VigiBase, Global ADR reporting and signal detection

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Pharmacovigilance in Eritrea

Drug Saf (2016) 39:763–768
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ORIGINAL RESEARCH ARTICLE

Artesunate/Amodiaquine-Induced Acute Extrapyramidal Reactions in Children and Younger Adults: Case Series Assessment

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Abstract

Introduction Several studies conducted in African countries reported the artesunate and amodiaquine (AS/AQ) tablet as a safe and well-tolerated anti-malarial drug in children and younger adults. The aim of this case series assessment was to assess the causal relationship between the AS/AQ tablet and extrapyramidal reactions in children and younger adults and to investigate the factor(s) predisposing to the adverse drug reactions.

Methods The causal relationship of all the cases was first assessed individually using the Naranjo Probability Scale and then subjected to a case series assessment using Austin Bradford–Hill criteria.

Results A total of 43 acute extrapyramidal reactions associated with the AS/AQ tablet were reported between 2012 and 16 November, 2015 to the Eritrean Pharmacovigilance Centre. The causality was found to be probable or highly probable for 33 (76.7 %) of the cases and the rest (10; 23.3 %) of the cases had a possible causal association. The extrapyramidal reactions had more or less similar clinical features in most of the cases and were characterized by abnormal involuntary contractions of muscles. The median age and body weight of the cases were 15 years and 40 kg, respectively, and 70 % of them were males. 90.7% of the reactions manifested in children and younger adults (aged <26 years). In most of the cases, reactions manifested in the third day from the start of treatment and 88.3 % of cases were hospitalized.

Conclusion The causal relationship between the AS/AQ tablet and extrapyramidal reactions in children and younger adults was found to be apparent and possibly owing to dose accumulation or an overdose of amodiaquine.

Key Points

The association of artesunate/amodiaquine (AS/AQ) and extrapyramidal reactions is not documented in the

Electronic supplementary material The online version of this

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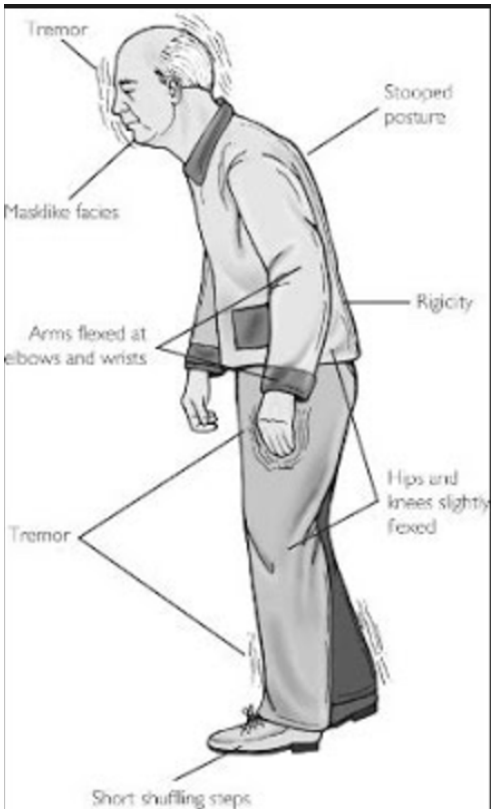
Artesunate;Amodiaquine for Malaria

Patients experienced:

involuntary muscle contractions in the neck, jaw, tongue, lips, extremities. Body stiffness, drowsiness, slurred speech, deviated gaze.



