

# ‘Papel’ do Ensino na Farmacovigilância

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# Where do I come from





# Stating the problem....

- Although medical and pharmacy students may recognize the importance of ADR reporting and express the intention to report ADR, **they are insufficiently prepared to handle ADRs and have inadequate pharmacovigilance competencies.**

Eur J Clin Pharmacol (2017) 73:891–899  
DOI 10.1007/s00228-017-2237-z



PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

## A global view of undergraduate education in pharmacovigilance

Jenny Hartman<sup>1</sup> · Linda Härmark<sup>1</sup> · Eugène van Puijenbroek<sup>1,2</sup>

DOI: 10.1590/S00080-623420140000400023

### Causes for the underreporting of adverse drug events by health professionals: a systematic review

CAUSAS DE LA SUBNOTIFICACIÓN DE LOS EVENTOS ADVERSOS A MEDICAMENTOS POR LOS PROFESIONALES DE LA SALUD: REVISIÓN SISTEMÁTICA

CAUSAS DE SUBNOTIFICAÇÃO DE EVENTOS ADVERSOS A MEDICAMENTOS POR PROFISSIONAIS DA SAÚDE: REVISÃO SISTEMÁTICA

Fabiana Rossi Varallo<sup>1</sup>, Synara de Oliveira Paim Guimarães<sup>2</sup>, Samir Antonio Rodrigues Abjaude<sup>3</sup>, Patricia de Carvalho Mastroianni<sup>4</sup>

ABSTRACT

Objective: Identify the main causes for

RESUMEN

Objetivo: Identificar las causas de la subnotificación

RESUMO

Objetivo: Identificar as causas de subnotificação

Hussain et al. *J of Pharm Policy and Pract* (2021) 14:5  
<https://doi.org/10.1186/s40545-020-00287-3>

Journal of Pharmaceutical  
Policy and Practice

RESEARCH

Open Access

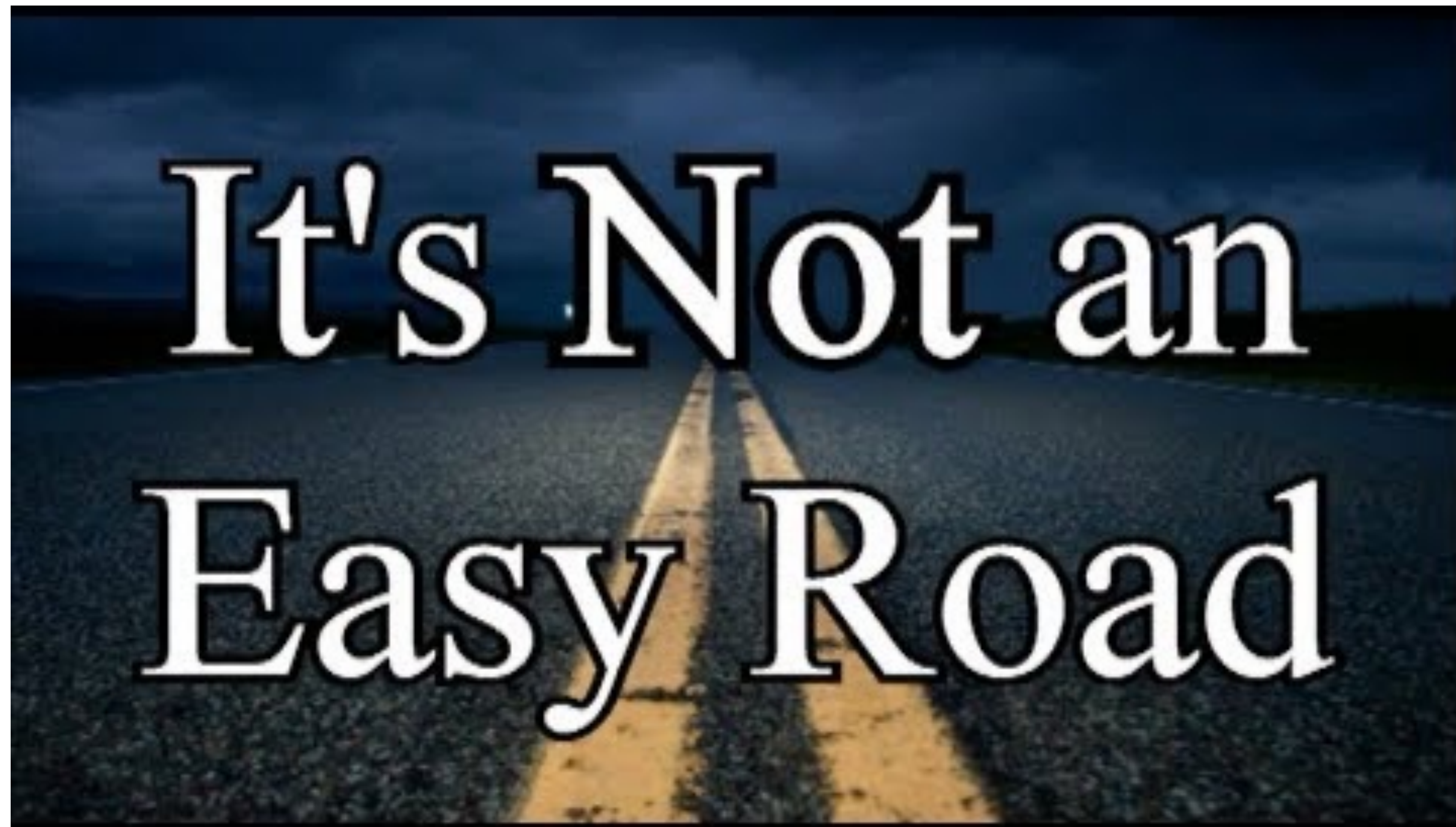
## Exploring healthcare professionals' knowledge, attitude, and practices towards pharmacovigilance: a cross-sectional survey

