
Uppsala
Monitoring
Centre

How RWE can better support pharmacovigilance signal management

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OHDSI Sweden 2025

Pharmaco**vigilance**

Individual case reports

ADRAC

Report of Suspected Adverse Drug Reaction including Birth Defects 224289

*(**Note:** Identities of Reporter, Patient and Institution will remain **Confidential**)*

Patient *(Initials or Record … only)*	Age	Sex	Weight	Height
[redacted] 05 DEC 2006	55	M	80	168

Adverse Reaction Description: DESC Date of Onset of Reaction: 29/11/06

PATIENT WITH A NON ST ELEVATION MI HAD DIAGNOSTIC ANGIOGRAM SHOWING SEVERE STENOSIS IN LAD. THE SAME DAY HAD PCI TO LAD DURING WHICH EXPERIENCED PROFOUND AND SUSTAI NED HYPOTENSION NOT BELIEVED WITH ARAMINE 6mg (SEVERAL 0.5mg SOLUSES) AND IABP. IMPROVED AFTER HYDROCONTISONE 200mg + PHENERGAN GIVEN. ??ALERGIC REACTION TO CONTRAST (ISOVUE 370)

All Drug Therapy Prior to Reaction Asterisk Suspected Drug(s) *(please use trade names)*	Daily Dosage and Route	Date Begun	Date Stopped	Reason for Use
S ASPIRIN	300mg O	29/11/06	—	NSTEMI
S CLOPIDOGREL	300mg LOADING DOSE	29/11/06	—	NSTEMI
TEMAZEPAM S	10mg	29/11/06		SEDATION
S TIROFIBAN	IV bolus + INFUSION	29/11/06	29/11/06	NSTEMI
S MIDAZOLAM	2mg IV	29/11/06	29/11/06	SEDATION
S OMNIPAQUE	90ml IC	29/11/06	29/11/06	} ANGIOGRAM
S ISOVUE 370		29/11/06	29/11/06	} ANGIOPLASTY

Treatment *(of reaction)*: R ARAMINE, HYDROCONTISONE PHENERGAN

Outcome: Recovered ☒ Not Yet Recovered ☐ Unknown ☐ Fatal ☐ Date of Death / /

Sequelae: No ☒ Yes ☐ *(describe)* MYOCARDIAL INFARCTION

Comments *(eg. relevant history, allergies, previous exposure to this drug)*:

NO KNOWN ALLERGIES before the episode. HAD ANGIOGRAM IN another hospital. then PCI SAME DAY. REACTION DURING PCI

