

Sources of European drug consumption data at a country level

Pili Ferrer · Elena Ballarín · Mònica Sabaté · Joan-Ramon Laporte ·
Marieke Schoonen · Marietta Rottenkolber · Joan Fortuny ·
Joerg Hasford · Iain Tatt · Luisa Ibáñez

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Abstract

Objectives This study aimed at outlining the characteristics of nationwide administrative databases monitoring drug consumption in Europe.

Methods Internet and bibliographic databases (April 2010) were searched and experts in drug utilization (DU) research interviewed to find nationwide administrative medicines consumption databases in Europe, with data for the out- and inpatient healthcare sector. A questionnaire was developed to gather additional information. We collected data providers, websites, accessibility, data sources, healthcare settings, population coverage, medicines-related data, patient and prescriber data, periods covered, and linkage to other databases.

Results Thirty-one administrative nationwide medicine consumption databases in 25 countries were identified. Questionnaires were responded for 20 databases. Eleven provided wholesalers' sales data, 11 on reimbursed, 5 on prescribed, and 4 on dispensing medicines. Fifteen databases provided inpatient drug consumption data, mainly wholesalers' sales.

Conclusions Nationwide administrative databases are of value to all stakeholders involved in the conduct and interpretation of post-marketing safety studies, and in the conduct of DU research. The endorsement of the anatomical therapeutic chemical/defined daily dose methodology by these databases contributes to data harmonization. However, there is still a lack of information on inpatient medicines consumption at a patient-level.

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P. Ferrer · E. Ballarín · M. Sabaté · J.-R. Laporte · L. Ibáñez
Fundació Institut Català de Farmacologia, Pg. Vall d'Hebron
119-129, 08035 Barcelona, Spain

E. Ballarín · M. Sabaté · J.-R. Laporte · L. Ibáñez
Servei de Farmacologia, Hospital Universitari Vall d'Hebron,
Barcelona, Spain

E. Ballarín · M. Sabaté · J.-R. Laporte · L. Ibáñez (✉)
Departament de Farmacologia, Terapèutica i Toxicologia,
Universitat Autònoma de Barcelona, Pg. Vall d'Hebron
119-129, 08035 Barcelona, Spain
e-mail: li@icf.uab.es

M. Schoonen
Center for Observational Research, Amgen Ltd., 1, Uxbridge
Business Park, Sanderson Road, Uxbridge, Middlesex, UK

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M. Rottenkolber · J. Hasford
Institute for Medical Information Sciences, Biometry and
Epidemiology, Ludwig Maximilians Universität-München,
Marchioninstr. 15, 81377 Munich, Germany

J. Fortuny
Global Clinical Epidemiology Department, Novartis Pharma
AG, Gran Vía Corts Catalanes, 764, 08013 Barcelona, Spain

I. Tatt
Information and Ophthalmology, EpiPRO, Grenzacherstrasse
124, Hoffmann-LA Roche, 4070 Basel, Switzerland

Introduction

Pharmaceutical expenditures have increasingly become a reason for concern for governments and healthcare providers. Studies published between 1995 and 2006 have shown that per capita medicine expenditures have increased an average of 50 % (Lu et al. 2011). Administrative registers, originally set up to monitor pharmaceutical expenditures, are currently a source of medicines consumption data for pharmacoepidemiological research (Furu et al. 2010). Parallel to the implementation of these medicines registers, different automated databases have been developed as a result of the increasing number of patient healthcare encounters that are now electronically registered and the possibility of establishing record linkage systems (Panneman et al. 2003).

Administrative databases offer several advantages: they cover large populations and the data are readily available and easy to access, enabling results to be obtained at lower costs and in less time (Schneeweiss and Avorn 2005). Most of these advantages apply, mainly, to databases with aggregated drug consumption data freely downloadable. Nevertheless, these databases also have downsides. First, not all variables regarded as potential confounders of an association may be collected (van Walraven and Austin 2012). Second, validity and accuracy of the data collected are not systematically assessed, and there is no standard set of rules on how and what data to collect. Third, the information is only registered for those individuals making use of the health services (Sorensen et al. 1996). Finally, institutions must guarantee anonymity, thereby hampering access to data.