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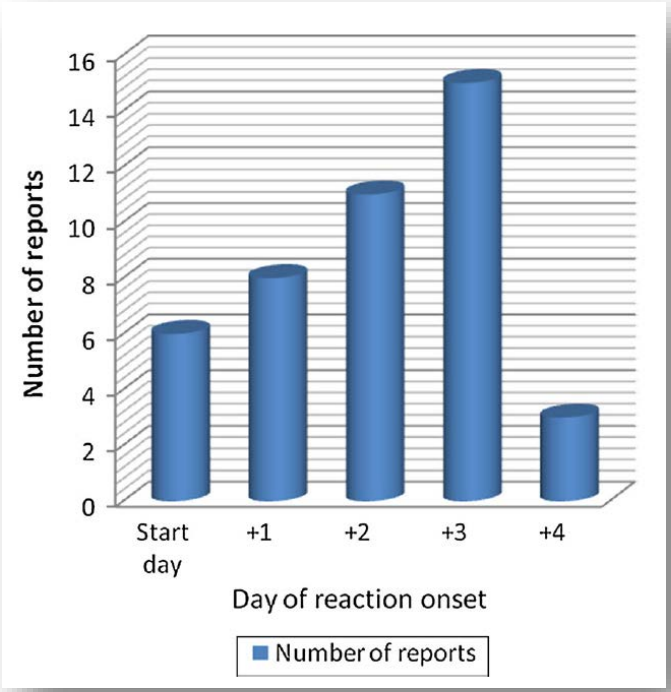
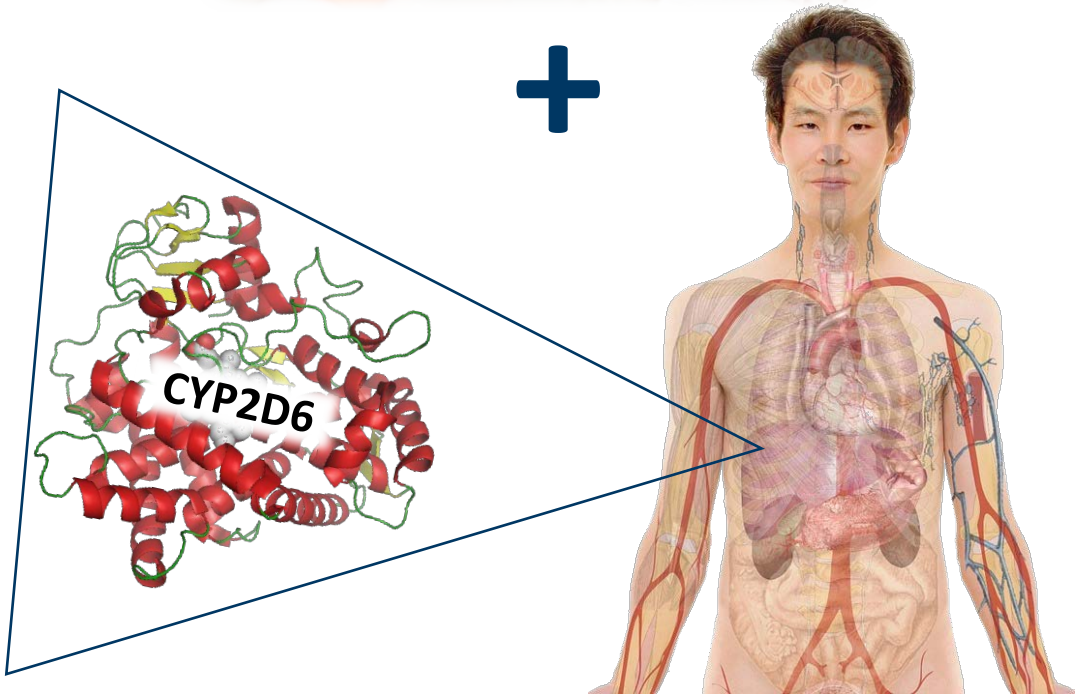
Artesunate;Amodiaquine



Why?



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Agenda

UMC intro

VigBase

Signal detection

Drug identification on ICSRs

Global exchange of drug data for ICSRs

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Uppsala Monitoring Centre (UMC) - a non-profit foundation

World Health Organization

WHO Programme for International Drug Monitoring

- Custodian for VigiBase
- PV training
- PV tools

- Signal detection
- PV research focusing on novel methodologies for data mining in large data sets
- Communication of potential safety issues

WHODrug

- Publishing and Maintenance organization
- Standardization and classification of global medicinal product data
- Medical coding expertise

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Disclaimer

VigiBase is a data set with a long history (over 40 years) and Pharmacovigilance and reporting practices have changed and developed since the start. Therefore data shown in this presentation may differ slightly to other results, depending on interpretation of the data.