Reporting Doctor, Pharmacist, etc: POSS

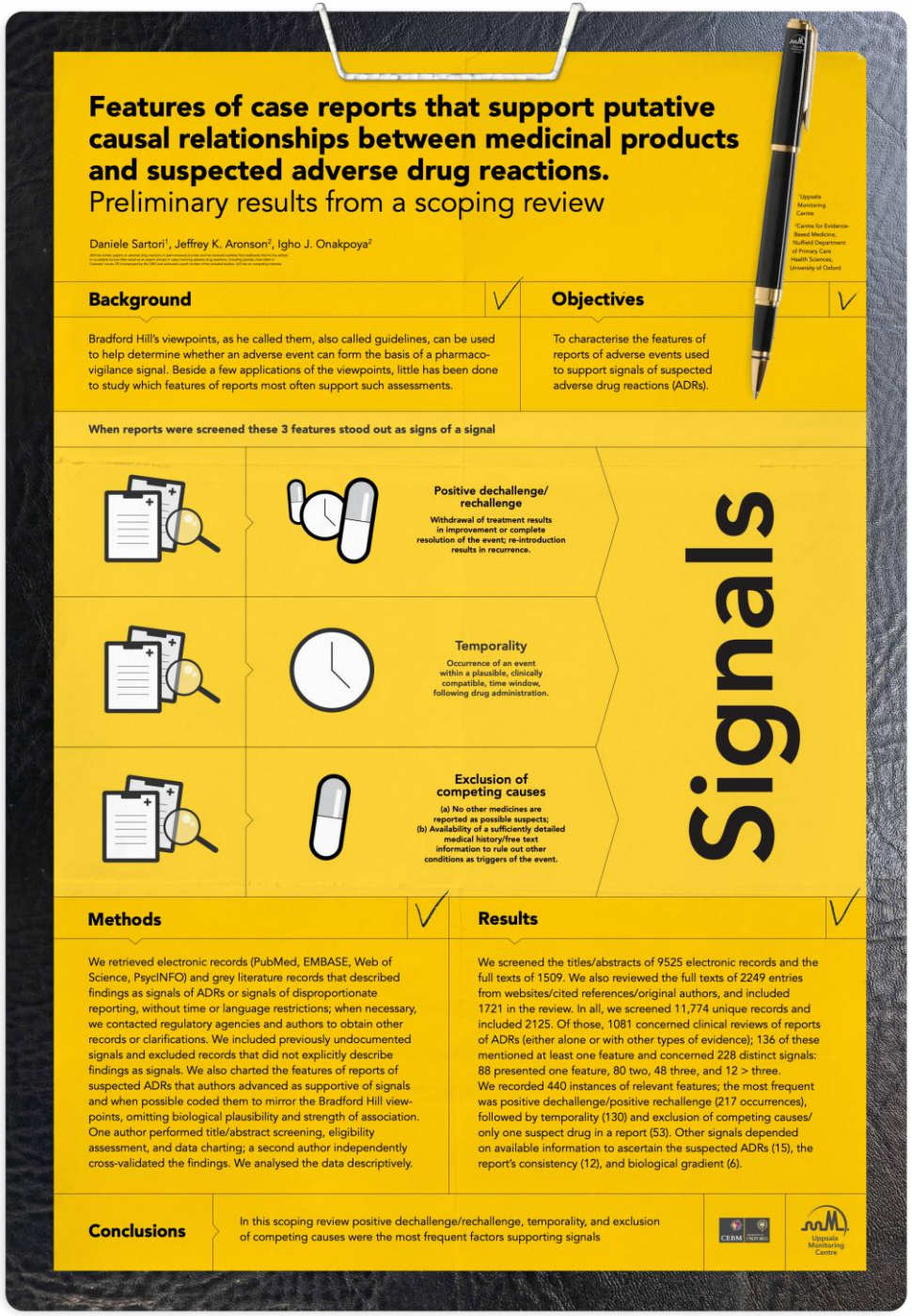
Name: [redacted]

Address: [redacted]

Signature [redacted] 30/11/06

Routinely collected health data

- Denominators
  - Number of patients exposed to medicine
  - Rates of adverse event with and without exposure to medicines
- Ability to assess more complex associations
  - Adjustment for biases and confounding
  - Incl due to indication or underlying disease
- Longitudinal data capture (before and after adverse event)



2025:

Case reports continue to dominate as a source of safety signals

How come?

Sartori et al. 2023

Drug Safety
https://doi.org/10.1007/s40264-022-01258-0

SCOPING REVIEW

Signals of Adverse Drug Reactions Communicated by Pharmacovigilance Stakeholders: A Scoping Review of the Global Literature

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Onakpoya et al. 2016

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Medicine and the Future of Health
RESEARCH ARTICLE Open Access

Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature

Igho J. Onakpoya*, Carl J. Heneghan and Jeffrey K. Aronson

Abstract

Background: There have been no studies of the patterns of post-marketing withdrawals of medicinal products to which adverse reactions have been attributed. We identified medicinal products that were withdrawn because of adverse drug reactions, examined the evidence to support such withdrawals, and explored the pattern of withdrawals across countries.

Methods: We searched PubMed, Google Scholar, the WHO's database of drugs, the websites of drug regulatory authorities, and textbooks. We included medicinal products withdrawn between 1950 and 2014 and assessed the levels of evidence used in making withdrawal decisions using the criteria of the Oxford Centre for Evidence Based Medicine.