For the past 15 years in Europe, different initiatives have evolved to compile information on the sources of medicines utilization (Walley 2003; EurMedStat Project 2007; Cross-National Comparison of Drug Utilization 2008). The objective, within the pharmacoepidemiological research on outcomes of therapeutics by a European Consortium (PROTECT) project is to review and compile knowledge regarding European sources of data on drug utilization (DU) in the out- and inpatient healthcare sector. The aim of this manuscript was to outline the main characteristics of European administrative sources of DU data at the country level.

Methods

We defined nationwide administrative medicines consumption databases as those population-based databases supported by governmental organizations or health insurance companies or sickness funds, all of which collect information on medicine sales at manufacturer or wholesaler levels and/or at the pharmacy level.

We conducted an Internet search in a hierarchical manner, from institutional European websites to governmental websites and to the websites of international and national research networks on DU (see Online resource 1). We also searched in the following bibliographic databases: PubMed (1975 to March 2010) and SIETES [Sistema de Información Esencial en Terapéutica y Salud, <http://www.sietes.org>, (1960 to March 2010)]. SIETES is a Spanish electronic database with a selected bibliography pertaining to clinical pharmacology and pharmacoepidemiology and is managed by the Catalan Institute of Pharmacology. We also searched Google (no date limits) free-access websites that did not require registration or passwords. There were no language restrictions. The following keywords were used: “pharmacoepidemiology”, “drug utilization”, “international cooperation”, “databases”, “Europe”, and the names of authors of published articles on DU. Informal contacts and interviews with European experts in the field of DU research completed this search.

The focus was on nationwide administrative databases monitoring drug consumption either in the out- or inpatient healthcare setting. Electronic medical-record databases were excluded. For operational purposes, we define Europe geographically and do not include Turkey or Israel.

Finally, 59 European national medicines agencies or ministries of health or sickness funds were approached by email. When a contact person was identified, an ad hoc questionnaire was sent (see Online Resource 2). The questionnaire was partially filled with information on databases that were available in-house and retrieved from the search. We asked each contact to complete the questionnaire and amend any errors.

Information was collected on data providers, websites, sources of medicines consumption data, healthcare settings, population coverage (the proportion in a particular database of a country’s inhabitants from which DU figures were compiled), information related to the medicines (packages, dosages, medicines codifications, measurement units, dates of prescription and dispensing, indications for which the medicines were dispensed or prescribed), sociodemographic and clinical characteristics of the patients, prescriber information, internal validity of each database, periods covered, potential record linkages with other databases, and external accessibility of the databases for research purposes.

Results

Thirty-one nationwide drug consumption databases and 31 contact persons were identified in 25 countries. Twenty contacts responded to the questionnaire. Table 1 provides a summary of the main characteristics of European

