Spontaneous Reporting Data: A Global Comparison Using An Online Database Resource

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BACKGROUND

- Spontaneous reports (SR) of suspected adverse events associated with biopharmaceuticals / medical products are key sources for identifying potential new drug hazards. SR data are the most important source of **signals from the total exposed population** BUT these data can also support hypotheses for pharmacoeconomic studies.
- Most regulatory agencies and large drug distribution projects utilize spontaneous reporting systems (SRS), yet there is **no standard method for developing a SRS,** and few tools are available to aid this process.
- WHO (OMS) collects SR data from >100 countries. Many databases (DBs) conform to **WHO's Council for International Organizations of Medical Sciences (CIOMS) standard data fields**.
- B.R.I.D.G.E. TO DATA® (www.bridgetodata.org), an **international resource of DB profiles**, can serve as a template and complement the CIOMS effort.

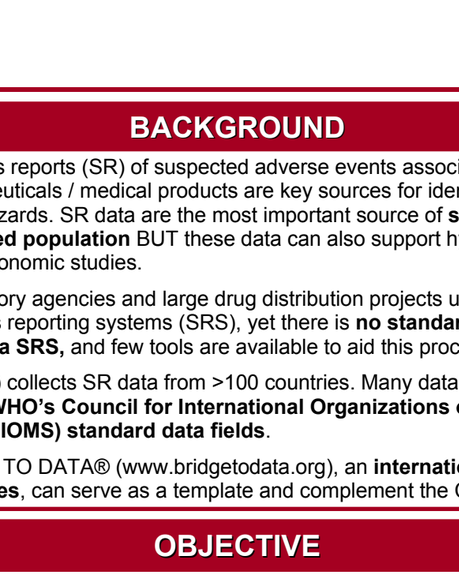
OBJECTIVE

To analyze SR databases and to characterize data elements useful for evaluating signals and for capturing different types of information.

METHODS

Box 1. We identified databases profiled in B.R.I.D.G.E. collecting SR data using two search criteria: ***Database Type = Spontaneous reporting systems;*** and ***Database Source = Spontaneous reports***

Figure 1. B.R.I.D.G.E. TO DATA® Search Page



Box 2. 20 of 209 profiles matched ≥1 criteria (**Figure 2**).

Box 3. The frequency of use of the 75 data fields (**Table 1**) used in B.R.I.D.G.E. structured profiles was compared among the 20 DBs.

Box 4. Based on use frequency, fields were categorized as:

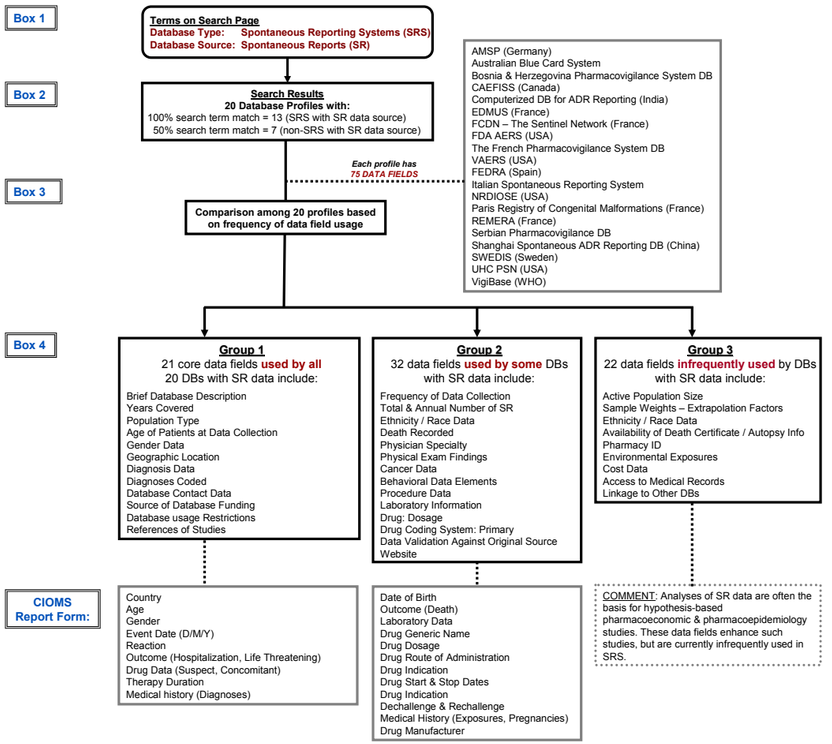
Group 1 (G1) – consensus in use of field among the set
Group 2 (G2) – use by ≥50% DBs
Group 3 (G3) – use by <50% DBs.

