Executive Summary

DRUG CONSUMPTION DATABASES IN EUROPE
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Different initiatives have arisen in Europe to gather information on drug utilisation (DU) for the last 25 years. Knowledge of the quantitative and qualitative patterns of drug use is a key element for the rational use of medicines, the rational assessment of the risk-benefit ratio and for decision-making on risk minimising actions for medicines.

In DU studies, information on prevalence, incidence, indication and duration of a treatment can be derived from different sources. First of all, there are data stemming from the different stages in the distribution chain of medicines: (i) dispensation with or without prescription, (ii) acquisition of medicines by hospital and community pharmacies or other outlets, straight from pharmaceutical manufacturers or through wholesalers, and (iii) reimbursement data. These data may be collected by governmental agencies or stored on pharmacies' databases or those of insurance companies. These sources of data are known as non-commercial drug data providers. In addition, data mining companies can conduct market surveys and thereafter sell the data stored in their databases. These sources of data are known as commercial data providers. In this report only IMS Health is mentioned as a commercial data provider. Secondly, there are sources of data on drug exposure obtained from the prescriptions registered on clinical databases. Thirdly, the current ingestion of medicines may be collected through interviews to patients. Finally, there are pharmacoepidemiological studies from which the utilisation rate for a class of drugs can be derived.

The databases cover large proportions of the population, the data are readily available and easy to access. However, these databases were initially created with an administrative purpose hampering their use in research. Not all variables regarded as potential confounders may be collected. Another problem is the inexistence of a standard method to evaluate the validity and accuracy of the data collected by these databases. Finally, the information is only registered for those individuals that reach the healthcare system, leaving out a segment of the population.

The objective of the Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium (PROTECT) project is to address the limitations of methods currently used in pharmacovigilance and pharmacoepidemiology, and to strengthen the monitoring of the benefit-risk assessment of medicines in Europe. The project is organised into seven workpackages (WP). The overall objective of WP2 “Framework for Pharmacoepidemiological Studies” is to develop, test and disseminate methodological standards for the design, conduct and analysis of pharmacoepidemiological studies. WP2 is organised into three working groups (WG). WG3 is in charge of reviewing and compiling knowledge about European sources of data on DU in the out- and inpatient healthcare sector. The project follows the recommendations from the World Health Organization (WHO) on the adoption of the Anatomical Therapeutic Chemical classification (ATC) of drugs and the measurement of drug exposure in Defined Daily Doses (DDDs). The PROTECT project includes the following adverse drug events: Calcium channel blockers (C08) - malignancies; antiepileptics (N03A) - suicide; benzodiazepine derivatives (N05BA,
N05CD) - hip fracture; antidepressants (N06A, N06CA) - hip fracture; beta-2-adrenergics (R03AC, R03AK) - acute myocardial infarction (AMI); macrolides (J01FA) and amoxicillin-clavulanic acid (J01CR02) - drug-induced liver injury.

To find out information on nationwide drug consumption databases we developed a search strategy that allowed for getting different sources of data on drug consumption considered of interest for drug utilisation studies: data providers, pricing and reimbursement agencies, information on marketed active substances, healthcare systems and reimbursement decisions adopted in each European country, and international drug utilisation working groups. As this is an ongoing study, we first limited the inventory to those European countries with a high population density, tradition in DU research and participation in the PROTECT project. First of all, we conducted a specific website search of global European institutions to country-specific governmental websites. Then, we searched bibliographic databases to find articles published by international working groups followed by a Google search, and finally we conducted interviews with experts in the field of DU. For each of the national drug consumption databases, the following information is provided: data provider, website, source of drug consumption, setting, population coverage, accessibility, drug codification, unit of measurement, drug-based information, prescriber and pharmacy information, potential confounders of a drug exposure, language of the database, record period and record linkage.

For the inpatient sector, the search strategy was slightly different. First of all, we reviewed the main available information on hospital drug utilisation for the drugs selected by PROTECT using a website and a bibliographic database search. Then, because of the importance of antibacterial consumption in the inpatient sector which is linked to the emergence and selection of antibiotic-resistant bacteria, a specific literature review was conducted to establish the availability of inpatient macrolides and amoxicillin-clavulanic acid consumption data in the selected PROTECT countries.

An area of special interest was to determine the validity of the national drug consumption data. Considering the bibliography available on the validity of drug consumption data and on the validity of automated databases in research, we developed a questionnaire including most of the items considered of relevance when measuring drug exposure. The key items referred to the definition of in- and outpatient drug consumption, population coverage, drug- and patient-based information, and database validity. However, these key items are also factors helping to interpret the results obtained when comparing drug consumption across countries and/or over time.