Table 1 Nationwide administrative drug consumption databases in Europe, 2013

Countries	Database name	Data providers	Website	Accessibility	Data source
Belgium	Pharmanet	National Institute for Health and Disability Institute (INAMI)	http://www.inami.fgov.be	Application: http://www.inami.fgov.be/drug/fr/statistics-scientific-information/pharmanet/request/index.htm	Reimbursed
Bulgaria	Not provided	Bulgarian Medicines Agency	http://www.bda.bg	Application: Medicines Use Control Department, Maria.popovada.bg	Sales
Croatia	Not provided	Croatian Drug Agency	http://www.almp.hr/?ln=en	Free online: http://www.halmed.hr/?ln=hr&w=publikacije&d=potrosnja_lijekova . Application: viola.maco@ic@halmed.hr	Sales
Czech Republic	Not provided	The State Institute for Drug Control	http://www.sukl.eu	Application: Press and Information Department, posta@sukl.cz	Sales (2006), dispensed (2011)
Denmark	Register of Medicinal Products Statistics	Danish Health and Medicines Authority	http://sundhedsstyrelsen.dk/en/about-us	Free online: http://www.medstat.dk . Further data: medicindata@ssi.dk	Dispensed
Denmark	Danish National Database of Reimbursed Medicines	Department of Clinical Epidemiology at Aarhus University Hospital	http://kea.au.dk/en/research/	theinternationaldatabaseofreimbursedprescriptions	Application: data available only for researchers all over Denmark
Reimbursed					
Estonia	Estonian Health Insurance Fund (EHIF) database	Estonian Health Insurance Fund	http://www.haigekassa.ee	Application: infor@haigekassa.ee	Reimbursed
Estonia	State Agency Medicines (SAM) database	State Agency of Medicines	http://www.sam.ee	Application: info@viamet.ee	Sales
Finland	Prescription register database	Social Insurance Institution	http://www.kela.fi	Application: Kela Research Department, tutkimus@kela.fi	Reimbursed
Finland	Drug sales register	Finnish Medicines Agency	http://www.fimea.fi	Application: communications@fimea.fi	Sales
France	Agence Nationale de la Sécurité des Médicaments (ANSM) database	National Agency of Medicines and Health Products Safety	http://www.ansm.sante.fr	Application: communications@ansm.sante.fr	Sales
France	ERASME database	National Insurance Fund for Salaried Employees-CNAMTS	http://www.ameli.fr/index.php	Application: http://www.ameli.fr/assurance-maladie/formulaire-de-contact.php	Reimbursed
Germany	Wissenschaftliches Institut der AOK (WiDO) database, Research Institute of the Statutory Health Insurance AOK	The Research Institute of the General Medical Insurance Plans (AOK)	http://wido.de/arzneiverordnungs-rep	Application: helmut.schroeder@wido.bv.aok.de, valentina.cocca@wido.bv.aok.de	Reimbursed
Hungary	Not provided	Directorate General of National Institute of Pharmacy	http://www.ogyi.hu	Application: ogyi@ogyi.hu	Sales
Iceland	Not provided	Icelandic Medicines Agency	http://www.lyfjastofnun.is	Free online: http://www.lyfjastofnun.is/Tolfractil/ , http://www.imca.is/fmea/statistics/nmr235	Sales
Iceland	The Icelandic Medicines Registry	Directorate of Health	http://www.landlaeknir.is/english/	Application: http://www.landlaeknir.is/english/	Dispensed
Ireland	Health Service Executive-Primary Care Reimbursement Services (HSE-PCRS) database	Department of Health and Children, Health Service Executive (HSE)	http://www.hse.ie/eng/stat/PCRS/	Application: pers@hse.ie	Reimbursed
Italy	OsMed database	Italian Medicines Agency, Medicines Utilisation Monitoring Centre	http://www.agenziafarmaco.gov.it/it/content/consumi-e-spese-farmacaceutica-e-attivita/C3%A0-hua	Application: farmaciline@aifa.gov.it	Dispensed