RESULTS

Table 1. Examples of Data Fields Used in Profiles (by Category)

Category	Data Fields
Summary	Database description, Database source, Years covered, Population type, Date of last update
Population Dynamics	Population size, Sample weights – Extrapolation factors
Demographic Data	Age, Gender, Date of birth, Death recorded, Other demographic data
Physician & Practitioner Info	Physician ID & Specialty, Pharmacy ID
Diagnoses/Signs & Symptoms	Diagnosis data, Diagnoses coded (coding systems), Max. number of codes, Physical exam findings, Environmental exposures, Behavioral data elements
Procedures	Procedure data, Procedures coded (coding systems), Laboratory information
Drug Information	Drug data, Drug dosage, Drug coding system(s), Additional drug information
Economic Data	Type of cost data (if applicable)
Validation & Linkage	Data validation, Access to medical records, Linkage to other databases
Administrative Data	Database contact data, Database usage restrictions, References of studies using/describing the database

Figure 2. Criteria-based search conducted in www.bridgetodata.org for DBs collecting SR data (209 Database Profiles worldwide as of May 10, 2013)



- ✓ Of the 75 data fields, 53 (71%) were frequently used among SR DBs: 21 (28%) were classified in G1; 32 (43%) were classified into G2.
- ✓ 22 (29%) fields utilized less frequently comprised G3. Analysis of G1 revealed that a majority of SR DBs are funded by government agencies, capture OTC & prescription drug use in inpatient & outpatient settings; however, diagnosis data are heterogeneously coded.
- ✓ Of the 25 fields on the CIOMS reporting form, 13 corresponded to G1, 10 to G2, and 2 overlapped with G1 & G2.

Table 2. Excerpt from B.R.I.D.G.E. TO DATA® comparing data elements within 3 selected databases

