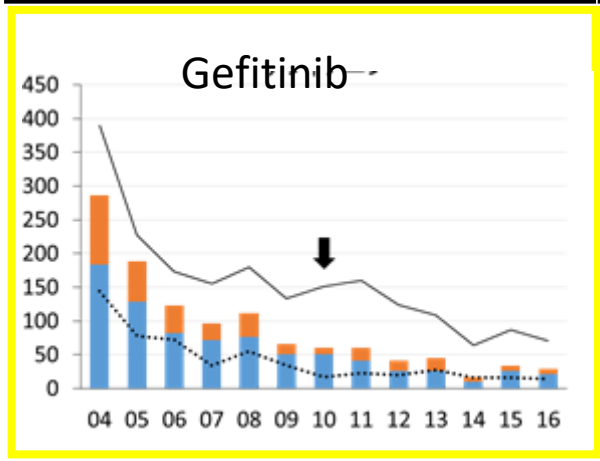
Most frequently reported, four suspected drug groups in ATC classification system level 4 of interstitial lung disease reports

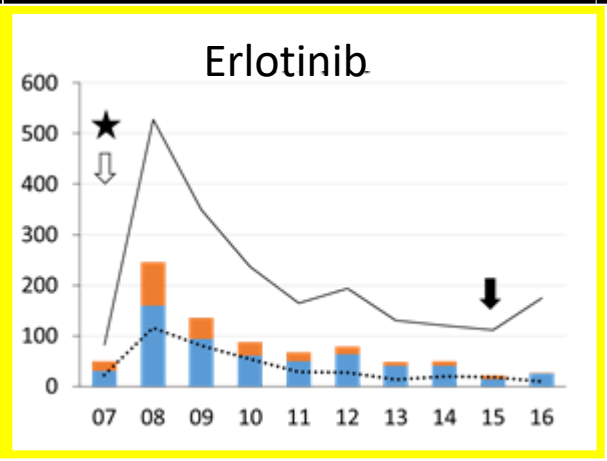


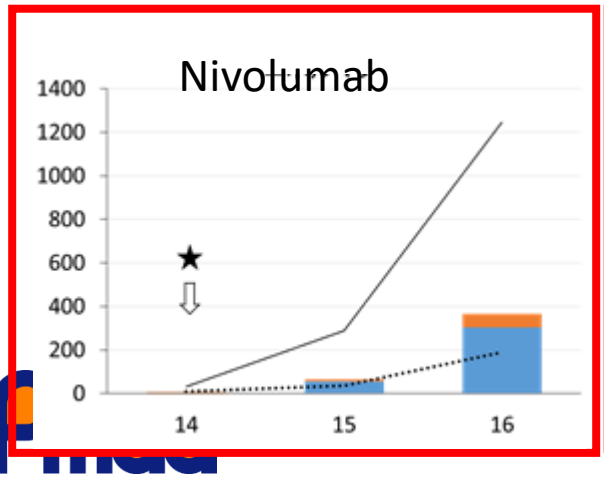


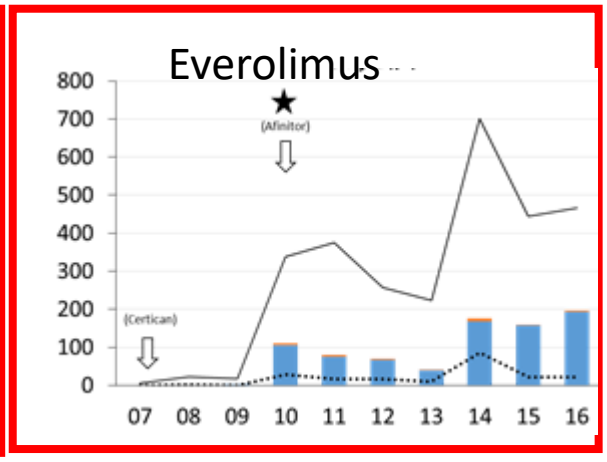












ILD fatal

ILD non-fatal

All reports non-fatal

All reports fatal

Re-examination started

The latest re-examination period expired

Set ILD as safety priority item

Frequency of ILD reporting
The horizontal axis: fiscal years

Summary

- Analysis of Japanese adverse event reporting patterns in a global context has revealed key features that may reflect possible pharmaco-ethnic vulnerabilities in the Japanese, as well as differences in adverse event reporting and clinical practice.
- Adverse events reported more often in Japan included interstitial lung disease, abnormal hepatic function, decreased platelet count, decreased neutrophil count and drug eruption.
- More reports from Japan had high completeness, were submitted by physicians and included a single adverseevent term
- The high rates of interstitial lung disease reporting derived from mainly the anatomical therapeutic chemicalclassification group L drugs.
- The regulatory system for those drugs may explain the high rates of interstitial lung disease reporting.
- In particular, the impact of solicited reports from useresults survey is found.