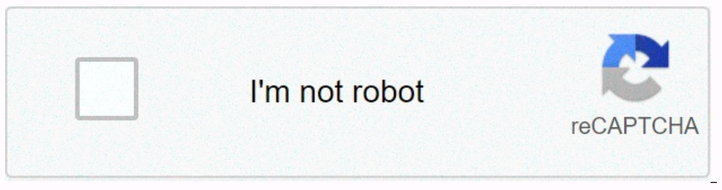

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Standardizing adverse drug event reporting data

Page 13 Sharing Citation: 2 current event reporting systems. Institute of Medicine. 2007. Reporting of adverse events in the field of drugs: Role of consumers and healthcare professionals: Summary of the seminar. Washington, DC: National Academies Press. Doi: 10.17226/11897. × of adverse events gives a signal or hypothesis that can be further evaluated by epidemiological methods and form the basis for additional epidemiological studies, where appropriate (FDA, 2005b). Manufacturers should report to the FDA the following serious and previously unknown adverse events within 15 days of their occurrence and conduct a follow-up investigation (FDA, 2005c): Events related to drug use in professional practice Events resulting from accidental or intentional overdose Events occurring in drug abuse events occurring in drug withdrawal Any failure of expected pharmacological action The analysis of serious adverse events identifies problems that should lead to changes in drug labels or that require notification to a doctor of adverse events. This information, as Anne Trontell, deputy director of the FDA's Office of Drug Safety, noted, allows the FDA, in collaboration with the manufacturer, to ensure that it has an effective product label to alert health professionals and patients to possible safety risks and areas of risk prevention. Daniel Troy, a partner at Sidley Austin LLP and the fda's former general counsel, added that once the drug is approved by the FDA, manufacturers must submit quarterly reports for the first three years and annual reports after that three-year period. The FDA may extend the three-month reporting period with written notice. The content of the reports shall include a summary of descriptiveness, an analysis of the information in the 15-day alert and a list of actions taken since the last report, such as labelling of changes or studies that have been initiated. The FDA can withdraw the approval of the drug if there has not been proper reporting. The FDA did not conclude from the submitted report that the drug was a direct cause of an adverse event, but rather that the event was related to drug use. The FDA does not impose legal requirements on doctors to report adverse events because it does not have the authority to regulate the practice of medicine, the responsibility of individual state governments. Currently, 20 states have mandatory reporting systems, but Mr. Troy said his experience is that there are cases of adverse reactions that are not reported. In countries without mandatory reporting systems, reporting is completely voluntary and therefore depends on the involvement of healthcare professionals. Possible reasons for under-reporting include the time it takes to complete a report, fear that event reporting will have a negative effect on practice medical and liability concerns. Mr Troy recommended that the AERS be streamlined to encourage reporting, for example 20 Sharing citation: 3 Active Surveillance Systems. Institute of Medicine. 2007. Reporting of adverse events in the field of drugs: Role of consumers and healthcare professionals: Summary of the seminar. Washington, DC: National Academies Press. Doi: 10.17226/11897. × voluntary reporting. By comparison, it is estimated that the ratio in public hospitals is 1 in every 80 events. These duke data show how voluntary reporting does not correspond to accurate coverage of the number of adverse events observed by patients, as 5 out of 6 events are missed. Dr Kilbridge said surveillance systems were limited by the available data. The data is extracted from many different sources and is highly variable in terms of quality. He also pointed out that the systems are resource-intensive, taking away both financial and human capital. The low specificity of the warning system creates too many alerts for human employees to respond to each one. Dr Kilbridge said the Duke system worked more than 60 triggers and sent the university hospital up to 60 to 70 signals a day, creating a significant amount of work for health care providers. Despite all this work, the current logic of the system leads to real anxiety only about one in six times that such events occur. Dr Kilbridge expressed hope that the rules could be developed with a sufficiently high predictive value to be effective as real-time intervention. We need to balance the possibility of real-time intervention with the practical aspects of the supplier workflow, Kilbridge said. Dr Kilbridge said that while the Duke University Pharmacy group made approximately 128 MedWatch reports in the past year, it received 1,500 automatically detected ADE reports and 4,000 voluntary reports from Duke University Hospital alone. Many of these adverse events are not necessarily reported to the