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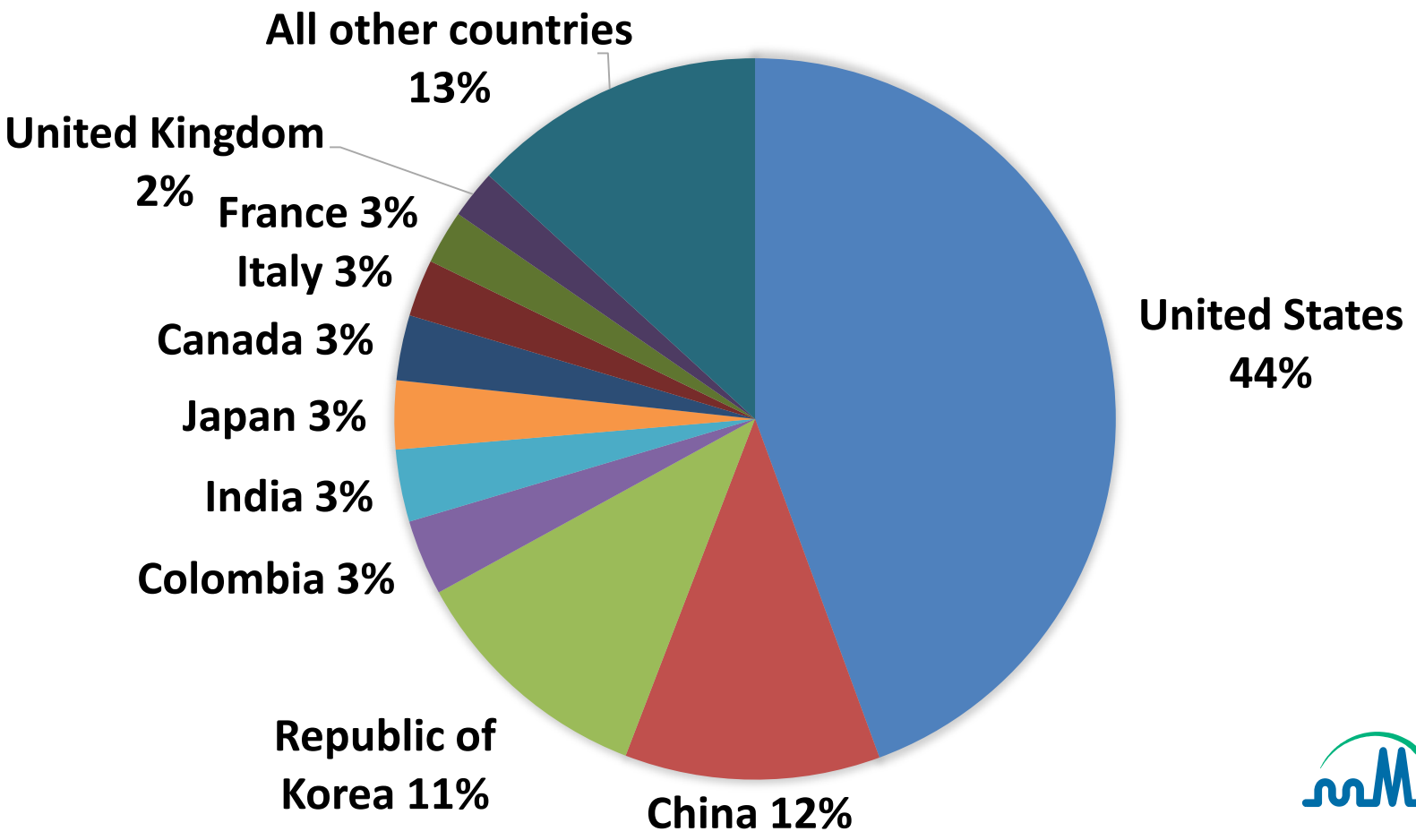
VigiBase – the world's largest database for spontaneous ICSRs

