Benefit-Risk Assessment Methodology Workshop

Statistical Issues in Medical Statistics, FMS/DSBS 5th Joint Workshop

7 June 2012, University Hospital, Malmö, Sweden, (Copenhagen area)

An increase in the use of quantitative Benefit-Risk Assessment methods has been proposed to aid in the evaluation of new medicinal products by regulatory bodies and reimbursement committees throughout the world. This workshop will provide a forum to hear about the latest developments in the applications of these methods from a world-leader in this area – keynote speaker Larry Phillips -- from representatives of European regulatory bodies, and from practitioners in the pharmaceutical industry and academia. The workshop includes presentations from each of these perspectives, as well as an opportunity to interact with the speakers in a panel discussion.

AGENDA

09.15-10.00	Registration, Coffee/Tea, Breakfast
10:00	**INTRODUCTION** from Keynote Speaker **Benefit-Risk Modelling of Pharmaceuticals: Where are we now?** Professor Lawrence Phillips – London School of Economics
10:30	**Quantitative Methods Across the Product Lifecycle - a Personal Perspective** Andrew Thompson – MHRA
11:00	**Comparison of different Benefit-Risk methodologies** Professor Johan Bring – Statisticon AB
11:30	**LUNCH**
13:00	**A Structured Approach with Focus on Transparency, Clinical Significance and Visualization** Dr. Sinan B. Sarac – Danish Health and Medicines Authority
13:30	**Post-marketing surveillance of drug safety in 2012: The EU Regulatory Framework** Dr. Doris Stenver – Danish Health and Medicines Authority
14:00	**Considerations for Implementing a Structured Benefit Assessment in Product Development** Dr. George Quartey – Genentech
14:30	**TEA/COFFEE**
15:00	**Cost/benefit evaluations in road safety… and in pharmaceutical pricing and reimbursement.** Professor Ulf Persson – Swedish Institute of Health Economics
15:30	**Benefit-Risk Modelling of Pharmaceuticals: Where are we going?** Professor Lawrence Phillips
16:00	**Panel Discussion** Lawrence Phillips, Andrew Thomson, George Quartey and Ulf Persson
17:00 Close	chaired by Carl-Fredrik Burman

Cost The registration fee is €150 Euros for participants from the industry and €75 Euros for participants from regulatory agencies and academia. **For full details and to register go to** **www.efspi.org**

SPEAKER ABSTRACTS

INTRODUCTION - Professor Lawrence Phillips – London School of Economics
Benefit-Risk modelling of pharmaceuticals:Where are we now?

This presentation introduces the current state of development by pharmaceutical companies, regulators and health technology agencies in the quantitative modelling of the benefit-risk balance for medicinal products. Two qualitative frameworks, UMBRA (formerly BRAT) and PrOACT-URL, will be explained as guidelines for assessing the benefit-risk balance. The key requirements for a comprehensive and coherent benefit-risk model leave just a few quantitative methodologies as satisfactory. Only a few pharmaceutical companies currently use them, and no regulators have accepted their use, despite their widespread acceptance outside the pharmaceutical sector.

Dr Andrew Thomson, Statistical Assessor, MHRA
Quantitative Methods Across the Product Lifecycle - a Personal Perspective

Quantitative methods for assessing whether medicinal products have a positive balance of benefits and risks are increasingly being vaunted as important tools to make important decisions. Various issues at the point of licensing that need to be considered include, but are not limited to: who constructs the models; who selects appropriate weights and how and when these are selected; and whether pre-specification can ever be suitably incorporated. The first half of the talk will address these points.
Once a positive decision has been made and a licence granted, data still continues to be generated whether through trials or more commonly through observational data. Incorporating this information within a quantitative framework presents more challenges and how we might begin to think about overcoming these challenges will be the focus of the second half of the talk.