FDA. Most of Duke's MedWatch reports originating from the pharmacy come from voluntary reporting by pharmacists who monitor events they think are unusual. We are being screened for things we already know as side effects of the drug, Said Dr Kilbridge. Robert Calif. commented that in the future, the most active surveillance systems will automatically report to both the pharmaceutical company and MedWatch. However, it raised the question of whether the FDA would be able to cope with the increased volume of reports. Computer data can be used to identify a signal that indicates the potential presence of an adverse event, after which humanitarian specialists can intervene (Bates et al., 2003). Several systems and approaches based on the allegations that provide this information were discussed (i3 Drug Safety, Department of Veterans Affairs [VA], and the Health Organization Research Center [HMORN]). According to Francesca Cunningham of these approaches benefit from understanding characteristics of the population as well as adverse events. Various recording systems patient information. All this information needs to be integrated to form complete patient health data. Arnold Chan of the Harvard School of Public Health highlighted page 3 Page 27 Share quote, suggested citation: 4 User involvement in reporting adverse events. Institute of Medicine. 2007. Reporting of adverse events in the field of drugs: Role of consumers and healthcare professionals: Summary of the seminar. Washington, DC: National Academies Press. Doi: 10.17226/11897. × risk for renal toxicity. In all likelihood, this is a direct result of the change in clinical practice, Mr. Katz said. In 2004, the IMF re-joined in educating patients about potential zoledronic acid-related adverse events after receiving a notice of a high incidence of osteonecrosis of the jaw in patients taking the drug. A study of the web-based study of myeloma and breast cancer, conducted in July 2004 by the IMF, found that the risk associated with time dependence was related to the drug (Durie et al., 2005). Public education programmes that raise public awareness and report tangible benefits of improving adverse reaction reporting systems are ways in which patient advocacy groups and even patients themselves can play a role in reducing adverse drug events (ESEs). The development of improved user reporting infrastructure will benefit from the increased contribution of those that the system was intended to serve. MedWatch captures only one part of the adverse events occurring, leaving the overall burden unknown. Alison Raine of the National Consumer League concluded that this was partly due to the lack of meaningful user engagement in the process and the fact that reporting mechanisms were divorced from routine practice. Dr Marvin Lipman of the Consumers Union said: In order for consumers to play a role, they need to be informed about the importance of reporting adverse effects of the drug, not only to their doctor and pharmacist, but also to the central body, the FDA. Ms Raine said MedWatch was not on most users' radar and was not integrated into the healthcare delivery system. It compared patient communication under the current MedWatch system with the new UK yellow card system (see Table 4-1). This system is managed by the Medicines and Healthcare Products

Regulatory Agency (MHRA) and supervises safety. Each report, which is actually a yellow card, is recognised and registered on receipt and then entered in the MHRA's adverse reaction database. The reports are evaluated by healthcare professionals in the pharmacovigilance group of the Post-Licensing Department of the MHRA. This assessment shall include the use of data from other sources, such as ex ante post-clinical trials, medical literature case reports, data from other drug regulatory agencies, epidemiological studies and registry contact databases. The Committee on Drug Safety and the Pharmacovigilance Subcommittee advise the MHRA on potential safety issues and appropriate regulatory The yellow card system allows users to report online, on prepaid letters and over the phone. Translation services are available to those who are page 4 Page 36 Share citing quoting suggested citation: 5 interactions of drugs and drugs. Institute of Medicine. 