Table 1 continued

Countries	Database name	Data providers	Website	Accessibility	Data source
Latvia	Not provided	State Agency of Medicines of Latvia	http://www.vza.gov.lv/index.php?id=305&sa=305&top=298	Application: info@vza.gov.lv	Sales
Lithuania	National Health Insurance Fund (NHIF) database	National Health Insurance Fund	http://www.vlk.lt/	Application: Kristina.Garnoliene@vlk.lt	Reimbursed
The Netherlands	Genes-en hulpmiddelen Informatie Project (GIP) databank	Health Care Insurance Board	http://www.gipdatabank.nl	Free online: http://www.gipdatabank.nl Further data: info@gip@cvz.nl	Reimbursed
The Netherlands	The Dutch Foundation for Pharmaceutical Statistics (SFK) database	Foundation for Pharmaceutical Statistics	http://www.sfk.nl	Application: info@sfk.nl	Dispensed
Norway	Norwegian Prescription Database (NorPD)	Norwegian Institute of Public Health	http://www.fhi.no	Free online: http://www.norpd.no Further data: datatilgang@fhi.no	Prescribed
Norway	Wholesalers drug statistics	Norwegian Institute of Public Health	http://www.fhi.no	Application: imfin@fhi.no	Sales
Poland	Not provided	National Health Fund	http://www.nfz.gov.pl	Application: rzecznikprasowy@nfz.gov.pl	Reimbursed ^b
Portugal	Infarmed database	National Authority of Medicines and Health Products, IP	http://www.infarmed.pt	Application: demps-amps@infarmed.pt	Prescribed, dispensed HOM ^d
Slovenia	Not provided	The National Institute of Public Health	http://www.ivz.si	Application: marjeta.jelenc@ivz-rs.si	Prescribed
Spain	Not provided	General Directorate of Pharmacy and Health Products	www.msc.es/profesionales/farmacia/organizacion.htm	Application: abenedi@mssi.es, oiaic@mssi.es	Reimbursed
Sweden	Swedish Prescribed Drug Register	The National Board of Health and Welfare	http://www.socialstyrelsen.se/	Free online: http://192.137.163.49/sdb/lak/va1.aspx . Further data: Andrejs.Leimamis@socialstyrelsen.se, Helena.Schioler@socialstyrelsen.se	Prescribed
Sweden	Not provided	Swedish eHealth Agency (from January 2014) (prior National Corporation of Swedish Pharmacies)	http://www.ehalsomyndigheten.se/ (from January 2014)	Free online: http://www.apotekensservice.se/lakemedelsstatistik/sok_statistik/sok_statistik_databaser/sokfunktion_recept/ . Further data: registrator@ehalsomyndigheten.se	Sales
United Kingdom	Electronic Prescribing Analyses Cost database	NHS Business Service Authority, Prescribing Services, Electronic Prescribing Analyses and Cost	http://www.nhsbsa.nhs.uk/PrescriptionServices.aspx	England: http://www.hscic.gov.uk/primary-care , Hospital data: http://www.hscic.gov.uk/article/2021/Website-Search?productId=9217&q=hospital+prescribing&ort=Relevance&size=10&page=1&area=both#top . Further data: enquires@hscic.gov.uk. Northern Ireland: http://www.hscbusiness.hscni.net/services/1806.htm . Further data: Admin.Office@hscni.net. Wales: http://wales.gov.uk/statistics-and-research/prescriptions-dispensed-community/?lang=en . Further data: stats.healthinfo@wales.gsi.gov.uk. Scotland ^e : http://www.isds.scotland.org/Health-Topics/Prescribing-and-Medicines/Community-Dispensing/Prescription-Cost-Analysis/ . Further data: nss.csd@nhs.net	Prescribed

Table 1 continued

Countries	Database name	Healthcare setting	Population coverage	ATC/DDD ^a	OTC	Data by age/gender	Record linkage
Belgium	Pharmanet	Outpatient	99 %	Yes	No	Yes	Yes (within INAMI)
Bulgaria	Not provided	Out/inpatient	100 %	Yes	Yes	No	No
Croatia	Not provided	Out/inpatient	100 %	Yes	Yes	No	No
Czech Republic	Not provided	Outpatient	100 %	Yes	Yes	Yes (since 2011)	No
Denmark	Register of Medicinal Products Statistics	Out/inpatient	100 %	Yes	Yes	Yes	Yes
Denmark	Danish National Database of Reimbursed Medicines	Outpatient	100 %	Yes	Yes	Yes	Yes
Estonia	Estonian Health Insurance Fund (EHIF) database	Outpatient	95 %	Yes	No	Yes	No
Estonia	State Agency Medicines (SAM) database	Out/inpatient	100 %	Yes	Yes	No	No
Finland	Prescription register database	Outpatient	100 %	Yes	No	Yes	Yes
Finland	Drug sales register	Out/inpatient	100 %	Yes	Yes	No	No
France	Agence Nationale de la Sécurité des Médicaments (ANSM) database	Out/inpatient	100 %	Yes	Yes	No	No
France	ERASME database	Outpatient	87 %	Yes	No	Yes	Yes
Germany	Wissenschaftliches Institut der AOK (WiDO) database, Research Institute of the Statutory Health Insurance AOK	Outpatient	85 %	Yes	No	Yes	Yes
Hungary	Not provided	Out/inpatient	>90 %	Yes	Yes	No	No
Iceland	Not provided	Out/inpatient	99 %	Yes	Yes	No	No
Iceland	The Icelandic Medicines Registry	Outpatient	93 %	Yes	Yes	Yes	Yes
Ireland	Health Service Executive-Primary Care Reimbursement Services (HSE-PCRS) database	Outpatient	37 %	Yes	No	Yes	Yes
Italy	OsMed database	Out/inpatient	100 %	Yes	Yes	Yes	Yes, at regional level
Latvia	Not provided	Out/inpatient	100 %	Yes	Yes	No	No
Lithuania	National Health Insurance Fund (NHIF) database	Outpatient	98 %	Yes	No	Yes	No
The Netherlands	Genees-en hulpmiddelen Informatie Project (GIP) databank	Outpatient	95 %	Yes	No	Yes	No
The Netherlands	The Dutch Foundation for Pharmaceutical Statistics (SFK) database	Outpatient	95 %	Yes	Yes (the 50 % of OTC drugs sold by pharmacies)	Yes	No
Norway	Norwegian Prescription Database (NorPD)	Outpatient	100 %	Yes	No	Yes	No
Norway	Wholesalers drug statistics	Out/inpatient	100 %	Yes	Yes	No	No
Poland	Not provided	Outpatient	100 %	Yes	No	Yes	No
Portugal	Informed database	Out/inpatient	100 %	Yes	Yes (sales)	No	No
Slovenia	Not provided	Outpatient	99 %	Yes	No	Yes	No
Spain	Not provided	Outpatient	100 %	Yes	No	No	No
Sweden	Swedish Prescribed Drug Register	Outpatient	100 %	Yes	No	Yes	Yes
Sweden	Not provided	Out/inpatient	95–100 %	Yes	Yes	Yes (for the outpatient sector)	No

