Glossary of terms used in Pharmacovigilance

Absolute risk

Risk in a population of exposed persons; the probability of an event affecting members of a particular population (e.g. 1 in 1,000). Absolute risk can be measured over time (*incidence*) or at a given time (prevalence).

See also attributable risk and relative risk

Adverse event

Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Synonym: adverse experience

Adverse (drug) reaction (ADR)

A response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. (WHO, 1972).

An adverse drug reaction, contrary to an adverse event, is characterized by the suspicion of a causal relationship between the drug and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

Allopathy

Non-traditional, western scientific therapy, usually using synthesised ingredients, but may also contain a purified active ingredient extracted from a plant or other natural source; usually in opposition to the disease. Compare *homeopathy*.

Association

Events associated in time but not necessarily linked as cause and effect.

Attributable risk

Difference between the risk in an exposed population (*absolute risk*) and the risk in an unexposed population (*reference risk*). Also referred to as excess risk.

Attributable risk is the result of an absolute comparison between outcome frequency measurements, such as incidence.

Examples: If the exposed persons with a particular outcome are A, the exposed persons without the outcome are B, the unexposed persons with the outcome are C and the unexposed persons with the outcome are D, then the attributable risk is calculated as :

$[A / (A+B)] - [C / (C+D)]$.

If, during the same time period, the incidence of rash in a population treated with medicine X is 35/1,500=0.023, and the incidence of rash in a population not treated with X is 5/2,000=0.0025, the attributable risk is (35/1,500) - (5/2,000) = 0.0205.

Benefit

An estimated gain for an individual or a population. See also *Effectiveness/Risk*.

Benefit - risk analysis

Examination of the favourable (beneficial) and unfavourable results of undertaking a specific course of action. (While this phrase is still commonly used, the more logical pairings of benefit-harm and effectiveness-risk are slowly replacing it).

Biological products

Medical products prepared from biological material of human, animal or microbiologic origin (such as blood products, vaccines, insulin).

Causality assessment

The evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction. Causality assessment is usually made according established algorithms.

Caveat document

The formal advisory warning accompanying data release from the WHO Database: it specifies the conditions and reservations applying to interpretations and use of the data.

Clinical trial

A systematic study on pharmaceutical products in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study the absorption, distribution, metabolism and excretion of the products with the objective of ascertaining their efficacy and safety.

Combinations database

Quarterly report of all drug-ADR associations produced by the BCPNN scan.

Common
In pharmacovigilance, an event with a frequency between 1 in 100 and 1 in 10.

Compliance
Faithful adherence by the patient to the prescriber's instructions.

Control group
The comparison group in drug-trials not being given the studied drug.

Critical terms
Some of the terms in WHO-ART are marked as 'Critical Terms'. These terms either refer to or might be indicative of serious disease states, and warrant special attention, because of their possible association with the risk of serious illness which may lead to more decisive action than reports on other terms.

See Serious adverse event or reaction.

Data-mining
At the UMC, the use of an automated tool, based on Bayesian logic, for the scanning of the WHO database (*Vigibase*) in the process of detecting drug-adverse reaction associations: the BCPNN. Knowledge-detection is the preferred term for the process.

Dechallenge
The withdrawal of a drug from a patient; the point at which the continuity, reduction or disappearance of adverse effects may be observed.

Effectiveness/risk
The balance between the rate of effectiveness of a medicine versus the risk of harm is a quantitative assessment of the merit of a medicine used in routine clinical practice. Comparative information between therapies is most useful. This is more useful than the efficacy and hazard predictions from pre-marketing information that is limited and based on selected subjects.

Efficacy
The ability of a drug to produce the intended effect as determined by scientific methods, for example in pre-clinical research conditions (opposite of hazard).

See also absolute risk, reference risk, attributable risk and relative risk.

Epidemiology
The science concerned with the study of the factors determining and influencing the frequency and distribution of disease, injury and other health-related events and their causes in a defined human population for the purpose of establishing programs to prevent and control their development and spread (Dorland's Illustrated Medical Dictionary).

See also pharmacoepidemiology

Essential medicines
Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. See www.who.int/medicines/default.shtml.

EudraVigilance
The European Union data-processing network and management system, established by the European Medicines Agency (EMEA) to support the electronic exchange, management, and scientific evaluation of Individual Case Safety Reports related to all medicinal products authorised in the European Economic Area (EEA). EudraVigilance also incorporates data analysis facilities.

Excipients
All materials included to make a pharmaceutical formulation (e.g. a tablet) except the active drug substance(s).

Formulary
A listing of medicinal drugs with their uses, methods of administration, available dose forms, side effects, etc, sometimes including their formulas and methods of preparation.

Generic (multisource product)
The term 'generic product' has somewhat different meanings in different jurisdictions. Generic products may be marketed either under the non-proprietary approved name or under a new brand (proprietary) name. They are usually intended to be interchangeable with the innovator product, which is usually manufactured without a license from the innovator company and marketed after the expiry of patent or other exclusivity rights.

Harm
The nature and extent of actual damage that could be caused by a drug. Not to be confused with risk.

Herbal medicine
Includes herbs, herbal materials, herbal preparations and finished herbal products.

Homeopathy
Homeopathy is a therapeutic system which works on the principle that 'like treats like'. An illness is treated with a medicine which could produce similar symptoms in a healthy person. The active ingredients are given in highly diluted form to avoid toxicity. Homeopathic remedies are virtually 100% safe. Compare *Allopathy*.

Incidence
The extent or rate of occurrence, especially the number of new cases of a disease in a population over a period of time.