COUNTRY DISTRIBUTION LAST YEAR



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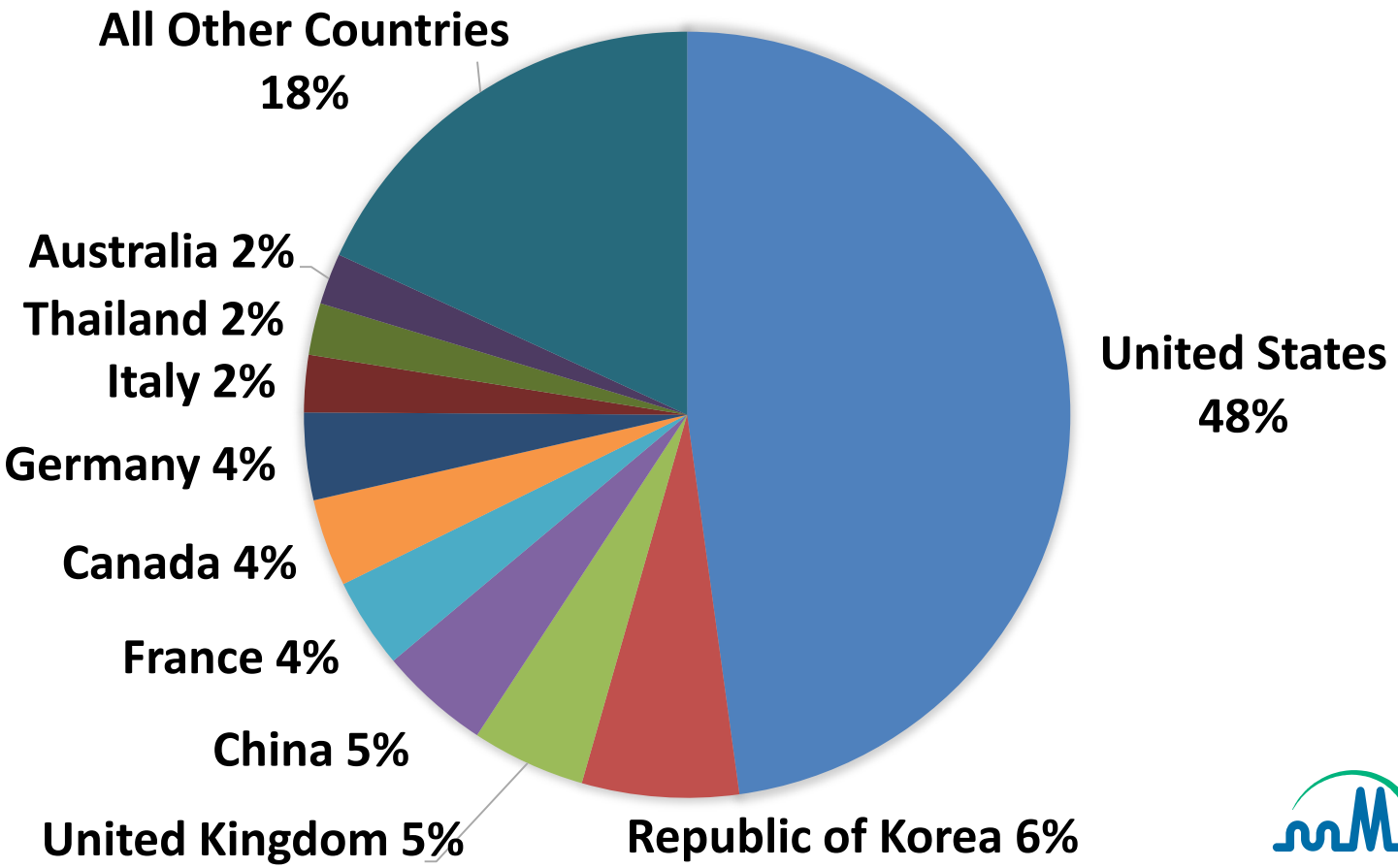
VigiBase

COUNTRY DISTRIBUTION SINCE 1968



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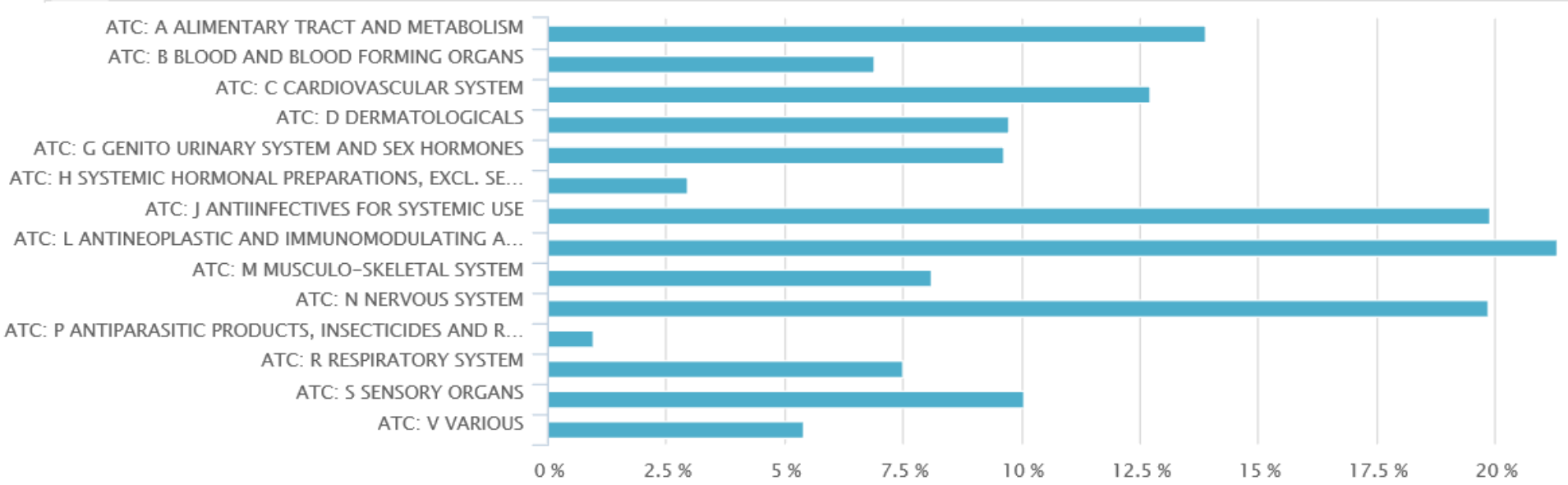
Drug class Distribution (# ICSRs 15.8 million)