Table 1 continued

Countries	Database name	Healthcare setting	Population coverage	ATC/DDD ^a	OTC	Data by age/gender	Record linkage
United Kingdom	Electronic Prescribing Analyses Cost database	Outpatient, inpatient data available for England	100 %	British National Formulary/average daily quantities. ATC/DDD upon request	No	No	No

OTC over the counter medicines, *HOM* Hospital-only medicines

^a Anatomical therapeutic chemical codification (ATC). Defined Daily Doses (DDD) as unit of measurement of drug use

^b Currently the National Health Insurance Fund of Poland only holds data on the value of medicines. Drug consumption data are retrieved from IMS (Personal communication)

^c In Scotland, there is the National Medicines Utilisation Unit set up in 2005 with patient-level data (<http://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/National-Medicines-Utilisation-Unit/>). Contact: m.bennie@nhs.net)

medicines consumption databases. Online resource 3 displays all database information retrieved via the questionnaire. Information was last updated in December 2013. All websites were last accessed on January 14, 2014. Switzerland and Russia do not have nationwide drug consumption databases.

Sources of data on medicines consumption were defined as described below: (a) sales: sales of medicinal products from wholesalers to the community or hospital pharmacies and other outlets. These are usually provided at an aggregate level. (b) Dispensed: medicines dispensed to patients at community pharmacies, either prescribed or not prescribed; therefore, these databases include data on over-the-counter (OTC) medicines. (c) Prescribed: prescription medicines dispensed at community pharmacies; this does not include OTC medicines, except when there is an authorised indication for which these OTC medicines may be prescribed. However, they include those medicines prescribed and dispensed but not reimbursed, e.g. oral contraceptives. (d) Reimbursed: medicines reimbursed by the health authorities or sickness funds; these medicines must be prescribed by a healthcare professional, dispensed at a pharmacy and reimbursed by the healthcare provider. OTC medicines and non-reimbursed prescription-only medicines are not included.

Discussion

We provided information on 31 nationwide sources of medicines consumption data in Europe. These databases were maintained either by governmental organizations such as national medicines and medical products agencies, or by health sickness funds. Most of the databases were originally created for administrative purposes. However, they are increasingly used in pharmacoepidemiology, especially in DU research (Schweeneiss and Avorn 2005).

The drug-data provider is closely linked to the country's health system organization and determines the sources of available drug consumption data. For instance, in France, on the one hand, the French Medicines Agency gives wholesalers' sales statistics because those who own the marketing authorization for a medicinal product must, by law, supply the agency with a declaration of the sales of that product in both out- and inpatient settings (Agence Nationale de Sécurité du Médicament et des Produits de Santé 2012). On the other hand, the French National Health Insurance provides information on reimbursed medicines in the outpatient sector (Assurance Maladie-France 2012).