ICSR Individual case safety report
A report that contains 'information describing a suspected adverse drug reaction related to the administration of one or more medicinal products to an individual patient…'. (*Volume 9 of the Rules Governing Medicinal Products for Human and Veterinary Use in the European Union*).

Knowledge-detection
Preferred term as the alternative to data mining; searching for combinations and patterns using BCPNN.

Martindale
One of the prime reference sources for information about drugs throughout the world. Published by the Pharmaceutical Press, UK.

Medical error
"An unintended act (either of omission or commission) or one that does not achieve its intended outcomes." Leape, Lucien. Error in Medicine. *Journal of the American Medical Association* 272(23):1851-57 (Dec. 21, 1994).

Member countries
Countries which comply with the criteria for, and have joined the WHO Programme for International Drug Monitoring.

National pharmacovigilance centres
Organisations recognised by governments to represent their country in the WHO Programme (usually the drug regulatory agency). A single, governmentally recognized centre (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyse and give advice on all information related to drug safety.

Neural network
A type of artificial intelligence used in the BCPNN to scan the WHO ADR database (*Vigibase*).

Over the counter (OTC)
Medicines which are available for purchase without prescription.

Pharmacoepidemiology
Study of the use and effects of drugs in large populations. See also *epidemiology*.

Pharmacology
Study of the uses, effects and modes of action of drugs.

Pharmacovigilance
The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

Phocomelia
Characteristic deformity caused by exposure to thalidomide in the womb, also very rarely occurring spontaneously. Meaning: limbs like a seal.

Phytotherapy
Western-style, scientific treatment using plant extracts or materials.

Placebo
An inactive substance (often called a sugar pill) given to a group being studied to compare results with the effects of the active drug.

Polypharmacy
The concomitant use of more than one drug, sometimes prescribed by different practitioners.

Post-marketing
The stage when a drug is generally available on the market.

Predisposing factors

Any aspect of the patient's history (other than the drug) which might explain reported adverse events (genetic factors, diet, alcohol consumption, disease history, polypharmacy or use of herbal medicines, for example).

Pre-marketing

The stage before a drug is available for prescription or sale to the public.

Prescription event monitoring (PEM)

System created to monitor adverse drug events in a population. Prescribers are requested to report all events, regardless of whether they are suspected adverse events, for identified patients receiving a specified drug. Also more accurately named 'cohort-event monitoring'.

Prescription only medicine (POM)

Medicinal product available to the public only on prescription.

Prophylaxis

Prevention or protection.

Rare

In pharmacovigilance an event with a probability between 1 in 10,000 and 1 in 1,000.

Rational drug use

An ideal of therapeutic practice in which drugs are prescribed and used in exact accordance with the best understanding of their appropriateness for the indication and the particular patient, and of their benefit, harm effectiveness and risk.

Rechallenge

The point at which a drug is again given to a patient after its previous withdrawal – see *dechallenge*.

Record linkage

Method of assembling information contained in two or more records, eg in different sets of medical charts, and in vital records such as birth and death certificates. This makes it possible to relate significant health events that are remote from one another in time and place.

Reference risk

Risk in a population of unexposed persons; also called baseline risk. Reference risk can be measured over time (*incidence*) or at a given time (*prevalence*). The unexposed population refers to a reference population, as closely comparable to the exposed population as possible, apart from the exposure.

Regulatory authority

The legal authority in any country with the responsibility of regulating all matters relating to drugs.

Relative risk

Ratio of the risk in an exposed population (*absolute risk*) and the risk in an unexposed population (*reference risk*). Relative risk is the result of a relative comparison between outcome frequency measurements, e.g. incidences.

Example: If the exposed persons with an outcome are A, the exposed persons without the outcome are B, the unexposed persons with the outcome are C, and the unexposed persons without the outcome are D, the relative risk is calculated as [A / (A+B)] / [C / (C+D)].

If the incidence of rash in a population treated with medicine X is 35/1,500=0.023, and the incidence of rash in a population which is not treated with X, during the same time period, is 5/2,000=0.0025, the relative risk is (35/1,500) / (5/2,000) = 9.3.

Risk

The probability of harm being caused; the probability (chance, odds) of an occurrence.

Serious Adverse Event or Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- results in death
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- is life-threatening

To ensure no confusion or misunderstanding of the difference between the terms 'serious' and 'severe', the following note of clarification is provided:

The term 'severe' is not synonymous with serious. In the English language, 'severe' is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache). Seriousness (not severity) which is based on patient/event outcome or action criteria serves as guide for defining regulatory reporting obligations.

Side effect

Any unintended effect of a pharmaceutical product occurring at normal dosage which is related to the pharmacological properties of the drug.

Signal

Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. The publication of a signal usually implies the need for some kind of review or action.

Spontaneous reporting

System whereby case reports of adverse drug events are voluntarily submitted from health professionals and pharmaceutical manufacturers to the national regulatory authority. *See ICSR.*

Thalidomide

Drug prescribed in the 1950s as a mild sleeping pill and remedy for morning-sickness for pregnant women. Led to serious birth defects. Returning to favour as a treatment for leprosy.

Traditional medicines

Traditional medicine is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness. *See also allopathic medicine.*

Uncommon

In pharmacovigilance an event with a frequency between 1 in 1.000 and 1 in 100.

Unexpected adverse reaction

An adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorization, or expected from characteristics of the drug.

Vigibase

The name for the WHO International ADR Database.

Vigiflow

VigiFlow (formerly called Vigibase Online) is a sophisticated case report management system created by the UMC, complying with GxP requirements.

Vigisearch

This is a custom search service offered by the UMC to third-party inquirers for which several types of standard presentation are available.

Vigimed

E-mail conferencing facility, exclusive to member countries of the WHO Programme for International Drug Monitoring.