THE ROLE OF PROTECT IN REGULATORY SCIENCE

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Regulatory science

Regulatory science consists of the areas of science that are used in the assessment of the quality, safety and efficacy of human and veterinary medicines **throughout their life-span**, as well as the scientific areas used in regulatory decision-making.

Source: EMA website

Why is regulatory science important?

- To support research in areas of emerging and innovative sciences and drug development for unmet medical needs

  eg. validated endpoints, surrogate endpoints, evaluation of safety and efficacy during drug development

- To develop and test methods for the assessment and monitoring of the benefits and risks of medicines during their life-cycle
- To evaluate and improve the effectiveness of regulatory activities and decisions
- To build capacity for benefit-risk monitoring.

A few examples…

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Adaptive Pathway / Life-span approach: Need for 'rapid learning systems'

Observational studies, Pharmacoepidemiology ➔ need for

- In-depth understanding of databases (strengths and weaknesses)
- In-depth understanding of methodology

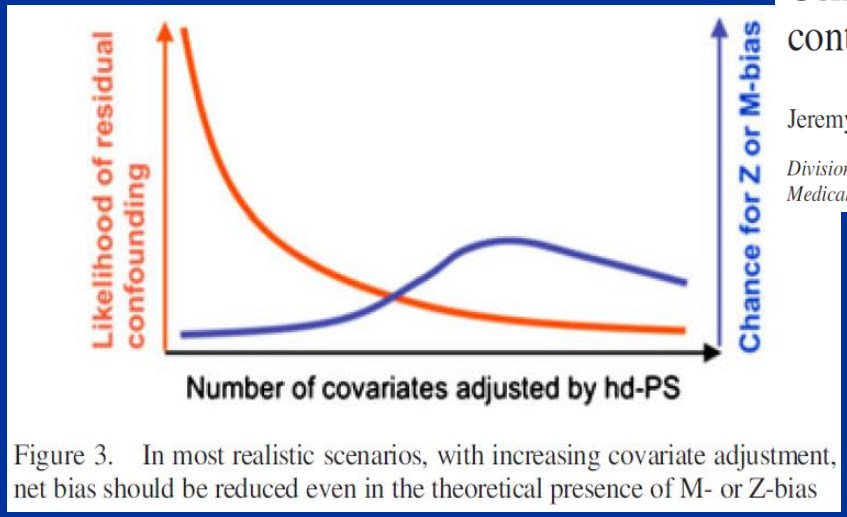


Figure 3. In most realistic scenarios, with increasing covariate adjustment, net bias should be reduced even in the theoretical presence of M- or Z-bias

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2012; **21**(S1): 41–49

Using high-dimensional propensity scores to automate confounding control in a distributed medical product safety surveillance system

Jeremy A. Rassen* and Sebastian Schneeweiss

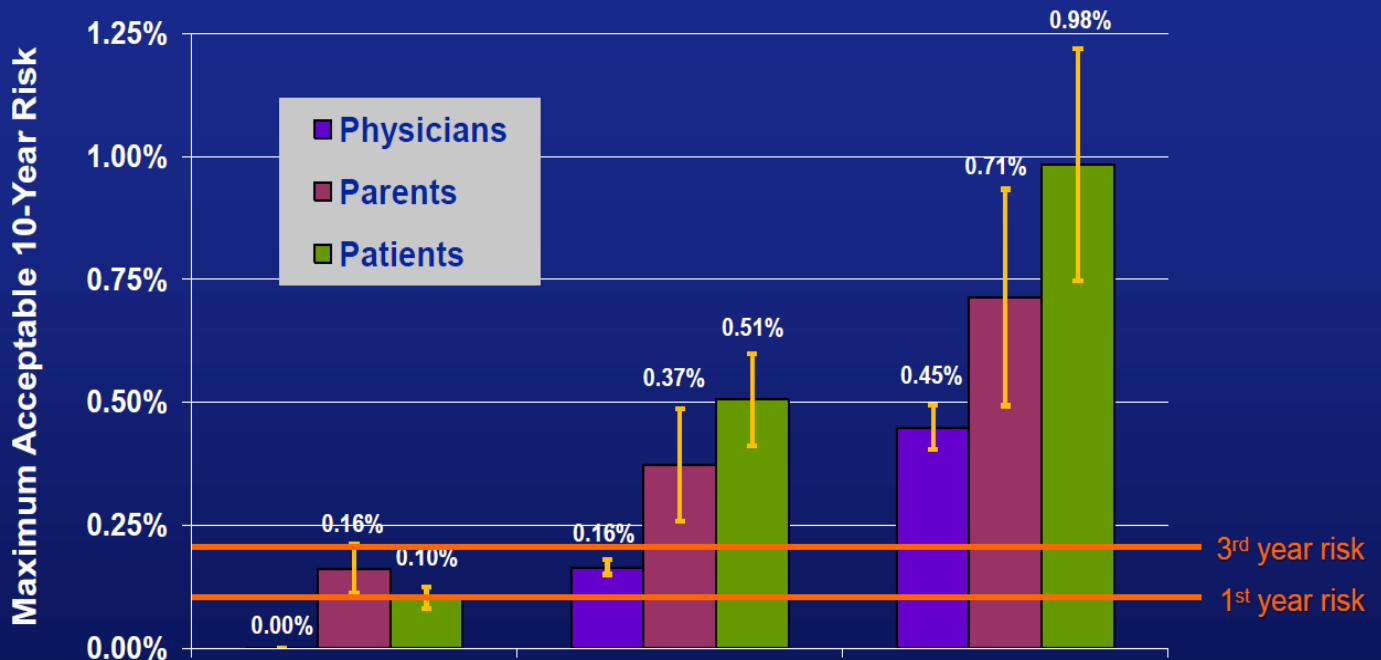
Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