Rabia Hussain<sup>1,2\*</sup>, Mohamed Azmi Hassali<sup>3</sup>, Furqan Hashmi<sup>4</sup> and Tayyaba Akram<sup>5</sup>



CRITICAL REVIEW







# What future healthcare professionals need to know about pharmacovigilance & risk management of medicines

Drug Saf (2018) 41:1003–1011  
<https://doi.org/10.1007/s40264-018-0681-z>



CURRENT OPINION

## What Future Healthcare Professionals Need to Know About Pharmacovigilance: Introduction of the WHO PV Core Curriculum for University Teaching with Focus on Clinical Aspects

Rike van Eekeren<sup>1,2</sup> · Leàn Rolfes<sup>1,2</sup> · Andries S. Koster<sup>3</sup> · Lara Magro<sup>4</sup> · Gurumurthy Parthasarathi<sup>5</sup> · Hussain Al Ramimmy<sup>6</sup> · Tim Schutte<sup>7,8</sup> · Daisuke Tanaka<sup>9</sup> · Eugène van Puijenbroek<sup>1,2</sup> · Linda Härmark<sup>1</sup>

Published online: 13 June 2018

Drug Saf (2014) 37:743–759  
DOI 10.1007/s40264-014-0216-1

SPECIAL ARTICLE

## Teaching Pharmacovigilance: the WHO-ISoP Core Elements of a Comprehensive Modular Curriculum

Jürgen Beckmann · Ulrich Hagemann · Priya Bahri · Andrew Bate · Ian W. Boyd · Gerald J. Dal Pan · Brian D. Edwards · I. Ralph Edwards · Kenneth Hartigan-Go · Marie Lindquist · John McEwen · Yola Moride · Sten Olsson · Shanthi N. Pal · Rachida Soulaymani-Bencheikh · Marco Tuccori · Claudia P. Vaca · Ian C. K. Wong

Published online: 30 August 2014  
© Springer International Publishing Switzerland 2014

# What future healthcare professionals need to know about pharmacovigilance & risk management of medicines

**Table 1** Summary of the key aspects and content of the World Health Organization pharmacovigilance core curriculum for university teaching

Key aspect	Knowledge	Skills	Attitude	Examples of teaching methods
Understanding the importance of PV	Drug-induced harm and hospital admissions Historical examples	Recognizing ADRs and their impact on individual patients	Open mindedness of adverse outcomes of drug use in pharmacotherapy	Story telling Patient interview
Preventing ADRs	General risk factors Individual risk factors Treatment guidelines and safety information	Choose right drug treatment	Safe prescribing/ dispensing	Problem solving Simulation, role play ADR monograph ADR report assessment
Recognizing ADRs	ADR classification Risk factors Confounding factors Epidemiology	Clinical reasoning Causality reasoning	Awareness of predictable and unexpected ADRs	Prescribing safety assessment Internship
Managing ADRs	ADR classification Seriousness Severity	Choose right actions; patient and HCP communication; recording of ADR data	Optimize risk-benefit balance in an individual patient	
Reporting ADRs	Limitations of premarketing phase Relevance of ADR reporting Documentation of ADRs	Recognizing ADRs in practice Complete reporting form	Responsibility for sharing (reporting) of ADRs	ADR reporting assignment



# Updated core competencies in pharmacoepidemiology to inform contemporary CV and training (academia, government and industry) – ISPE, 2022