This complex methodology yielded a list of comprehensive and more specific institutional European websites (see Table 3), and international networks on DU studies (see Table 3). From them, we derived what we term background data: list of national medicines agencies (see Table 4), healthcare systems (see Appendix 8.3), pricing and reimbursement agencies (see Table 5), pharmaceutical data sources by country (see Table 6) and international networks and working groups in pharmacoepidemiology (see Appendix 8.4 and 8.5). For each of the international working groups, the following information was collected: website, definition,
objectives, record period, country-participants, funding and publications. These international networks have been divided into those offering general information: general research groups, and specific research groups, i.e. those studying either specific diseases or groups of drugs of interest for the PROTECT project.

Information on national drug consumption databases in Europe is provided for Belgium, Bulgaria, The Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Norway, Poland, Portugal, Spain, Sweden, The Netherlands and The United Kingdom (see Table 9 and 10). Few countries can provide data on the inpatient sector at a national level. In 2009, the consumption at ATC level 1 for the cardiovascular system (C), nervous system (N) and respiratory system (R) for the inpatient sector gave results in Denmark of < 4%, for ATC level 3 or 4; in Sweden of < 3%, and in France of <7% (see Appendix 8.6). From the bibliographic database search in the inpatient sector, the majority of articles were set in the outpatient setting and expressed drug consumption as a percentage of the active substance. For inpatient antibacterial consumption data sources see Appendix 8.8.

Questionnaires were received from Belgium, The Czech Republic, Denmark, France, Hungary, Italy, Norway, The Netherlands and Sweden. See Tables 13-15 for a summary of the information retrieved from the questionnaire.

The PROTECT inventory provides information on 19 European working groups and 20 nationwide drug consumption databases. In addition, sources of inpatient antibacterial consumption were identified in 7 countries and 1 region of Spain. For Denmark, France, Italy, Norway and Sweden inpatient drug consumption is available for drugs other than antibacterials. As expected, the Nordic countries and The Netherlands with their long tradition in drug utilisation research, are the ones to provide drug consumption data online which is free to download. For the rest of the countries, information should be applied for. Finland requires 1-1.5 years of notice before divulging such information.

The interest in compiling such information has evolved in the last 25 years from the EuroMedicines project that elaborated a drug directory for 14 European countries, to the EUROMEDSTAT project, the CNC (Cross National Comparison) project, the EuroDURG-ISPE (European drug utilisation group and International Society of Pharmacoepidemiology) collaboration and the ENCePP (European Network of Centres for Pharmacoepidemiology and Pharmacovigilance). Several specific international working groups have also been established to deal with a specific disease or a group of drugs that indirectly involve drug utilisation research.

Generally speaking, there is a scarcity of nationwide hospital drug consumption information, mainly attributed to the high heterogeneity in the management of medicines at a hospital level. In addition, when studying drug consumption in inpatient settings, the recommendations from the WHO for adjusting drug consumption to clinical activity are barely followed. In contrast to this lack of information on inpatient drug utilisation from non-commercial data providers, in 2008, IMS Health started the Hospital Audit Prescription which collects information on drugs
dispensed from hospital pharmacies to the patient, containing more clinical information (diagnostic) which is of interest in research.

The evaluation of validity of drug consumption data provides enough information to determine the comparability of the results in drug consumption across different countries or over time. Three European databases collect dispensed medicines which best assess drug exposure, as they include over-the-counter (OTC) drugs. Five databases collect reimbursed data, and three prescription data. The rest of the databases collect information on sales from wholesalers. The population coverage of most of these databases reaches 100%. ATC/DDD methodology has been adopted by all these databases, including the British ePACT database which collects information according to the British National Formulary (BNF) and measures drug consumption with Average Daily Quantities (ADQs). The ePACT database provides ATC codes and DDDS upon request. Most of the databases update retrospectively the ATC codes and DDD according to the WHO guidelines released every year. The problem with the ATC/DDD methodology has already been pointed out. First of all, the lack of an ATC code or the non assignment of a DDD to some of the marketed drugs. In this case, the strategy adopted for each of the databases varied considerably. Secondly, there is the fact that the DDD does not correspond to the prescribed daily dose (PDD), and that there are no DDDs assigned to children.

The questionnaire allowed us to evaluate the different degrees of ascertainment of those variables considered potential confounders of drug exposure. Very few databases provide the age and gender of the patient, though some provide information on the prescriber and the community pharmacy where the patient purchased the drug. However, some databases allow the development of a record linkage system.

The PROTECT inventory is a comprehensive and structured source of information on drug consumption that should promote the correct interpretation of the results of a study comparing different European countries. In addition, a brief summary of the data provided by IMS Health is available. For academic researchers PROTECT offers a basis for future collaborations while giving regulatory agencies and pharmaceutical companies the possibility of supporting post-marketing and safety studies. Such an inventory would not have been possible without the previous initiatives that compiled this information and knowledge.