Monitoring trends of medicines consumption could estimate the prevalence, incidence, and duration of exposure to particular drugs. These measures can best be derived from those databases gathering information on the

number of users of particular medicinal products (Schneeweiss and Avorn 2005), such as the Nordic databases. Sales from wholesalers that include pharmacy stock movements and parallel trade may overestimate drug consumption. Conversely, reimbursement data may underestimate medicines consumption, as it does not include OTC medicines or prescribed non-reimbursed medicines. The over- or underestimation of drug consumption in each data source may depend on the group of medicines under study. For instance, approximately 30 % of antibacterials for systemic use are sold OTC in countries like Spain and Italy (Gagliotti et al. 2009). Therefore, sales of medicines may offer a more accurate estimate of population exposed to antibacterials than reimbursed antibacterials. Oral contraceptives, which must be prescribed but may not be reimbursed, may be underestimated in databases providing reimbursement data (Stolk et al. 2008). Dispensing databases may provide better estimates of the proportion of population exposed to NSAIDs (Bernard et al. 2012).

These databases cover almost the entire population of a given country, except for the ERASME database in France (87 %), the WiDO database in Germany (85 %), and the Health Services Executive-Primary Care Reimbursement Services' (HSE-PCRS) pharmacy claims database in Ireland (37 %). The ERASME database represents the largest health insurer in France. However, there are two additional reimbursement databases covering farm and agricultural workers and civil servants. In Germany, the WiDO database covers prescriptions provided to the German population and covered by the largest Statutory Health Insurance. Although the HSE-PCRS database covers only the population that is eligible for the General Medical Services (GMS) scheme, it captures more than two-thirds of the prescriptions issued in the country (Brewer et al. 2013). Eligibility for the GMS scheme depends on the patient's income for patients <70 years old and free for those ≥ 70 years old. It overrepresents children, women, the elderly and people on low incomes (Zaharan et al. 2013). The Dutch databases also covered <100 % of the population, but only the GIP database provided the weighting methodology used.

All databases could be a source for the study of patterns of drug use over time and across countries. As every database provides drug consumption data following the anatomical therapeutic chemical (ATC) classification of drugs and the defined daily dose (DDD) recommended by the WHO Collaborating Centre for Drug Statistics Methodology. Outpatient consumption is usually expressed in DDD per 1,000 inhabitants and per day or per year (WHO Collaborating Centre for Drug Statistics Methodology 2014). However, for inpatient medicine consumption, several denominators have been proposed, as follows: bed-

days (Capellà 1993), patient-days (United States Center for Disease Control and Prevention 2011), admissions (Filius et al. 2005), discharges (VinCat database methodology 2011), and finished consultant episodes (Curtis et al. 2004). In the United Kingdom, the ePACT database codes the medicines according to the British National Formulary (BNF) chapters and measures the consumption in average daily quantities and DDDs. Nevertheless, an ATC booklet is provided to facilitate cross-comparisons with the BNF classification of medicines.

The major limitation of every database is that there is always a lower or higher degree of exposure misclassification because no database captures patient compliance. Only the Danish prescription register can to some extent estimate primary non-compliance, i.e. the percentage of electronic prescriptions transmitted to the pharmacies that remained unclaimed. Some authors state that uncollected prescriptions from the pharmacy may not be of importance when estimating drug exposure (Tobi et al. 2004), whereas other authors have found differences in redemption rates by age, gender, and group of medicines (Ekedahl and Månsson 2004). Studies of sensitivity and specificity comparing the drug consumption captured with these databases and the intake of drugs reported by the patient himself have been conducted for several of these databases (Richardson et al. 2013; Kildemoes et al. 2011). These studies have been conducted for specific groups of drugs or population subgroups, and it is difficult to know whether they are generalizable to the rest of the groups of medicines and population subgroups.