- 1) Epidemiology
- 2) Clinical Pharmacology
- 3) Regulatory Science
- 4) Communication and other professional skills
- 5) Statistics, analysis of data and science
- 6) New competencies (Judith Jones *et al*, 2012): digital health

Updated core competencies in pharmacoepidemiology to inform contemporary curricula and training for academia, government, and industry

Vicki Osborne<sup>1</sup>, Deborah Layton<sup>2</sup>, Amie Goodin<sup>3</sup>, Almut G Winterstein<sup>3</sup>, Andrew Bate<sup>4</sup>, Catherine Cohet<sup>5</sup>, Xavier Kurz<sup>5</sup>, Lisa Pont<sup>6</sup>, David Moeny<sup>7</sup>, Olaf Klungel<sup>8</sup>, Simone Pinheiro<sup>9</sup>, John Seeger<sup>10</sup>, K. Arnold Chan<sup>11</sup>, Joshua Brown<sup>3, 12</sup>

<sup>1</sup> GW, part of Jazz Pharmaceuticals; <sup>2</sup> PEPI Consultancy Ltd, UK; <sup>3</sup> University of Florida; <sup>4</sup> GSK; <sup>5</sup> European Medicines Agency; <sup>6</sup> University of Technology Sydney; <sup>7</sup> Food and Drugs Administration; <sup>8</sup> Utrecht University; <sup>9</sup> AbbVie; <sup>10</sup> Optum; <sup>11</sup> National Taiwan University; <sup>12</sup> Pfizer

Disclosures: Funding for the manuscript project provided by ISPE. The following personal or financial relationships relevant to this presentation existed during the past 12 months/during the conduct of the study: Employment: GW Pharmaceuticals; IQVIA; GSK; Pfizer; AbbVie. Consultant/Advisory Board: Arbor Pharmaceuticals; Genentech Inc. Research Grant: Merck, Sharpe, Dohme; Amgen; Boehringer Ingelheim; MSD; Takeda.

Background

The first paper to specify the core content of pharmacoepidemiology as a profession was published by an ISPE workgroup in 2012.<sup>1</sup> Pharmacovigilance, analysis of exposure data, epidemiologic methods, and communication skills were the original core competency groups identified from this work. The ISPE strategic plan 2016-2019 considered the identification and development of the field a priority for the society due to the broad and evolving scope of pharmacoepidemiology.

A joint ISPE Academic Council /Education Committee working group was established in 2017. The aim was to review and propose updates to the core competencies that could be used to inform education program curricula and thus provide well trained pharmacoepidemiologists in academic, government, and industry.

Funding was secured from the ISPE Call for Manuscripts in 2020. To ensure applicability of findings to multiple areas, the group consisted of 14 ISPE members with positions in academia, industry, government, and other settings. Experience ranged from early to advanced career professionals, representing multiple countries across 4 continents. Many had significant experience in development of curricula within Higher Education and/or teaching thereof.

<sup>1</sup> Jones JK et al. PDS 2012; 21(7):677-689

Methods

All competencies outlined by Jones et al<sup>1</sup> were extracted from the manuscript and presented to the work group.

Following the Delphi technique principle, the working group were asked to a) independently consider which competencies could still be considered "core" b) which were optional c) whether any further competencies should be added to the list and d) the grouping to which the core competencies could be mapped.

These expert-based judgements were collated and used to identify consensus. It was noted that some competencies could contribute to multiple groups and could be directly or indirectly related to a group. Key-words were also identified to assist in mapping.

Results

Five core domains were proposed (Table 1):

(1) Epidemiology,

(2) Clinical Pharmacology,

(3) Regulatory Science,

(4) Communication and other professional skills, and

(5) Statistics, analysis and data science.

In comparison to the original work by Jones et al, this presented a shift over the past 10 years. In total, 53 individual competencies were proposed, of which many overlapped with the original competencies but also included some new competencies (e.g. basic principles of digital health).

Some individual competencies were considered after core domains were defined, though there was scope for revision if they did not accurately reflect individual competencies

Table 1. Updated core competencies in pharmacoepidemiology, mapped to five core domains