FIELD NAMES	Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) (Canada)	FEDRA (Spanish Pharmacovigilance Data of Adverse Reactions) (Spain)	VigiBase (WHO Adverse Drug Report (ADR) database) (Sweden)
Region	All 13 provinces and territories of Canada	17 Autonomous Communities and 2 Autonomous Cities of Spain.	More than 100 countries from all parts of the world, especially from Europe and North America
Database Type	Spontaneous Reporting System (Enhanced in situations where an AEFI signal has been identified, or in mass immunization campaigns like pandemic H1N1 immunization.) In addition to the voluntary reporting system (CAEFISS), Canada also has an active surveillance system for serious AEs following immunization, vaccination failures and selected infectious diseases known as IMPACT (Immunization Monitoring Program ACTive).	Spontaneous Reporting System	Spontaneous Reporting System (VigiBase is primarily intended to be a spontaneous adverse drug reaction (ADR) report system; however, the database includes cases with a varying degree of suspicion, both on the level of the initial reporter, and on the causality ascertainment made by the national center.)
Database Source	Spontaneous Reports Spontaneous Reporting and Active Reporting by IMPACT nurse monitors The AEFI Report Form is used nationally; Provinces and territories may have different versions. In the passive system, HCPs report to local, provincial and/or territorial public health authorities AEs that follow immunization or may have been due to the administration of a vaccine. These authorities, as well as vaccine manufacturers, forward all such reports to the Public Health Agency of Canada. All reports received from both active & passive surveillance systems are aggregated and stored in a computerized, web-enabled AEFI database at the Agency.	Spontaneous Reports (77% Yellow Card (YC) 12% Industry 10% Health professional studies 1% Regional Pharmacovigilance Centres Literature Review)	Spontaneous Reports The ICSRs in VigiBase come from both regulatory & voluntary sources, depending on the PV system. Some national centers accept reports only from medical practitioners; others accept reports from a wider spectrum of health professionals. Some national centers include reports from pharmaceutical companies in the information submitted to the collaboration center. Some reports also come from consumers. Case reports from studies or special monitoring are also included, when provided. These categories are flagged, so that they can be distinguished from other report categories.
Frequency of Data Collection	Ongoing: Other severe or unusual events are also solicited and reported if the health care provider feels it may have been due to the administration of a vaccine. The reports are entered into an electronic database.	Ongoing	Ongoing: VigiBase is updated with incoming ICSRs on a continuous basis. National centers are recommended to send reports weekly (new guidelines since 2010). Previously the frequency was at least once a quarter which most centers adhered to, and several reported more frequently.
Years Covered	1987- Present	1992 - Present	1968 - Present
Total number of spontaneous reports	<200,000 reports to date	14,750 cases were received in 2011, but this number varies from year to year	VigiBase holds more than 6 million ICSRs contributed by the national centers, as of June 2011
Age of Patients at Data Collection	Yes (DOB) Some jurisdictions send data on DOB, some only indicate age (when provided)	Yes Age can be captured in four ways: (1) Date of Birth (most precise), (2) Age (when the reaction starts), (3) Age Group, or (4) Gestation Period (for fetuses).	Yes [Age at onset of reaction, age group of onset of reaction, date of birth (DOB, MOB orYOB)]
Death Recorded	Yes: YYYY / MM / DD	Yes	Yes: Both cause and date of death are recorded
Diagnoses Coded	MedDRA: Since October 2009; prior to that WHOART was being used	MedDRA: LLT Other: The verbatim of the original term as reported by the original reporter is also recorded when the exact term cannot be matched with MedDRA dictionary.	MedDRA / WHO-ART ICD
Laboratory Information	Yes: If indicated, the laboratory information will be coded in MedDRA.	Yes: Coded with MedDRA	Yes: Using MedDRA or ICD
Drug Data	Yes: Vaccines, treatment related to the current AEFIs, and concomitant medication are all captured in different sections of the database	Yes: Prescription & OTC Information on biologicals and vaccines is also included	Yes: Prescription drugs and to some extent OTC, pharmacist-dispensed products, herbal medicinal products, vaccines, biotech & blood products, diagnostics, and contrast media.
Drug: Regimen & Route	Yes: The route of administration is captured only for vaccines. However, if the ATC code includes the route, it is captured.	Yes: Form of drug; Frequency of Administration; Units per Dose; Number of Doses Taken, and Route.	Yes
Drug: Manufacturer	Yes: Only for vaccines, though	Yes: Manufacturer or Laboratory, Dossier number, and Lot Number are all available, when the suspected drug is a trade name	Yes: Product name is included, as well as name source and source version, company, country, active ingredients, and CAS numbers
Drug: Dosage	Yes: Only for vaccines. If the dose information is provided for the drugs, they will be captured in the comment section and not coded as they are for vaccines.	Yes: Also recorded are Modifications to the Drug Dosage post-ADR and medical progress, as well as Drug Challenge, Re-Challenge, De-Challenge or Stop	Yes: When reported
Drug: Days Supply	Yes: If indicated	Yes: Drug Start and Stop Dates and Time to ADR are recorded.	No
Drug: Generic Name	Yes: ATC-WHO is used for drugs. Right now, CAEFISS has a combination of generic and trade names, but it may change in the near future.	Yes	Yes
Drug: Additional Information	Yes: For vaccines - Lot number; date vaccine was administered; information re: vaccination errors such as: given outside the recommended age limits, product expired, dose # exceeded thank recommended for age, incorrect route, wrong vaccine given, etc.	Yes: Also recorded are the Type of Drug; Therapeutic group; Drug Indication; Country of Authorization; Country of Acquisition; Suspect Level; Drug Formulation; and Lot number.	Yes: Product name is included, as well as name source and source version, company, country, active ingredients, and CAS numbers
Cost Data	No	No	No
Access to Medical Records	No: However, in special circumstances when a serious AEFI is under review, some information is requested from the province of residence	Yes	No: All reports have a unique ID which can be traced back to the medical record but not publicly accessible.
Linkage to Other Databases	No	Yes: Data are exchanged with several databases: EudraVigilance - PM, Vigibase, and Pharmaceutical industry databases.	Yes: This database is a composite of data from national centers' databases.
Sponsoring Government Agency	Public Health Agency of Canada	Spanish Ministry of Health and Consumption (Agencia Española de Medicamentos y Productos Sanitarios [AEMPS])	N/A (VigiBase is self-funded by a nonprofit foundation at the WHO Collaborating Centre for International Drug Monitoring)

LIMITATIONS

This analysis was done using DBs currently profiled within B.R.I.D.G.E. More profiles of data sources are continually being added to this resource.

CONCLUSION

In this analysis, B.R.I.D.G.E. TO DATA served as a tool to categorize data fields used in SR databases and to identify additional fields to complement the CIOMS effort (e.g., data on cost, procedures, environmental exposures). We believe that important capabilities such as access to medical records, cost data and DB linkages can enhance ad hoc pharmacoeconomic studies, yet are currently infrequently used in SRS. With increasing interest in SRS, it is likely that the use of these data fields will also increase, and the methods for collecting SR data may be instructive for database design.

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