Results: We identified 462 medicinal products that were withdrawn from the market between 1953 and 2013, the most common reason being hepatotoxicity. The supporting evidence in 72 % of cases consisted of anecdotal reports. Only 43 (9.34 %) drugs were withdrawn worldwide and 179 (39 %) were withdrawn in one country only. Withdrawal was significantly less likely in Africa than in other continents (Europe, the Americas, Asia, and Australasia and Oceania). The median interval between the first reported adverse reaction and the year of first withdrawal was 6 years (IQR, 1–15) and the interval did not consistently shorten over time.

Conclusion: There are discrepancies in the patterns of withdrawal of medicinal products from the market when adverse reactions are suspected, and withdrawals are inconsistent across countries. Greater co-ordination among drug regulatory authorities and increased transparency in reporting suspected adverse drug reactions would help improve current decision-making processes.

Keywords: Adverse drug reaction, Drug withdrawal, Systematic review, Voluntary recall

Background

Drug regulatory authorities award marketing authorizations that license pharmaceutical companies to market medicinal products when there is sufficient evidence that the product has a favourable benefit-to-harm balance [1]. If a new adverse drug reaction is suspected after approval, several courses of action can be taken by the regulator and/or manufacturer, including adding a new product label with specific warnings [2], adding a new contraindication [3], issuing a Direct Healthcare Professional Communication [4], allowing patients to decide whether they will take the drug [5], and in the most serious cases, withdrawal or revocation of the licence [6].

Post-approval withdrawal of medicinal products because of adverse drug reactions can be triggered by evidence obtained from various sources – anecdotal reports, observational studies, clinical trials, systematic reviews, or animal data. The removal of previously approved products from the market can result in loss of confidence in medicines by the public, loss of effective

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Pharmacoepidemiology and Drug Safety

WILEY

REVIEW OPEN ACCESS

Recommendations to Enable Broader Use of Real-World Evidence to Inform Decision-Making Throughout Pharmacovigilance Signal Management

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Keywords: decision-making | pharmacovigilance | real-world data | real-world evidence | regulatory science | signal management

ABSTRACT

Introduction: Despite substantial investments in analytical infrastructure and scientific research related to the development and analysis of real-world evidence in support of signal management, the impact on routine pharmacovigilance activities has been limited. Most organizations still rely largely on analyses of individual case reports and pre-existing evidence – especially during signal detection and validation.

Objective: This paper presents a set of recommendations for efforts to enable broader use of real-world evidence throughout pharmacovigilance signal management, in the future.

Outcome: The recommendations regard streamlined data access, data harmonization and use of reproducible analytical workflows to enable rapid and robust evidence generation. They emphasize the need for cross-disciplinary collaboration and for organizational adaptations to ensure adequate competence and supporting processes, including principles for how to integrate new types of evidence in decision-making. The execution of pilot studies under realistic conditions and the dissemination of their findings are highlighted as important steps toward defining the proposed change and driving progress in this area. This manuscript is endorsed by the International Society for Pharmacoepidemiology (ISPE).