1=Directly related to category; 2=Indirectly related to category

Core competency	Key word	Epidemiology	Clinical Pharmacology	Regulatory Science	Communication and Other Professional Skills	Statistics, analysis and Data Science
Advanced statistical modelling techniques (e.g. GLM, GEE, MSM)	Advanced Modelling Methods	2				1
Double robustness	Advanced Modelling Methods	?				1
Multi-group comparisons	Advanced Modelling Methods	?			2	1
Benefit-Risk assessment methods	Benefit-Risk		2	1	2	2
Causal mediation analysis	Causal Mediation Analysis	2				1
Fundamental principles of comparative clinical trials, key decisions of design, delivery and assessment, reporting and meta-analysis	Clinical Trials	1		2		
Distributed data networks and use of Common Data Models	Common Data Model	2				1
Appraisal of pharmacoepidemiological research	Critical Appraisal	1	2		2	1
Data mining techniques	Data Mining	2	2			1
Embedding prospective data collection in secondary databases for additional data collection	Data Sources	2				1
Data sources and types of data in pharmacoepidemiology	Data Sources	1	2		1	1
Quality and validation of data sources	Data Sources	1			2	1
Policy, public health and regulatory decision making	Decision Making	2	2	1	1	
Demographic analysis	Demographic Analysis	1				1
Basic principles of digital health	Digital Health	2	2		1	
Global burden of communicable and noncommunicable disease and public health intervention strategies	Disease Prevalence			1		
Disease prevention strategies (inc screening)	Disease Prevention			1		
Drug utilization, adherence, and switching	Drug Utilisation	1	2		2	1
Geriatrics, pediatric, pregnancy and other specific and special populations	Drug Utilisation		1			
Ethical issues in pharmacoepidemiology	Ethics				2	
Good Pharmacoepidemiology Practices guidelines	Good Practice	1		1	2	
Health economics modelling approaches	Health Economics	2				1
Written communication of study methods, results and interpretation	Interpretation of results	1			1	
Oral presentation of study methods, results and interpretation	Interpretation of results	1			1	
Interpreting epidemiologic data: chance, bias, confounding, effect modification	Interpretation of results	1				2
Machine learning techniques	Machine learning	2				1
Missing data and data imputation	Missing data	2				1
Applications of omics data in epidemiology and public health	Omics		2			
Common drug associated conditions, symptoms and syndromes	Pharmacology		1		2	
Types of adverse events (A/E) by mechanism/classification system	Pharmacology		1		2	
Basic principles of drug actions, pharmacokinetics and pharmacodynamics	Pharmacology		1		2	
Variability in drug response due to drug-drug interactions, pharmacogenomics/genetics	Pharmacology		1		2	
Professional networking skills	Professional skills				1	
Statistical programming skills	Programming skills	2				1
Qualitative methods in health research	Qualitative methods	2				1
Quantitative bias analysis	Quantitative Bias analysis	1			2	1
Regulatory reporting requirements	Regulatory			1		
Basic phases of drug development and information obtained	Regulatory		2	1	2	
Drug regulatory process and agencies	Regulatory			1	2	
Risk management	Regulatory			1	2	



# A single tale of two stories

## RANDOMIZED TRIALS OR OBSERVATIONAL TRIBULATIONS?

THE role of observational studies in the evaluation of treatments is a long-standing and contentious topic.<sup>1</sup> In this issue of the *Journal*, Concato et al.<sup>2</sup> and Benson and Hartz<sup>3</sup> report that observational studies give results similar to those of randomized, controlled trials. If these claims lead to more observational studies of therapeutic interventions and fewer randomized, controlled trials, we see considerable dangers to clinical research and even to the well-being of patients.

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London WC1E 7HT, United Kingdom



Ready-Made Bouquet, *Rene Magritte (1956)*



# Teaching uncertainties...

*“The education of young physicians should overcome the level of the few questions in a crash course. Of course, they should not all become methodologic or theoretical experts. (...) But they should at least be familiar with the **terms of the debate, the way of arguing, so that they can recognize what arguments are used in what circumstances, and whether they want to be swayed by them.***

*In the end, they should recall that “**the art is long, life short**” meaning in this instance that medical history has shown repeatedly that erring is possible, despite the best arguments. We should not be afraid to teaching them uncertainty”.*



# WHO PV Core CV for University Teaching

**Fig. 2** Example of curriculum levels of competence in PV education. The pyramid shows increasing complexity of key PV aspects during university education. Depending on the local situation and structure of the educational programme, a Bachelor/Master division may be absent. Apart from the structure, increasingly complex learning outcomes can be offered throughout the programme. *ADR* adverse drug reaction, *PV* pharmacovigilance. Adapted from Koster et al. [36]

## **MASTER: The student .....**

- ..... is able to anticipate on potential adverse drug reactions when prescribing or designing a pharmacotherapeutic treatment plan for an individual patient;
- ..... is able to recognize and interpret (expected and unexpected) adverse drug reactions, occurring in real-life patients;
- ..... is able to design effective treatment interventions for patients, suffering from adverse drug reactions;
- ..... is able to report adverse drug reactions to the locally recognized authorities.