Another limitation of estimating drug exposure at the aggregated level is that, at most, patterns of drugs use may be stratified by age, gender, and region. Only Danish, Swedish, Norwegian and Finnish databases enabled a record-linkage system to be established with other nationwide databases through unique personal identification numbers. Belgian, German and French reimbursement databases also established a linkage with other databases within a particular sickness funds organization, through an identification number. In addition, in Germany, people have a unique personal lifelong health-insurance number that allows continuity of information for patients who switch from one health insurance provider to another (Buchnera et al. 2013).

For inpatient healthcare settings, with the exception of Italy, all nationwide administrative databases that we found registered sales from wholesalers. In Italy, all medicines dispensed to a patient during her or his stay in a hospital are reimbursed by the local health authorities and are, therefore, registered in the appropriate regional databases. The inexistence of a centralized collection of inpatient dispensed data may be explained by the high heterogeneity in the management of medicines at a hospital level. The

medicines chain distribution may vary between different types of hospitals, and not all hospitals may have a hospital pharmacy. Moreover, in some countries, the absolute number of hospitals remains unknown (Vogler et al. 2010). Not registering exposure to medicines during hospital stays, especially for long stays, also introduces exposure misclassification. Even if it were possible to link outpatient databases with hospital discharge files, exposure misclassification would remain a concern, as most hospital discharge files have no information on drug exposure (Schneeweiss and Avorn 2005). Medicines consumption during hospital stays is also important, as it has been claimed that medicines prescribed in hospitals impact the prescribing behaviour of general practitioners (Bradley 1992), as well as patient's compliance. Approximately 60 % of patients experience changes in their medications during hospital stays (Himmel et al. 2004).

Focusing on the outpatient healthcare setting is understandable, as the outpatient sector represents the highest share of pharmaceutical costs. Medicines consumption in the inpatient healthcare setting ranges between 3 and 14 % of the total medicines consumption in a country (Vogler et al. 2010). Most of health policy research is conducted in the outpatient setting. The availability of inpatient drug consumption databases registering medicines dispensed to patients at a country level would certainly help to promote the rational use of medicines through cost-containment policies on the prescriber side and would improve the safety and quality of prescribing medicines.

A controversial issue, when using these administrative databases, is the definition of out- and inpatient drug consumption data. Apart from medicines dispensed to patients staying in hospitals, some countries may include those medicines prescribed by specialists or hospital-only medicines (HOM) dispensed to outpatients or medicines prescribed in long-term healthcare institutions, such as nursing homes and psychiatric clinics. In Portugal, the dispensation of HOM to outpatients is registered as inpatient drug consumption. As exemplified in Denmark, drug consumption in nursing homes is registered at the patient rather than the institutional level. For instance, a study on the use of antiepileptic drugs in institutionalized and community-dwelling elderly patients showed that 9 % of institutionalized elderly patients consumed antiepileptic drugs compared to only 2 % of their community-dwelling counterparts (Johnell and Fastbom 2011). Studies on the appropriateness of prescription of antiepileptic drugs should consider both settings separately, as health policy measures implemented to improve rational prescribing would likely differ between these two elderly populations.

The definition of healthcare setting needs to be considered, especially when conducting cross-national comparison studies of DU. On the one hand, this would help us to

understand the reasons for variations in drug use. On the other hand, it may elucidate potential relationships between variations in medicines consumption and other variables such as healthcare system features, cultural differences, population characteristics, burdens of disease, and clinical guidelines.

Among the main strengths of the present work is its compilation of such a high number of nationwide administrative databases that monitor drug consumption in Europe and its systematic description of their characteristics. Emphasis is put on the accessibility of medicines consumption data for research purposes, providing an up-to-date contact if it were publicly available on the website. In general the Nordic countries and the Netherlands, with their long tradition in DU research, offer aggregated drug consumption data that are freely available online. Researchers may apply for further data at the individual level. Usually a fee is required for these requests. Second, the completed questionnaires provided valuable information that enabled assessment of the degree of comparability of drug consumption data across countries and over time. Moreover, information obtained via the questionnaires was a means to confirm information collected through published manuscripts and/or databases websites. Although we do not present drug consumption information for the whole of Europe, we have compiled information for all those countries with the biggest populations. Another remarkable point is the scarcity of nationwide inpatient databases at the patient level. There is bound to be more information on inpatient DU at a national level, though this information is either not publicly available or not easily accessible making it almost invisible. A recently published review on the use of inpatient healthcare databases in observational studies confirmed that there were not nationwide administrative databases monitoring the consumption of drugs in the inpatient healthcare sector, in Europe (Larsen et al. 2013).