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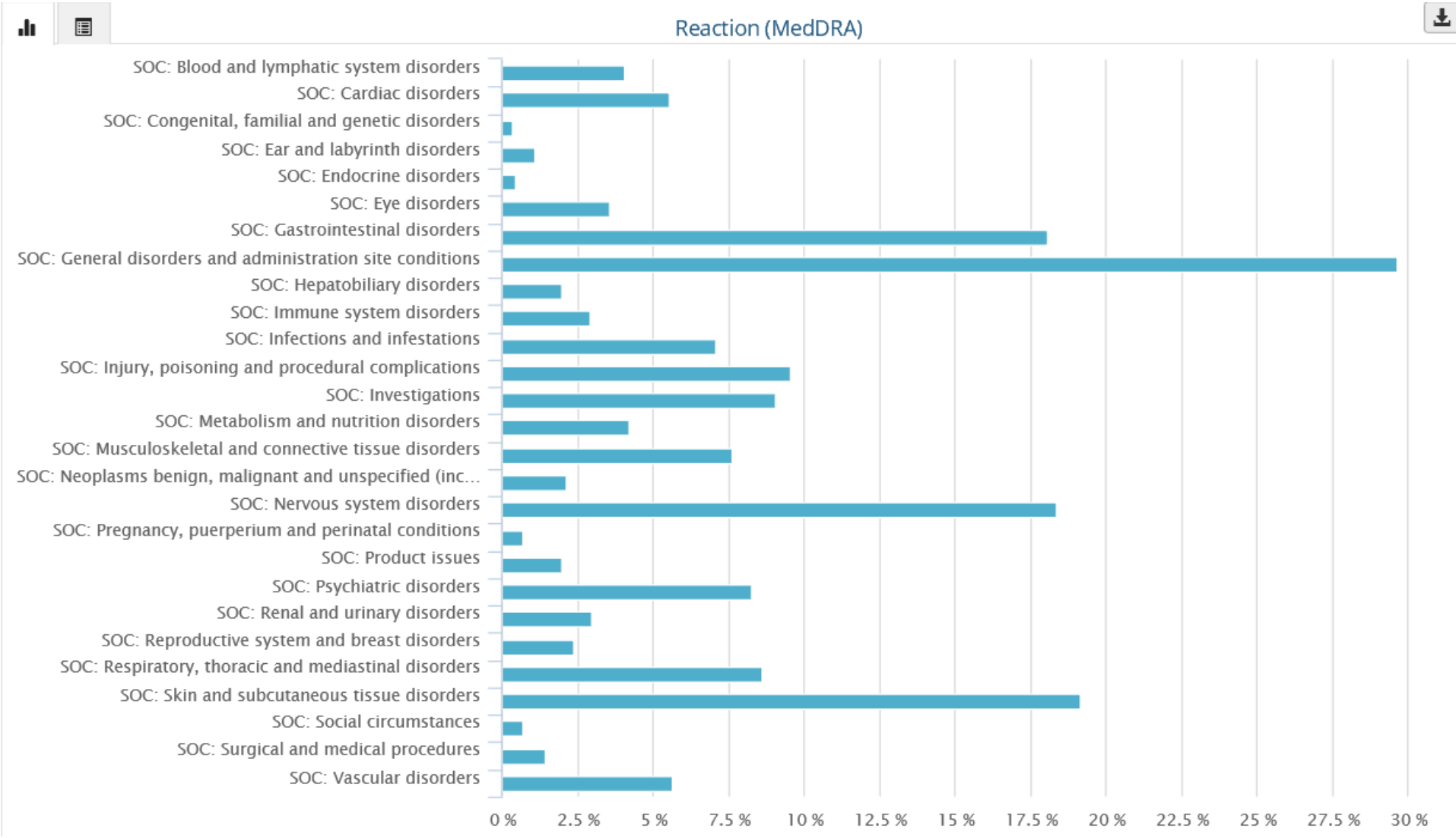
Adverse event distribution