## **BACHELOR: The student.....**

- ..... is able to identify adverse drug reactions in authentic descriptions or examples of (relatively simple) patient cases;
- ..... is able to explain the mechanism of relatively simple adverse drug reactions in terms of pharmacological, toxicological principles and/or individual risk factors;
- ..... is able to suggest pharmacotherapeutic interventions for relatively simple cases of adverse drug reactions.

## **YEAR 1: The student .....**

- ..... knows the concept 'pharmacovigilance' and is able to describe the importance of preventing, recognizing, managing and reporting adverse drug reactions;
- ..... is able to give historical and current examples of drug-induced harm.



# Undergraduate level – Integrated Master in Pharmaceutical Sciences (FFUL)

## Mandatory

- Pharmacology I and II (3<sup>rd</sup> Year)
- Pharmacotherapy I (4<sup>th</sup> Year) and Pharmacotherapy II (5<sup>th</sup> year)
- **Risk Management of Medicines and Health Products (5<sup>th</sup> year)**



2022/23

## Option

- **Pharmacoepidemiology & Pharmacovigilance (new 2022/3: Health Technology Assessment)**



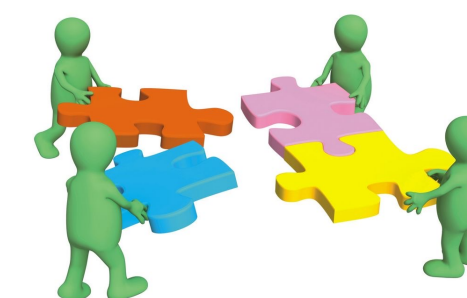


# Teaching environment



The therapist, *Rene Magritte (1937)*

- **Academia**
- **Regulators (INFARMED, EMA)**
- **Regional Pharmacovigilance Units (UFLSS)**
- **Public Health Institute (INSA, IP)**
- **Pharmaceutical Industry & CROs**
- **Health-care providers**
- **Patients' organizations**
- **(...)**