EUROPEAN MEDICINES AGENCY

Listening to the patient's voice:

Maximum Acceptable PML Risk

Crohn's Disease



PROTECT: the Vision

EUROPEAN MEDICINES AGENCY

To strengthen the monitoring of benefit-risk of medicines in Europe by developing innovative methods

To enhance early detection and assessment of adverse drug reactions from different data sources (clinical trials, spontaneous reporting and observational studies)

To enable the integration and presentation of data on benefits and risks

PROTECT: Goals

Data collection

- ✓ efficient and simple methods for early data collection directly from patients
- ✓ non-prescribed medicines
- ✓ linkage to health event databases

Signal detection

- ✓ spontaneous reports: in-depth analysis of methods and good practice recommendations
- ✓ better use of electronic health records and clinical trials

Risk assessment

- ✓ understanding the variability in results of studies of a same safety issue in different data sources, supporting decision-making
- ✓ detailed guidance and standards regarding design, conduct and analysis of pharmacoepidemiological studies for evaluation of safety concerns

Benefit-risk assessment

- ✓ analysis , testing and recommendations of methods for integrating and communicating data on benefits and risks from clinical trials, observational studies and drug reaction reports
- ✓ benefit-risk assessment based on patients and prescribers' perspectives

PROTECT

SHAPING OBJECTIVES INTO A WORK PROGRAMME

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GlaxoSmithKline R & D Ltd
Deputy Co-ordinator, PROTECT

Observations by IMI Pharmacovigilance Stakeholder Group

A wealth of epidemiological data on drug exposure and outcomes is available in the EU, but

- ✓ No central repository of such data
- ✓ Different data sources do not communicate
- ✓ Data cannot be combined

Systems and networks for pharmacovigilance are used for regulation, not for research (reactive not pro-active)

Methods of pharmacovigilance have remained unchanged for two decades

Risk minimisation methods are not yet available for testing

Effectiveness of risk communication is put into question

PROTECT: Partners (34)

PUBLIC

REGULATORS:

EMA (Co-ordinator)
DKMA (DK)
AEMPS (ES)
MHRA (UK

ACADEMIC INSTITUTIONS:

University of Munich
FICF (Barcelona)
INSERM (Paris)
Mario Negri Institute (Milan)
University of Groningen
University of Utrecht
Imperial College London
University of Newcastle Upon Tyne
University of Aarhus
University of Poznan (Poland)

OTHERS:

WHO UMC
GPRD
IAPO
CEIFE

SMES:

Outcome Europe
PGRx

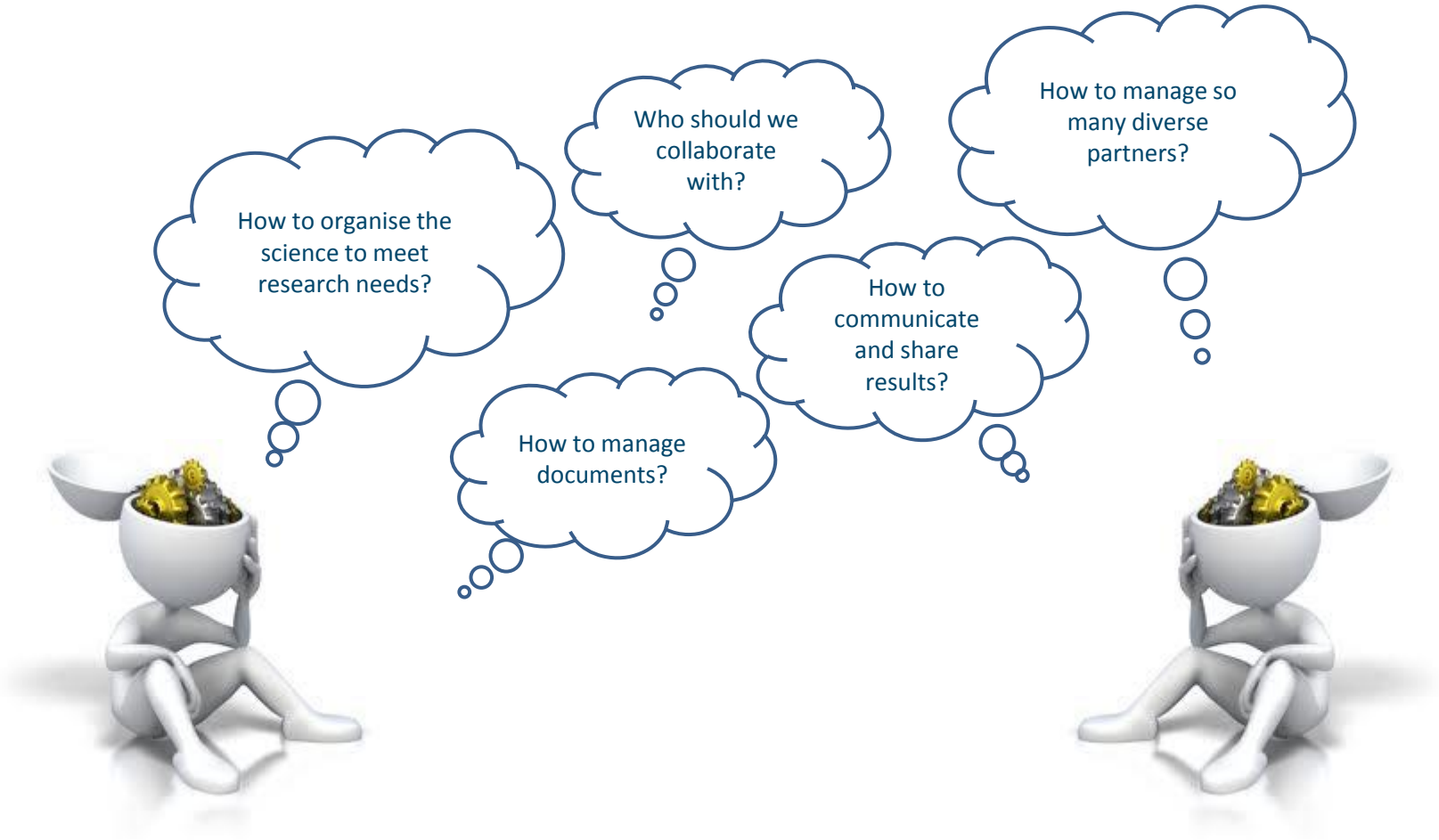
PRIVATE

GSK (Deputy Co-ordinator)
Sanofi- Aventis
Roche
Novartis
Pfizer
Amgen
Genzyme
Merck Serono
Bayer Schering
Astra Zeneca
Lundbeck
NovoNordisk
Takeda
Eli Lilly

PROTECT: Partners

1st Consortium Assembly, 15 May 2009

PROTECT: The challenge



Decision to group work in 6 MODULES

- DATA COLLECTION FROM PATIENTS
- SIGNAL DETECTION
- SIGNAL EVALUATION
- BENEFIT-RISK INTEGRATION AND REPRESENTATION
- VALIDATION STUDIES
- TRAINING & EDUCATION

How we organised the project

WP1: Project Management and Administration

Objective	To create and maintain the conditions needed to achieve the objectives and deliverables of the PROTECT project

Scientific steer towards the overall project objectives and strategy	Quality Control and Assurance measures	Administrative, organisational and financial support	Track work progress in line with the work programme	Financial monitoring and accountancy	Knowledge management tools and strategies