2007. Reporting of adverse events in the field of drugs: Role of consumers and healthcare professionals: Summary of the seminar. Washington, DC: National Academies Press. Doi: 10.17226/11897. × interactions of greatest clinical importance, noted Jacob Abarca of the University of Arizona College of Pharmacy. A recent analysis carried out by Dr. Abarza noted a limited agreement between drug interactions considered to be of greatest clinical importance (i.e. major drug interactions) (Abarca et al., 2004). Four commonly used drug interaction compensations were selected for analysis: Drug Interaction Assessments (2001), Drug Interaction Facts (Mangini, 2001), Drug Interactions: Analysis and Management (Hansten and Horn, 2001), and the DRUG-REAX Program (Moore, etc., 2001). The analysis found 406 DPI that were classified as of greatest clinical importance in at least one of these references. Only 2% are listed in the four compensations. The interclass correlation coefficient is 0.09, which indicates a very low arrangement on the classification of major drug interactions. Russell Teagarden of Medco Health Solutions, Inc., recommends establishing single interaction and adverse drug response criteria to reduce variability in determining what constitutes a major interaction. Mr Teagarden, who has contributed to the facts of drug interaction (Mangini, 2001), pointed out that there is variability not only among sources, but often within groups working on each individual source. He said existing databases are not integrated, so clinically important information does not come from a single, easily accessible system. The establishment of single criteria for drug interactions and adverse drug reactions may refer to problems with strength and co-health among the sources of information. Dr. Kahn noted that standardized terminology for equally evaluating interactions for their clinical significance is a necessity, because if you can't describe it, then you can't analyze it. The variable quality of the data makes much of the collected knowledge unusable. Although databases may alert doctors and pharmacists to dangerous interactions, healthcare providers are unable to respond to any alarm while still performing their clinical duties. Doctors may become subject to emergency fatigue, which can cause notifications to be bypassed or turned off. Dr. Weingarth noted that some systems are too sensitive, which leads to many alarms; this results in performance of the pharmacist. Using computerized systems creates the ability to issue alerts for potential DDIs. However, these signals are embedded in other medication signals that can make it easy to ignore DDIs. Up to 88 per cent of all by public pharmacists (Chui and Rupp, 2000), said Dr. Abarca, and only one in nine signals is considered useful by suppliers, according to a 2005 study (Spina et al., 2005). I think if we send a warning to a pharmacy that said your pharmacy will explode in five seconds, they'll just overexcit it and switch to the next prescription, Mr Teagarden said. Pharmacists and suppliers, however, believe that DDI signals are more useful than other types of drug use signals (Abarca et al., 2006). 5 He added: The end result is that the information currently available does not help prescribers in managing patients in real time. Because DDIs includes at least two drugs, interaction information can be placed on the label for the newer product in an interactive pair, but not for the older drug. The side effects listed on the label give no indication that the likelihood of occurrence of these symptoms is higher when taking the drug or placebo. Robert Calif. stressed the need for a third party (neither the FDA nor the pharmaceutical industry) to decide what information is relevant to consumers and useful to prescribers and should therefore be included in the labeling. I wouldn't want the content of the label to be a market-oriented issue or an opinion poll, Dr. Calif. said. Mr Teagarden offered the United States Pharmacopoeia (USP) as a good environment for developing an official list of drug interactions derived from its official content monograph. The USP has already defined a medical error through its National Coordination Council for Drug Reporting and Prevention (ICC MERP). The USP founded NCC MERP in 1995 and its membership includes 22 patient safety groups (SCC MERP, 2005). NCC MERP argues that its definition of drug errors is a successful development. According to the NCC's MERP, an error in drug therapy is any preventable event that can cause or cause inappropriate use of drugs or harm the patient while the drug is under the supervision of a healthcare professional, patient or user. Such events may relate to professional practice, healthcare products, procedures and systems, including prescribing; communication with the order; labelling, packaging and product nomenclature; mixing; submission of distribution; the application of education; monitoring; (SME of the SCC, 2005). This definition has been adopted by the FDA, Centers for Media Social Services and Medicaid Services (CMS) and USP. The development of a common nomenclature has the potential to improve the ability of different institutions to exchange information. A working group using NCC MSP information as a model could improve the information provided to the prescriber. The group can bring together experts from academia, practice, pharmacy and industry, as well as regulatory bodies. It may be improving the tools that are already available to