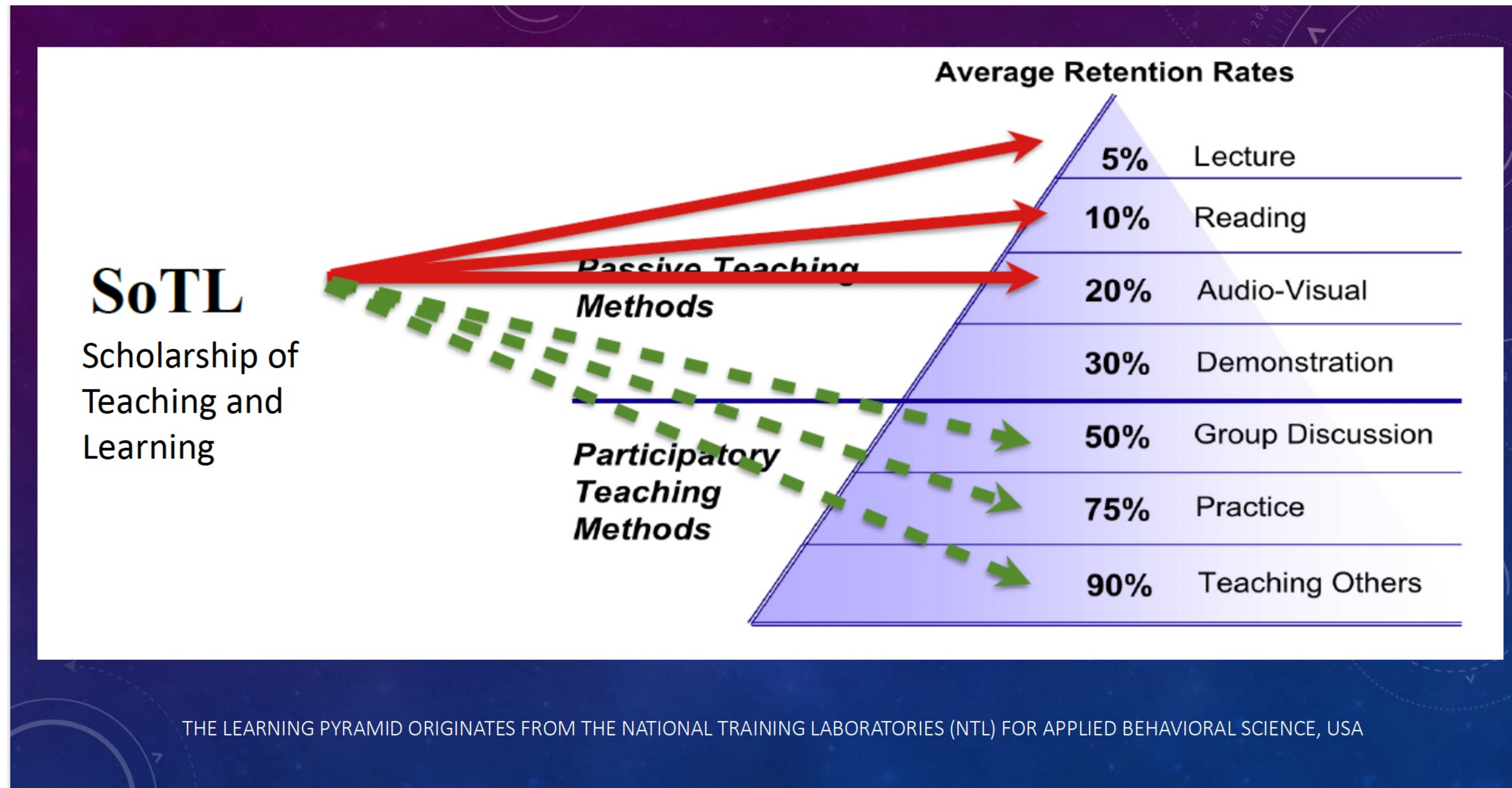


# New scenarios?...





# ...new learning approaches





# Teaching methodologies

## Projecto de Investigação UC Farmacoepidemiologia / Farmacovigilância

### **Tema 1:** *Estudo pós-autorização de efetividade e segurança da vacina Imvanex®*

Objectivo: desenho de um protocolo de estudo destinado a dar resposta a uma questão concreta de investigação, em contexto real de utilização de um medicamento.

O Comité de Medicamentos de Uso Humano (CHMP) da Agência Europeia de Medicamentos recomendou, em julho de 2022, a aprovação da vacina Imvanex®, já autorizada para uso contra a varíola em adultos, de forma a estender a sua utilização contra a

A decisão de recomendação de aprovação desta vacina baseou-se nos resultados laboratoriais (dados não clínicos) que sugerem que a vacina desencadeia a produção de anticorpos que visam o vírus da varíola dos macacos e podem assim ajudar a proteger contra

No âmbito da sua autorização, foi solicitado pela EMA a realização de estudos observacionais (incluindo um *European Public Assessment Report*) com objetivo de recolher dados que clarifiquem a relação benefício-risco em contexto real de utilização. Neste sentido, a companhia responsável pela vacina adjudicou a realização deste Estudo a uma multinacional, tendo sido constituída para este efeito uma equipa de investigação que integrará farmacoepidemiologistas de diversos países europeus. Portugal representar-se-á nesta equipa, através de um conjunto de peritos selecionados pelo INSA, os quais terão como missão, a elaboração de um protocolo deste estudo e a sua implementação no território nacional.



O estudo terá, entre outros, compreender a abordagem dos seguintes

questões e objetivos do Estudo de acordo com os requisitos

do estudo (e.g. critérios de inclusão e exclusão), fontes de

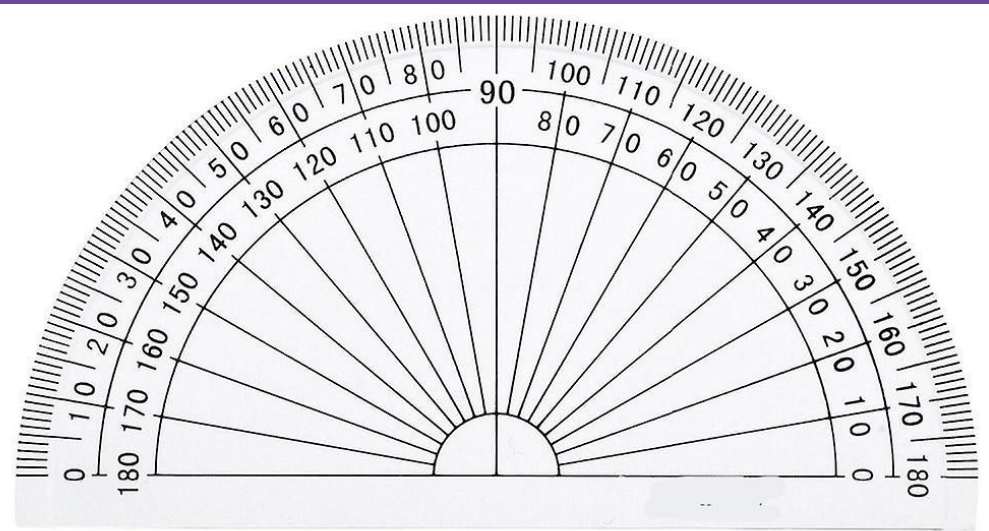
dados e quais *outcomes* (segurança e efetividade) / investigar e

identificar as vantagens e limitações metodológicas do Estudo proposto;