External Advisory Board - members

Name	Affiliation	Expertise
Corinne De Vries, PhD	Department of Pharmacy and Pharmacology, University of Bath, UK	Pharmacoepidemiology
Helen Dolk, MD	Epidemiology and Health Sciences research centre for Maternal , Foetal and Infant Research , University of Ulster , UK	Epidemiology and Health Service Research , Maternal , Foetal and Infant Research
Trevor Gibbs, MD	Former Head of Global Pharmacovigilance and Product Safety, GSK, UK; Pharmacovigilance Consultant	Pharmacovigilance, Health Outcomes, Public Health
David Haerry	European AIDS Treatment Group (EATG), Brussels, Belgium	Public Health Patients' preference
Vicky Hogan, PhD	Director, Office of Risk Management and Science, Marketed Health Products Directorate (MHPD), Health Canada	Benefit-risk assessment
Michael Lewis, MD	EPES Epidemiology, Pharmacoepidemiology and Systems Research GmbH, Berlin, Germany	Pharmacoepidemiology
Allen Mitchell, MD	Slone Epidemiology Center, Boston, USA	Perinatal epidemiology Pharmacoepidemiology
Marcus Müllner, MD	Head of AGES PharmMed (Austrian Medicines and Medical Devices Agency), Austria	Benefit-risk assessment Clinical epidemiology Pharmacovigilance
Gerald Dal Pan, MD, M.H.S.	Director, Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research (CDER), Food and Drug Administration (FDA), USA	Pharmacovigilance, Drug development, Public Health & Risk management
Munir Pirmohamed, MD	Department of Pharmacology and Therapeutics, University of Liverpool, UK	Pharmacology Pharmacovigilance
Samy Suissa, PhD	Department of Epidemiology/Biostatistics, McGill University, Montreal, Canada	Biostatistics Pharmacoepidemiology

External Advisory Board - role

- ✓ Identification of any critical step, activity or missing element that may represent a risk for the project, or that may affect its quality or implementation; proposal of possible remedial actions to the Steering Committee
- ✓ General guidance and recommendations regarding scientific, technical and ethical aspects of the work programme
- ✓ Recommendations to the Steering Committee
- ✓ Input to the Steering Committee regarding non-European research programmes with similar objectives and scope, and advice on opportunities for collaboration
- ✓ Advice to the Steering Committee on the communication and dissemination of outcomes achieved by the consortium

Sharing the results

- Commitment to share all the outputs of PROTECT

PROTECT WEB PORTAL

A website accessible to the general public where relevant deliverables for public use will be posted http://www.imi-protect.eu

PUBLICATIONS

Most deliverables of the project will be produced initially as reports delivered to the IMI JU and they will also be published and disseminated through the appropriate mediums

ENCEPP NETWORK

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance is a project led by the EMA intended to further strengthen the post-authorisation monitoring of medicinal products in Europe. The results of the PROTECT programme made available to all ENCePP members http://www.encepp.eu/

Links with other projects

- Interactions with a number of other international research programmes with overlapping or complementary research agenda

  - ✓ Drug Safety and Effectiveness Network (DSEN)
  - ✓ Eu2P: European Programme in Pharmacovigilance and Pharmacoepidemiology
  - ✓ EU-ADR: Exploring and Understanding Adverse Drug Reactions by Integrative Mining of Clinical Records and Biomedical Knowledge
  - ✓ European Drug Utilization Research Group (EuroDURG)
  - ✓ European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)
  - ✓ FDA's Sentinel Initiative
  - ✓ Observational Medical Outcomes Partnership (OMOP)
  - ✓ EUPATI - European Patients' Academy on Therapeutic Innovation

Key Success Factors

- Wide range of complementary expertise due to multi disciplinary , multi-stakeholder contribution
- High levels of commitment and expertise

- First rate project management at EMA and in each work package
- Links to e.g. IMI EU2P so that learning from PROTECT turned into teaching materials
- Excellent website for management of project and communication


Thank You
Mahalo
Kiitos
Tack
Toda
Grazie
Obrigado
Thanks
Takk
Merci
Gracias

ULTIMATE JUDGE OF SUCCESS IS WHETHER THE EXCELLENT RESEARCH RESULTS (OUTPUTS) ARE CONVERTED INTO OUTCOMES FOR INNOVATION AND PUBLIC HEALTH