communicate interactions between drugs and their likely effects, Dr Kahn said. The FDA has several related regulatory initiatives to the safety of drugs. The e-labeling rule requires the industry to submit electronic labels to the FDA starting in June 2006. MedWatchPlus will merge adverse events page 6 HHS (Ministry of Health and Human Services) Office for Human Research Protection 2005. Request for public comment on ohrp's draft recommendation on the reporting and review of adverse events and dislike problems related to risks to participants or others . [Online]. Available: [accessed March 7, 2006]. Hillestad R, Bigelow J, Bower A, Girosi F, Meili R, Scoville R, Taylor R. 2005. Can electronic medical records systems transform health care? Potential health, savings and cost benefits. Healthcare 24:1103–1117. 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Medical Journal of Australia Australia medicines and healthcare products (MHRA). 2005. What happens with a yellow card. Available: [accessed March 6, 2006]. Mitchell AA. 2003. Systematic identification of medicines causing birth defects – New possibility. New England Journal of Medicine 349(26):2556-2559. Moore L, Minna K, Moore KB. 2001. Drug reaction system. [Online]. Available: [accessed February 21, 2006]. NCC MERP (National Coordination Council for Reporting and Prevention of Drug Errors). 2005 ICC ICC: the first ten years. Identifying the problem and developing solutions: Summary. [Online]. Available: [Accessed February 15, 2006]. 2005. Cash safety—Risk monitoring in approved medicines. New England Journal of Medicine 352(12):1173-1176. Page 7, page 53 Share the quote: Seminar program. Institute of Medicine. 2007. Reporting of adverse events in the field of drugs: Role of consumers and healthcare professionals: Summary of the seminar. Washington, DC: National Academies Press. Doi: 10.17226/11897. × Seminar Daily Forum for Discovery, Development and Translation The role of consumers and health professionals in reporting adverse events in the field of drugs – main challenges and opportunitiesNew opportunities 3–4, 2005 Phoenix Park Hotel 520 North Capitol Street, NW Washington, DC 20001 Thursday, November 3, 2005 8:30 a.m. Opening notes Jeffrey M. Dryson, New England Journal of Medicine Topic 1: Recognition and Reporting of Adverse Drug Reactions by Physicians, Including Stimuli and Deterrents (e.g. Churg-Strauss Syndrome with Anti-Leukothriene; Liver Failure with Anti-Diabetic Drugs; Immunomodulators). 8:40 am Daniel E. Troy, Jade Sidley Austin Brown &wood LLP Anne E. Trontell, MD, MPH U.S. Food and Drug Administration Richard Platt, MD, MS Harvard Medical School Page 8 agenda. Dr. Hunt, who is licensed to practice medicine in the District of Columbia, has been certified by the American Board of Surgery and has been an associate of the American College of Surgeons since 1993. Practicing surgery in both private and academic settings, Dr. Hunt was a clinical assistant professor of surgery at Howard University, as well as chair of surgical peer review at various hospitals in the Washington metropolitan area. Saira A. 1. PharmD, MS , is director of clinical programs, pharmacy management, at Horizon Blue Cross Blue Shield of New Jersey (BCBSNJ), where it is associated with pharmacist management, formula management, patient safety initiatives drug information, usage analysis, research and clinical outcomes, and disease management condition. She is also director of the postgraduate pharmacy program at Horizon BCBS. She is actively engaged in research and is director of In 2000, Dr. Yang received a master's degree in pharmacology from St. John's University in New York and her Farm from Rudgers, New Jersey State University. He graduated from Harvard Medical School. After completing his training in internal medicine, he completed a program in clinical pharmacology and was a fellow in clinical pharmacology. BCDSP is a pioneer in the use of automated databases in drug safety studies. Dr Jack, along with his colleagues at BCDSP, published more than 300 studies over a 35-year period. In addition, he organised several international seminars on post-marketing medicine research, the 21st of which took place in France in June 2005, collecting experts in the field to share information on recent developments in pharmacoepidemiology. Dr Sidney Khan is a major factor in the development of pharmacovigilance, risk assessment and risk management. After 17 years in the academic laboratory medicine in the UK and US as director of laboratory and principal investigator, he spent the next 13 years at Bristol-Myers Squibb and Johnson & Johnson working to assess the safety of medicinal products throughout their lifecycle. In July 2002, it established Pharmacovigilance Risk Management (Inc. Inc.). During his time as industrial ruler, Dr. Khan was actively involved in several United States and international