- <https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-18-21-july-2022>
- EPAR Imvanex®: <https://www.ema.europa.eu/en/medicines/human/EPAR/imvanex>



# Teaching methodologies





Faculdade de Farmácia da Universidade de Lisboa  
Mestrado Integrado em Ciências Farmacêuticas  
U.C. Gestão de Risco de Medicamentos e Produtos de Saúde; 5º ano, 1º semestre



Plano de  
Gestão de Risco



LISBOA  
UNIVERSIDADE DE LISBOA

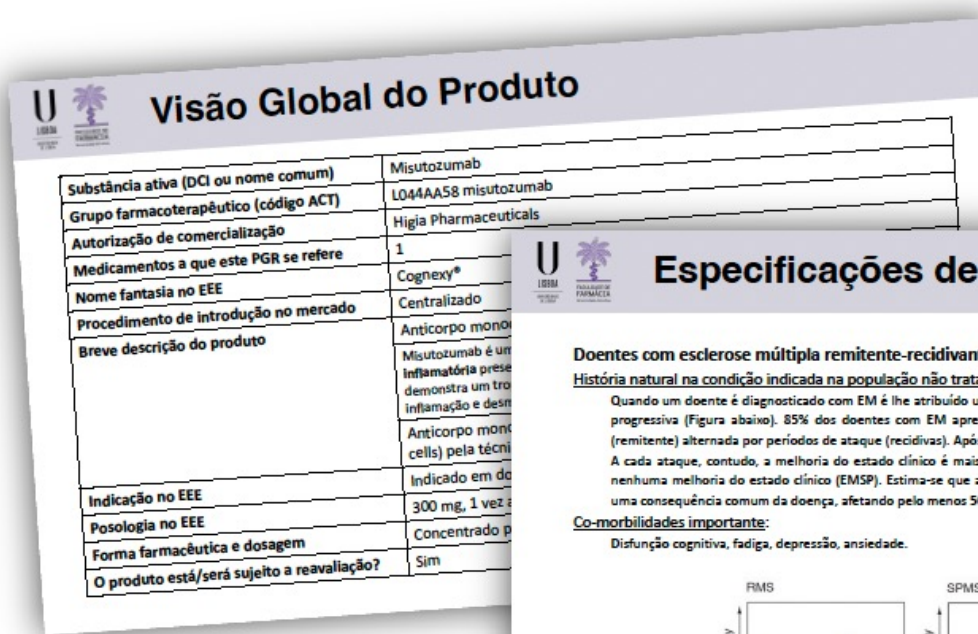


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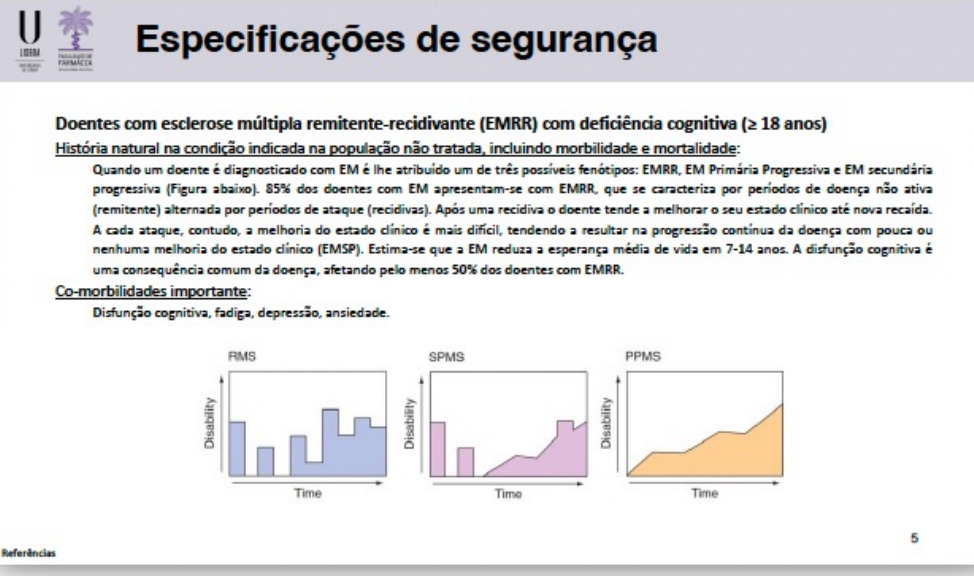
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- Parte I Visão Global do Produto
- Parte II Especificações de Segurança
- Parte III Plano de Farmacovigilância
- Parte IV Planos para Estudos de Eficácia Pós-autorização
- Parte V Medidas de Minimização do Risco (incluindo avaliação da eficácia das medidas de minimização do risco)
- Parte VI Sumário do Plano de Gestão do Risco

