Exploring patient reported information in signal detection within a global database

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Background

There is limited published evidence of whether it is possible to identify drug safety signals from globally collected individual case safety reports (ICSRs) submitted by patients.

Objectives

To explore the contribution of globally collected patient reports to signal detection.

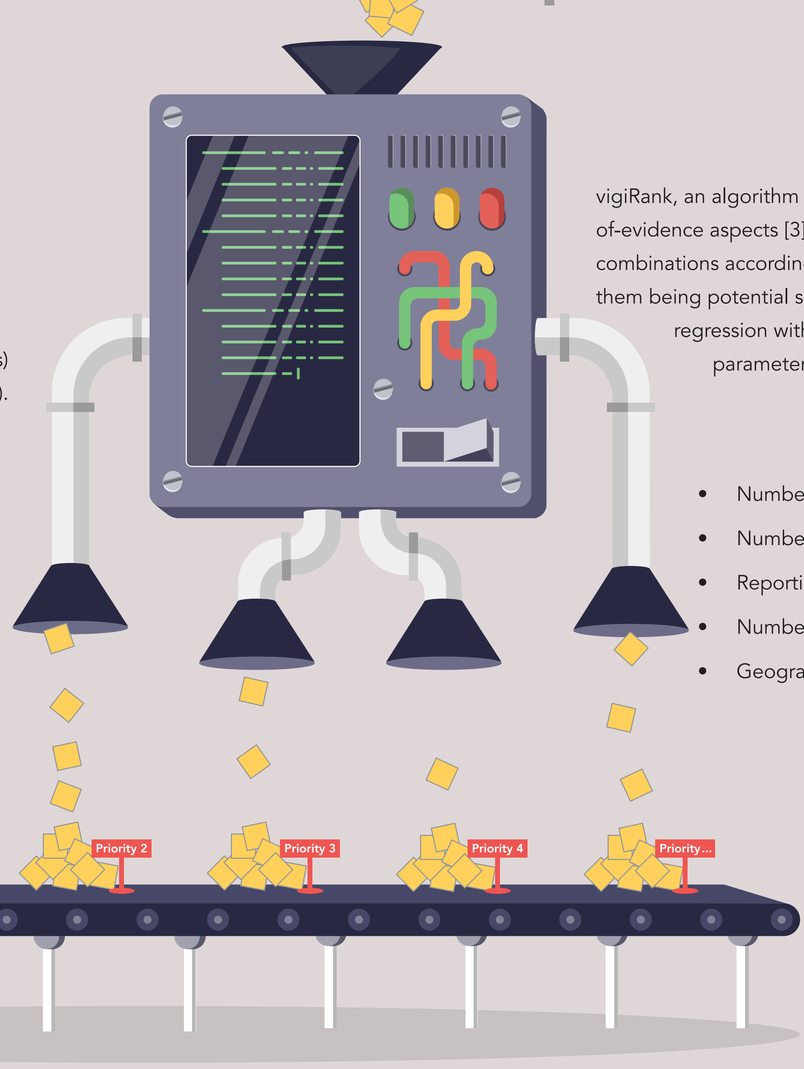
Methods

Data was retrieved from the WHO global ICSR database, VigiBase, in September 2016. 'Patient reports' were defined by reporter type "Consumer/Non health professional" according to the E2B reporting standard, and **consisted of 3.6 million reports.**

Drug – adverse drug reaction (ADR) combinations were generated and restricted to a series of reports in which the patient reports constituted more than 50% of all available reports for the combination in the full database. Next, each combination was restricted to include at least one report received in or after 2014, from at least 2 countries, and no more than 30 patient reports in total.

vigiRank, an algorithm using multiple strength-of-evidence aspects [3], was used to rank the combinations according to the likelihood of them being potential signals. It uses a logistic regression with the following parameters:

- Number of informative reports
- Number of recent reports
- Reporting disproportionality
- Number of reports with narratives
- Geographical spread



New signals:

- **Desloratadine** – Depression
- **Desogestrel** – Panic reaction, suicidal ideation and self-injurious behavior
- **Pregabalin** – Color vision distortion
- **Levothyroxine** – Panic attacks
- **Amitriptyline** – Dry eyes

New aspects of previously known ADRs:

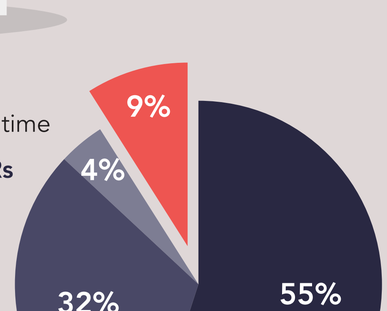
- **Systemic hormonal contraceptives** – Loss of libido
- **Sodium glucose linked transporters subtype 2 (SGLT-2) inhibitors** – Genital puritus
- **Noscapine** – Headache, stomach ache and chest pain

The list of Drug-ADR combinations **was manually assessed by a multidisciplinary team from UMC and Lareb**, investigating the presence and adequacy of the labelling of the adverse reactions in the patient information leaflets (PILs) and the summary of medical product characteristics (SmPCs). Assessors classified the combinations as being labelled/non-signal/to be kept under review (KUR)/potential signal.

Potential signals found were subsequently clinically evaluated in-depth to determine whether a signal should be communicated.

Results

A total of 212 combinations were manually assessed during the four-day allocated time for the signal detection workshop. The proportion of adequately **PIL-labelled ADRs was 55%, non-signal 32%, keep-under-review (KUR), i.e. requiring further monitoring,4% and potential signals 9%**. After widening some signals to include similar ADRs or drugs, 11 potential signals underwent in-depth clinical evaluation. This resulted in one non-signal, two KURs and eight signals that have been communicated within the WHO programme for international drug monitoring. These signals revealed five new suspected ADRs and three new aspects of previously known ADRs, e.g. regarding severity and previously inadequately described adverse reactions.



Conclusions

Patient reports were a valuable resource in global signal detection and identified important additional information about already known ADRs and new suspected ADRs. It is possible to use statistical methods to prioritize patient reports in a meaningful way.

References

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[2] Norén GN, et al. Data Mining and Knowledge Discovery. 2007;14:305-28.
[3] Caster O, et al. Drug Safety 2014;37:617-28.

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