1 | Background

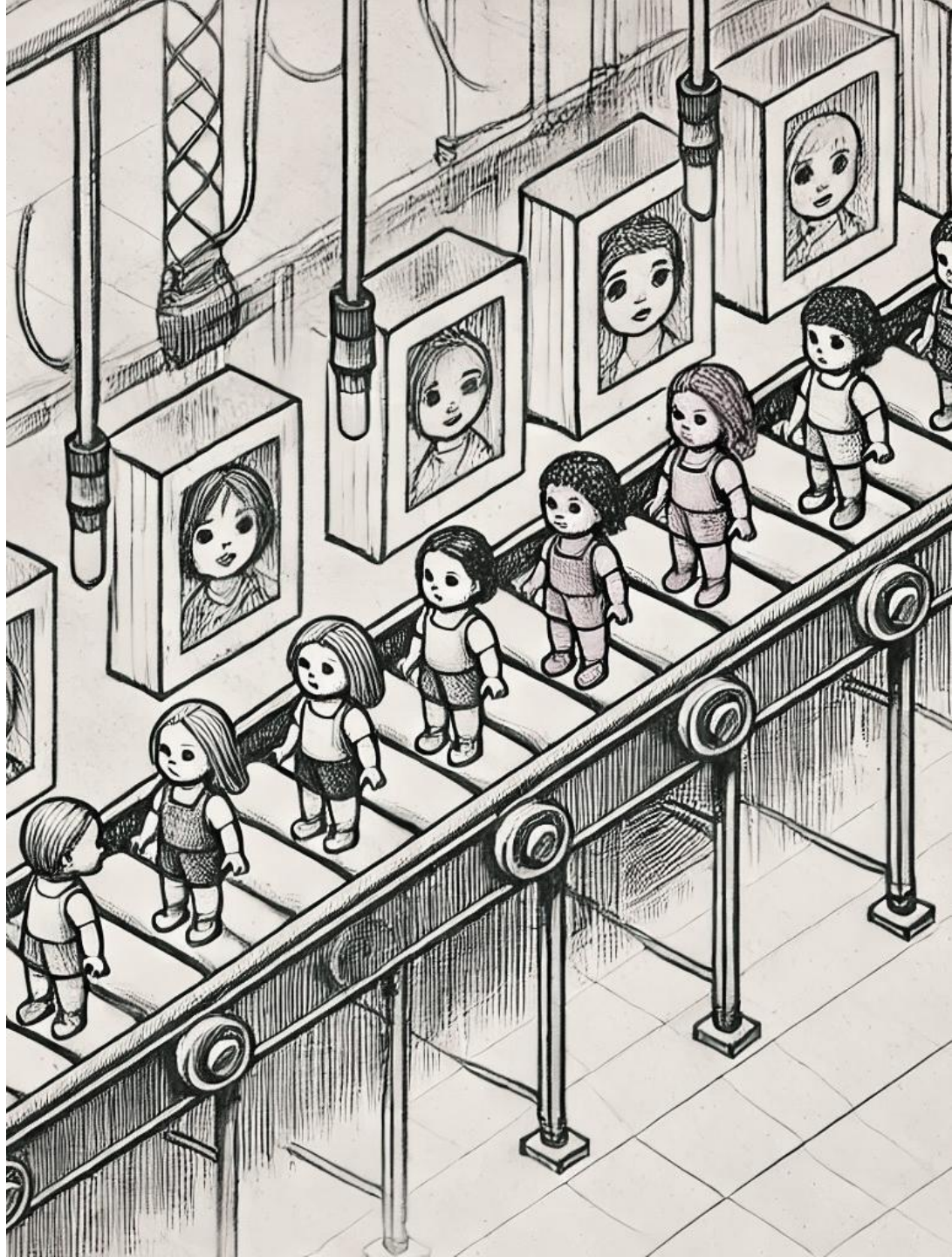
Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other problem related to medicinal products. Medicinal products approved for regular clinical use must be continually monitored for new information that may alter their benefit–risk balance overall and/or in different settings and populations. To this end, regulatory authorities, pharmaceutical companies, and other stakeholders analyze an array of data sources to detect information that may suggest previously unknown risks of adverse effects or new information about

Summary

- Substantial investments have been made to support the development and analysis of real-world evidence for regulatory decision-making
- Even so, most pharmacovigilance organizations rely primarily on individual case reports and preexisting evidence during signal management
- Streamlined access to fit-for-purpose data, data harmonization, and the use of reproducible analytical workflows are identified as enablers of rapid and robust evidence generation using real-world data
- Impact on pharmacovigilance decision-making may depend on cross-disciplinary collaboration and the establishment of principles for evidence integration
- The execution of pilot studies and dissemination of their findings can help drive progress

