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Background: Active surveillance for unknown adverse drug effects may be carried out by applying epidemiological techniques to large administrative databases. Self-controlled designs have the advantages over conventional cohort designs of not requiring a defined comparison group and adjustment by design for confounders that are stable over time.

Objectives: To implement and describe the output of a comprehensive symmetry screening of a large population-based dataset on elderly patients.

Methods: We applied a symmetry design to a dataset containing all drug dispensings and all hospital diagnoses in Denmark during the period 1995–2012 for persons born before 1950. The approach compares the incidence rate of a given outcome during a symmetrical period before and after initiation of a drug. We analyzed all drug–drug sequences and all drug–disease sequences (more than 200×10^9) occurring during the study period. The identified associations were ranked according to the number of outcomes that could be attributed to the exposure. We then reviewed the top ranked associations to evaluate whether the association was known, unknown, or likely to be due to reverse causation.

Results: In the main analysis, 29,891,212 incident drug therapies, and 21,300,000 incident diagnoses were included. Out of 186,758 associations evaluated in the main analysis, 43,575 (23.3%) had nominal *p*-values <0.05 . Of the top 200 drug–drug associations, 53% were interpreted as possible unknown adverse drug reactions, 16% as known adverse drug reactions, and 26% as being due to confounding or reverse causation. For the top 200 drug–disease associations these proportions were 34%, 14%, and 53%, respectively.

Conclusions: While most signals concern already known adverse drug reactions or aspects of routine clinical practice, a substantial proportion reflect associations that might represent unsuspected adverse drug effects. Open-ended screening by symmetry analysis can be a useful pharmacovigilance tool, when coupled with a systematic post-hoc review of potential signals.

524. 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 safety signals of globally collected individual case safety reports (ICSRs) from patients.

Objectives: To explore the contribution of globally collected patient ICSR to signal detection.

Methods: Data were retrieved from the WHO global ICSR database, VigiBase, in September 2016. "Patient reports" were defined by ICSR type "Consumer/Non health professional" according to the E2B reporting standard. Among the 3.5 million reports, suspected duplicate reports and reports from studies were excluded. Drug–adverse drug reaction (ADR) combinations were generated using both patient and non-patient reports. The combinations were then restricted to report series with at least 50% patient reports. Each combination was required to include at least one patient report received after 2014, ≥ 2 countries, ≤ 30 patient reports in total. *vigiRank*, an algorithm using multiple-strength-of-evidence aspects, was used to rank the combinations according to the likelihood of the combinations being potential signals. Each combination was manually assessed by a multidisciplinary team, investigating causality and the adequacy of the labelling of the adverse reactions in the patient information leaflets (PILs). Assessors classified the combinations as being labelled, non-signal, to be kept under review (KUR), i.e. requiring further monitoring, or potential signal. Potential signals were subsequently clinically evaluated in-depth to determine whether a signal should be communicated.

Results: A total of 212 combinations were assessed during the four day allocated time for the signal detection sprint. The proportion of adequately PIL-labelled

ADRs were 55%, non-signals 32%, KUR 4% and potential signals 9%. After grouping similar ADRs and drugs, eleven potential signals underwent in-depth clinical evaluation. This resulted in two non-signals, one KUR and eight signals that will be communicated within the WHO Programme for International Drug Monitoring. Five signals described new suspected ADRs and three described new aspects for 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 highlighted new suspected ADRs as well as important additional information about already known ADRs.

525. Characteristics and Quality of Spontaneous ADR Reports Submitted via the WEB-RADR App

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Background: Spontaneous reporting of suspected ADRs is key for efficient post-marketing safety surveillance. However, existing reporting tools are sometimes perceived as complex or inaccessible. As a complement, the WEB-RADR consortium developed a mobile phone app based on a simplified reporting form.

Objectives: To evaluate the characteristics and quality of reports submitted via the WEB-RADR app.

Methods: The app was launched in UK in July 2015, Netherlands in January 2016, and Croatia in May 2016. This study includes reports submitted up to September 2016 that (i) were spontaneous, (ii) had a single notifier, and (iii) were submitted directly by a health care professional or patient. For each country separately, the app reports were compared to a set of reference reports, submitted via conventional means during the same period, and meeting the inclusion criteria. The following report characteristics were analysed: the proportions of patient reports and reports concerning females (chi-squared tests), and the median

patient age (Mann–Whitney U test). In addition, a set of 100 app reports and 100 reference reports (for Croatia 37 and 68 reports, respectively) was randomly sampled, stratified by the proportion of patient reports among the app reports. Blinded assessors scored the quality of reports in this subset using a tool called ClinDoc, and the proportion of reports of at least moderate quality was compared (chi-squared test).

Results: A significantly higher proportion of app reports were submitted by patients in UK (28% vs 18%; $p < 0.01$) and Croatia (32% vs 7%; $p < 0.01$), whereas in the Netherlands the difference was small (60% vs 57%; $p = 0.5$). The proportion of female patients among app reports was relatively similar to the reference group, in all countries: 53% vs 60% in UK; 59% vs 64% in the Netherlands; and 76% vs 66% in Croatia ($p > 0.1$ for all). Median patient ages were also similar: 60 vs 55 years in UK; 48 vs 48 years in the Netherlands and 56 vs 56 years in Croatia ($p > 0.05$ for all). The proportion of reports of at least moderate quality was high in both groups, for all countries, but relatively lower for app reports: 83% vs 92% in UK ($p = 0.08$); 85% vs 98% in the Netherlands ($p < 0.01$); and 78% vs 78% in Croatia ($p = 1.0$).

Conclusions: The WEB-RADR app offers a new complementary route of spontaneous reporting that has been shown to attract patients and that could become an important tool in the future. Patient demographics are similar to conventional reporting routes, and report quality is sufficient despite a simplified reporting form.

526. Medication Error Reporting in European Regulatory Database EudraVigilance: A Descriptive Study

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Background: Medication errors are the most common preventable cause of adverse events in health care and a major public-health burden. It is essential to understand the causes, contributing factors and consequences of medication errors. EudraVigilance (EV) is a large database collecting individual case safety reports (ICSR) worldwide resulting in a large dataset from which much information can be obtained. The EU pharmacovigilance legislation (2012) provides a clear legal framework for sharing data on medication errors causing harm.