Professor Johan Bring, Statisticon AB
Comparison of different Benefit-Risk methodologies

A good decision-model could be of help in the complicated process to decide whether to approve a NDA or not. Also in the decision to withdraw a drug from the market it should be useful to have a structured process to handle all relevant information. There are many different models available: MCDA, BRAT, Impact numbers, PrOACT, SMAA etc. In this talk Johan will discuss important characteristics of different models and also highlight some of the main difficulties associated with their use.

Dr. Sinan B. Sarac – Danish Health and Medicines Authority
A Structured Approach with Focus on Transparency, Clinical Significance and Visualization

Benefit-risk assessment of medicines, treatments, etc., consumes enormous resources, and the outcome often seems to depend on personal experience and expertise. The purpose is to demonstrate how clinical data can be weighted, scored and presented by the use of a quantitative benefit-risk assessment method. Our aim is to present a comprehensive approach that is simple to apply, allows direct comparison of different types of risks and benefits, quantifies clinical significance, and is tailored for the comparison of different options, treatments, etc. The methodology is demonstrated by analysing a cohort of 302 patients with colorectal cancer treated at the Copenhagen University Hospital (Rigshospitalet).

Dr. Doris Stenver – Danish Health and Medicines Authority

Post-marketing surveillance of drug safety in 2012: The EU Regulatory Framework

The European Medicines Agency and national regulatory agencies work closely together within an extensive EU network for approval and post-marketing surveillance (pharmacovigilance) of new medicinal products. This presentation will describe the network, and will focus on the tasks and responsibilities of the regulatory authorities, their co-operation with the pharmaceutical industry, the most important tools available, e.g. periodic safety update reports and risk management plans, and major objectives of the new European pharmacovigilance legislation, which comes into force in July 2012.

Dr. George Quartey – Genentech, US

Considerations for Implementing a Structured Benefit Assessment in Product Development

Benefit–risk assessment (BRA) is a fundamental element of drug development with the aim to strengthen decision making for the benefit of public health. BRA provides crucial information for decision-making by regulators as well as producers during the development and subsequent approval phase of a new drug product and for the post approval re-assessment of marketed medicines. Recently there has been an increased interest in developing a framework to evaluate the benefit and risk profile of medicinal products. We intend to explore some recent developments in the quantitative and qualitative framework settings and present some case studies that will provide the opportunity to discuss various aspects of B-R assessment during product development.

Professor Ulf Persson – Swedish Institute of Health Economics

Cost/benefit evaluations in road safety … and in pharmaceutical pricing and reimbursement

Benefit cost evaluation have been used by the Swedish National Road Administration in the transport sector since 1970s. However, in the health care sector benefit cost evaluation was not in use by any agency until 2002 when the Value Based Pricing (VBP) system for pharmaceuticals was adopted by the Pharmaceutical Benefit Board – LFN (now called the Dental and Pharmaceutical Benefits agency-TLV). In transport benefit cost analysis is used to allocate resources to building new safer roads and to prioritize between different traffic safety measures. In health care sector benefit cost analysis mainly are used for evaluating pharmaceutical treatments but also in the development of treatment guidelines. The valuation of the benefit in transport safety, i.e. the value of risk reduction per see - the Value of a Statistical Life (VSL), have many similarities to the valuation of health – the value of a Quality Adjusted Life Year (QALY) in the health care sector. In fact the valuation of a QALY is derived from the VSL in transport and both are linked to the individual willingness to pay for Safety and health in Sweden.

Professor Lawrence Phillips

Benefit-Risk Modelling of Pharmaceuticals: Where are we going?

Why has the medical profession been so reluctant to apply any of the benefit-risk balancing methodologies? This talk suggests five reasons, but then shows there are cracks in medical and regulatory practice that might enable these approaches to become more attractive as decision aids. The capability of the models to extend human capability through an integration of modern statistical and decision-theoretic practice will be explored.

Panel Discussion

Lawrence Phillips, Andrew Thomson, George Quartey and Ulf Persson chaired by Carl-Fredrik Burman