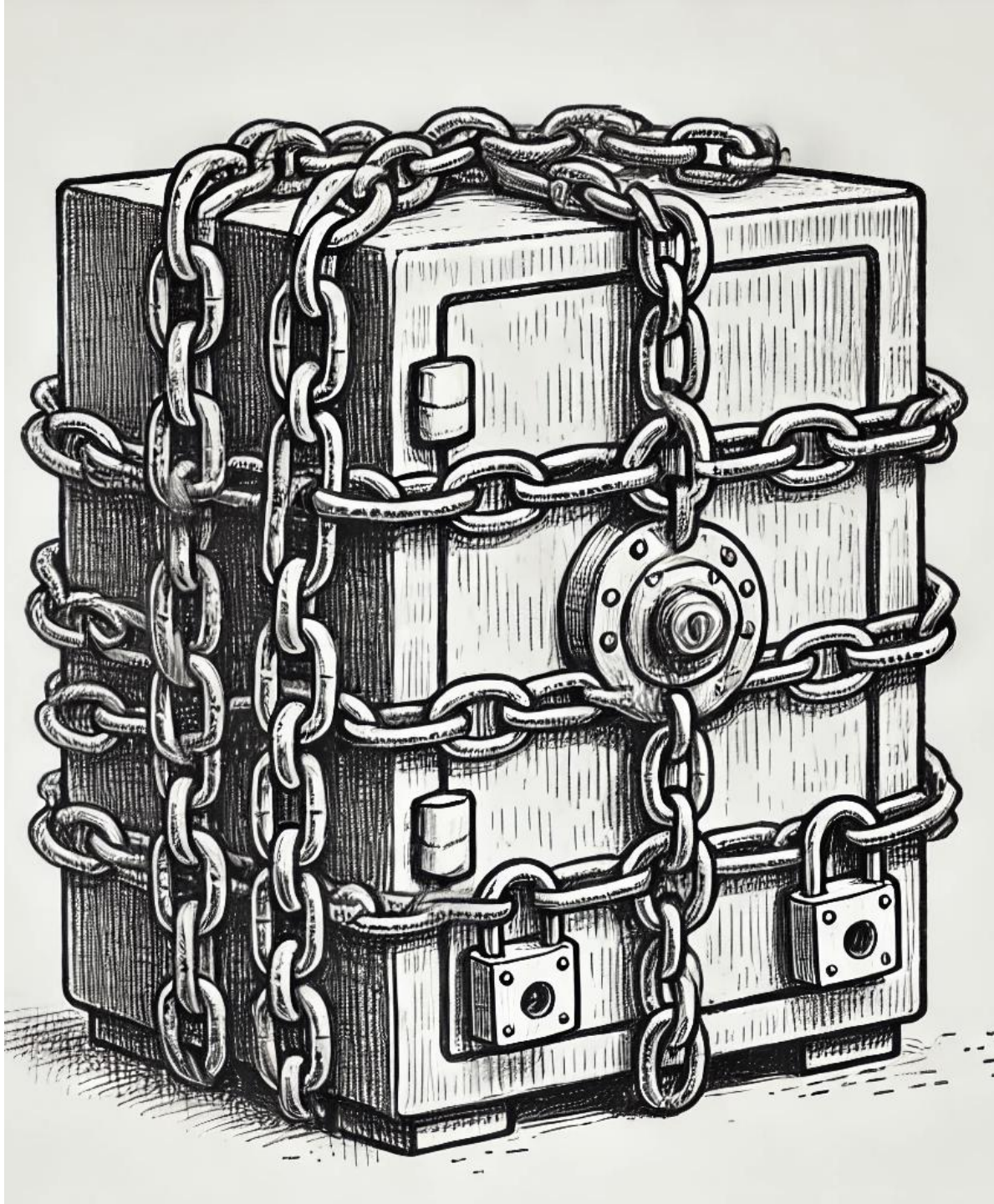
Needed: Rapid and reliable evidence-generation

- Datasets mapped to broadly used Common Data Models, including their standard vocabularies
- Reproducible analytical workflows with possibility to customise design parameters for pharmacovigilance use case
- Validated phenotypes for broad range of outcomes and covariates
- + capability to develop and deploy new phenotypes in response to findings



Needed: Timely access to fit-for-purpose data

- Data on relevant medicinal products and adverse events for the right patient populations
- Streamlined data access approval processes
- Harmonized requirements for study protocols across RWD sources
- Data access approval for overarching study designs/master protocols for pharmacovigilance use cases



Needed: Process adaptations

- Collaboration between pharmacovigilance, epidemiology, and RWD expertise
- Guidance on how to integrate new types of evidence in current processes

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