PHARMO Newsletter March 2012

The PHARMO Institute for Drug Outcomes Research specialises in the collection and analysis of complex, longitudinal patient-centric data, detailing the relationship between drug exposure, outcomes and burden of disease in real-life settings.

We invite you to read our newsletter.

New PHARMO European Collaborations

In December 2011, PHARMO entered two projects requested and awarded by the European Medicines Agency (EMA). In the context of on-going safety monitoring of drugs in the European Union, the EMA issued a restricted invitation to tender to a number of candidates across Europe.

One project will evaluate patterns and determinants of use of oral contraceptives, and the other project is a drug safety study exploring an association between cardiac valve disorders and the use of bisphosphonates.

Patterns and determinants of use of oral contraceptives (OC) in the European Union
Since their introduction in the early 60s, OC have evolved, with modifications of hormone doses, types and combinations, dosage regimes and administration schedules. As the science of OC evolves, it is specially important to understand the impact of OC use in women with elevated cardiovascular risk due to hypertension, lipid abnormalities, diabetes, smoking, obesity or older age and in women who have autoimmune diseases or other special health problems (e.g. asthma, osteoporosis). In this context, an assessment of the current patterns and determinants of use of OC among women of reproductive age is needed for a valid safety evaluation.

Bisphosphonates and cardiac valve disorders
A signal of disproportionate reporting concerning the risk of cardiac valve calcification leading to a cardiac valve insufficiency associated with the use of bisphosphonates was found in EudraVigilance. A similar association between the use of bisphosphonates and the presence of heart calcification in women has also been discovered in a cohort study conducted in the United States of America (MESA study, November 2010 in the Journal of the American College of Cardiology).
The primary objective of the present study is to confirm or refute the presence of a possible risk of cardiac valve disease in patients treated with bisphosphonates. An etiological study will be performed if the signal is confirmed.

Other participants
Besides PHARMO, participants in these projects are:

- the Erasmus Medical Center with the primary care databases of the Integrated Primary Care Information (IPCI)
- The Health Improvement Network (THIN)
- the University of Milano-Bicocca (UNIMIB) with the demographic and healthcare database of Lombardy
- the Agenzia regionale di sanità della Toscana (ARS) with the demographic and healthcare database of Tuscany
- the Società Italiana di Medicina Generale with the Health Search Database (HSD).

European Commission 7th Framework Programme

EU-ADR and SOS
PHARMO participates in the EU-ADR project and the SOS project, both funded by the European Commission under the 7th Framework Programme. PHARMO is one of the data suppliers and contributes to the statistical analyses.
The EU-ADR project started in February 2008 and recently ended in January 2012 after an extension of 6 months. The SOS project started in November 2008; the project has been extended 6 months beyond the initial 3 years planned and therefore it will last until the 30th of April 2012.
The latest results of the EU-ADR project and the SOS project will be presented at ICPE 2012 in Barcelona.

EU-ADR project
The EU-ADR project aims to develop an innovative computerized system to detect adverse drug reactions, supplementing spontaneous reporting systems. To achieve this objective, EU-ADR exploits clinical data from electronic healthcare records (EHRs) of over 30 million patients from several European countries (the Netherlands, Denmark, United Kingdom and Italy). In this project a variety of text mining, epidemiological and other computational techniques are used to analyze the EHRs in order to detect 'signals' (combinations of drugs and suspected adverse events that warrant further investigation).
EU-ADR is carried out by an interdisciplinary team of researchers who share the ultimate objective to demonstrate that an earlier detection of adverse side effects of drugs is possible by using modern biomedical

informatics technologies to efficiently exploit both the massive amounts of available EHRs, and the ever-increasing biological and molecular knowledge.
The project should demonstrate that scientific and clinical evidence can quickly and directly be translated into patient safety and, thus, health benefit.

SOS project
The -Safety Of non-Steroidal anti-inflammatory drugs- project aims to asses and compare the risk of cardiovascular and gastrointestinal events of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) with the ultimate goal of providing decision models to clinicians and regulatory authorities, such as medicine agencies.

The strategy followed consists on first systematically reviewing and analyzing previously published clinical trials and observational studies. Then, the methodological issues and knowledge gaps are identified. Subsequently, a multi-country observational study is designed and conducted in existing health care databases in the UK, the Netherlands, Germany and Italy. The project partners provide information of more than 35 million individuals from the general population, including an ample representation of children.
This study is the largest observational study on NSAID safety that has ever been performed and permits the unique possibility to investigate the effects of several individual NSAIDs.
Finally the knowledge generated allows the development of the aforementioned decision models, which are needed in clinical practice to decide the type of NSAID that would yield the lowest gastrointestinal and cardiovascular risk for an individual patient. Decision models for regulatory agencies will focus on the public health risk.

Publications

We would like to draw your attention to recently published studies using PHARMO data and/or publications by PHARMO staff:

Cardiovascular diseases/diabetes:
- The risk of new onset heart failure associated with dopamine agonist use in Parkinson's disease. Mokhles MM, Trifirò G, Dieleman JP et al., Pharmacol Res, 2012, 65(3): 358-64.
- Risk of cardiac valve regurgitation with dopamine agonist use in Parkinson's disease and hyperprolactinaemia: a multi-country, nested case-control study. Trifirò G, Mokhles MM, Dieleman JP et al., Drug Saf, 2012, 35(2): 159-71.
- Use of thiazolidinediones and risk of osteoporotic fracture: disease or drugs? Bazelier MT, Gallagher AM, van Staa TP et al., Pharmacoepidemiol Drug Saf, 2012, in press.

Oncology:
- Lower risk of cancer in patients on metformin in comparison with those on sulfonylurea derivates: results from a large population-based follow-up study. Ruiter R, Visser LE, van Herk-Sukel MP et al., Diabetes Care, 2012, 35(1): 119-24.

Other:
- Knee arthroplasty and risk of hip fracture: a population-based, case-control study. Lalmohamed A, Opdam F, Arden NK et al., Calcif Tissue Int, 2012, 90(2): 144-50.
- Electronic healthcare databases for active drug safety surveillance: is there enough leverage? Coloma PM, Trifirò G, Schuemie MJ et al., Pharmacoepidemiol Drug Saf, 2012, in press.

Congresses

PHARMO will attend the ISPOR 17th Annual International Meeting, June 2-6, 2012, Washington, USA, where we will present our latest research:
- Trends in prevalence of ADHD drug treatment in the Netherlands from 2000 until 2010
- Male/female incidence ratio of ADHD drug treatment in the Netherlands from 2000 until 2010
- Medication use and hospital admission rates among preterm born infants compared to full term born infants