This work faces some limitations. First, this is not a systematic review, but a broad overview of the current state of nationwide administrative databases monitoring drug consumption in Europe. Second, the questionnaire was returned by 20 databases, hindering the validation of the information obtained. Third, the majority of the information provided is for the outpatient healthcare setting. This is consistent not only with the administrative nature of the databases, but also because most of the policies dealing with pharmaceutical costs are directed to the outpatient sector. Fourth, compilation of such a large amount of information is a challenging task. Previous European initiatives have been a useful resource. Unless this information is kept updated, all this record-keeping will quickly become meaningless and the results out-of-date. To channel these efforts into the right direction, funding is a

must. Fifth, linked to the aforementioned limitation, contact names provided in this manuscript are the ones publicly available from the websites, and people change positions; thus there is a need to update this information. Finally, there are other databases used in DU research and pharmacoepidemiology in general, such as clinical databases built on a sample of anonymised medical records collected by general practitioners (Clinical Practice Research Datalink, The Health Improvement Network database in England) or databases built on a linkage record system [PHARMO database in the Netherlands, Medicines Monitoring Unit (MEMO) in Scotland]. However, the latter databases were out of the scope of the present work, which focused on databases representative of the whole country.

This catalogue of European medicines consumption databases is the framework for DU studies in the assessment of the benefit-risk of a drug (Kurz 2011) which is the main objective of the PROTECT project. The use of these databases provides the denominators of populations exposed to particular drugs when calculating adverse drug reaction rates from spontaneous notifications (Lapi et al. 2010) or when conducting case-population studies that in certain circumstances estimate early risks and their public health impact (Capellà et al. 2002). Such databases may be used to identify discrepancies between patients taking a medicine after market authorization and patients who participated in clinical trials before the drug was launched. In 2002, desmopressin was approved in Denmark for the treatment of nocturia in adults and the summary of product characteristics warned of hyponatremia in elderly patients. A DU study found that desmopressin was mainly prescribed for patients >80 years (Callréus 2007). Such details are useful in the detection of misuse of groups of medicines affecting safety, for instance, whether the prescription of a medicine is adjusted to clinical guidelines (Donoghue and Tylee 1996; Brewer et al. 2013). These data can be used to calculate the public health impact of adverse drug reactions, as it has been done for benzodiazepines and antidepressants, and hip fractures (Khong et al. 2012; Prieto-Alhambra et al. 2014). Moreover, these databases may be helpful in assessing the effectiveness of health-policy decisions, such as the use of generics (Godman et al. 2010) and conducting cross-national comparisons as the European Surveillance of Antimicrobial Consumption group have already done, collecting data on the outpatient healthcare sector for 31 countries (Adriaenssens 2010).

Conclusion

Promoting the rational use of medicines is the ultimate goal of drug utilization research. These European national databases play a key role when conducting this research. This article presents information on sources of drug

consumption data of value to all stakeholders—researchers, pharmaceutical industries and regulators—involved in the conduct and interpretation of not only drug utilization research, but also of post-marketing safety studies. Since 2004 with the launch of the EURO-MED-STAT recommendations on the minimal contents of datasets and the promotion of the ATC/DDD methodology to harmonize data for monitoring drug consumption, there have not been other similar projects. This article showed that the ATC/DDD methodology was adopted by almost all databases. In addition, in Sweden, Scotland, Catalonia and Norway, health authorities are currently implementing programs with the aim of coordinating a patient's pharmacotherapy between the out- and inpatient healthcare setting. These programs should call for countries to monitor nationally representative data on inpatient medicines consumption at an individual level. The availability of nationwide and standardized out- and inpatient sources of medicines consumption data at an individual level would enhance quantitative and qualitative drug utilization studies.

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