Signal detection at UMC

A signal is essentially a hypothesis of a risk with a medicine with data and arguments that support it

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Signal detection at UMC

- **Step 1: Disproportionality analysis**
  - Drug* – reaction pairs
- **Step 2: manual analysis and evaluation**

"what is reported more often than expected?"

*Substance name

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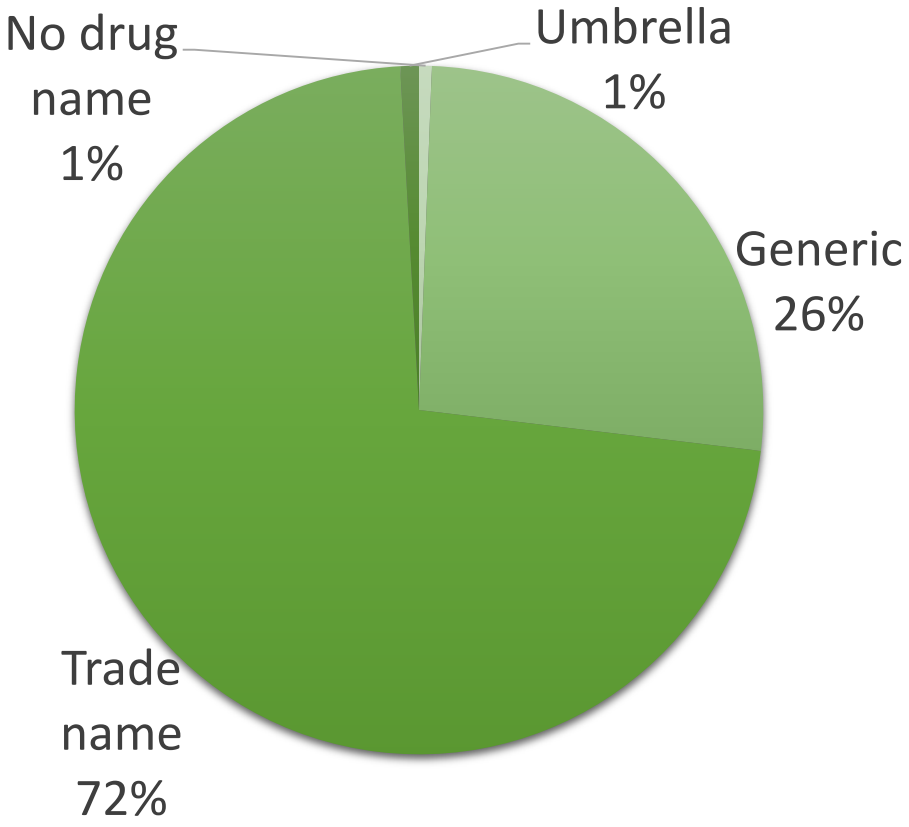
Identification of drug on ICSRs

Drug names on VigiBase ICSRs



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Identification of drug on ICSR

	All VigiBase	Reports 2012-2017
Industry reports	52%	55%
Non-industry reports	48%	45%

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Identification of drug on ICSR

	All VigiBase	Reports 2012-2017
Batch number	18%	22%
No batch number	82%	78%

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WHODrug

Originally developed to help analysis in VigiBase ICSRs

Used by industry and national authorities to structure and understand data

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Drug identification levels for global exchange of ICSRs - WHODrug

Trade name

Substance

- INN, USAN, JAN

Formulation

- Changing to EDQM standard

Strength

- UCUM

PhPID

Classification/drug charachteristics

- ATC (Anatomical, Therapeutic, Chemical)
- SDG (Standardised Dug Grouping)

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How would GSRS and IDMP data improve signal analysis?

Allow for more advanced data mining

- Chemical structures
- Protein characteristics
- Manufacturing methods
- …

Gives more context in manual evaluation

IF reported on the detailed level

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Thank you!

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