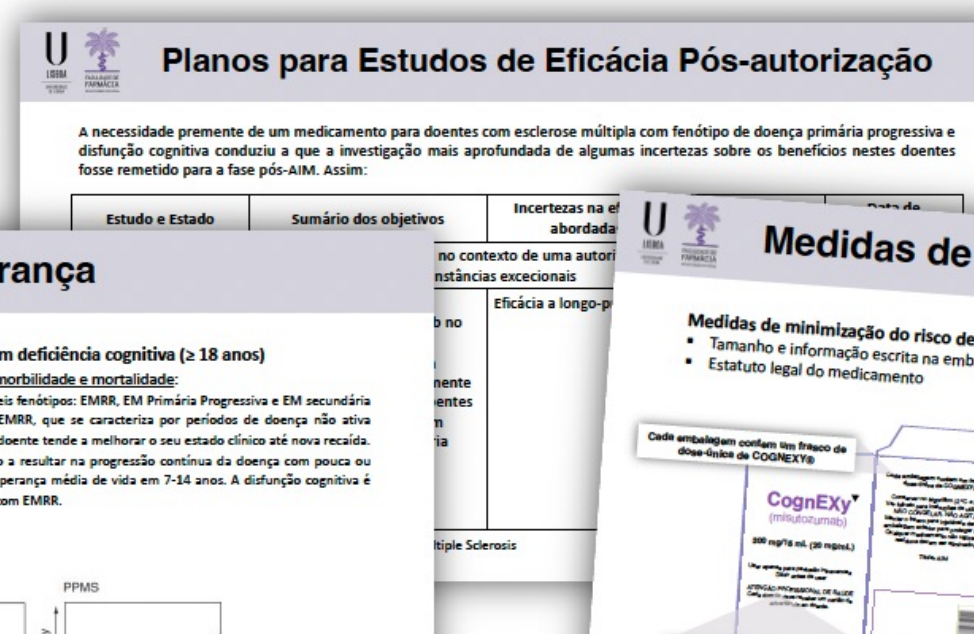





Visão Global do Produto



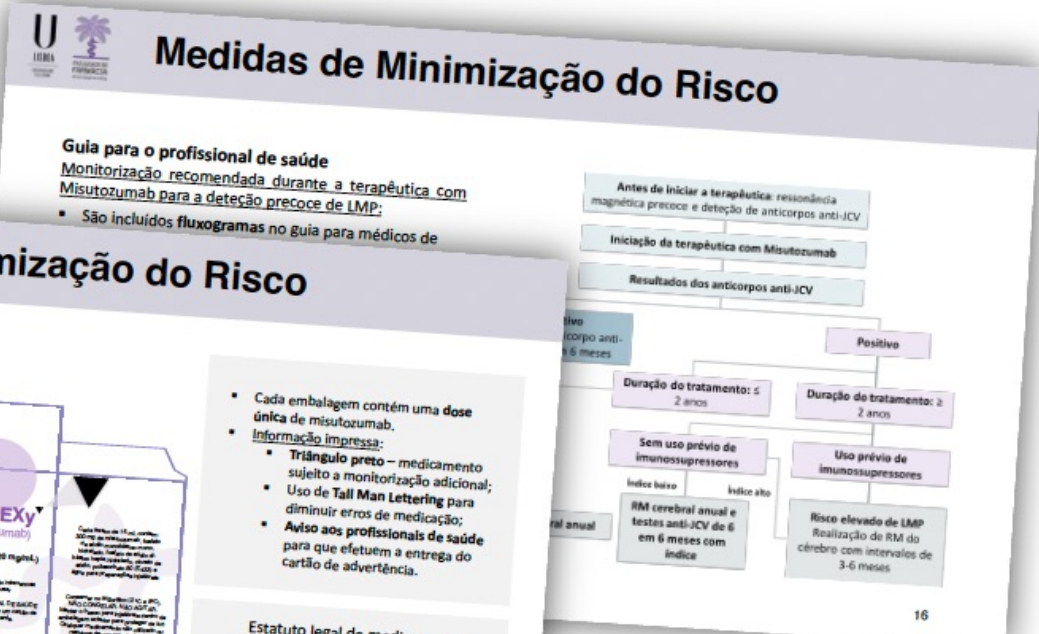
Especificações de segurança



Planos para Estudos de Eficácia Pós-autorização



Medidas de Minimização do Risco



Medidas de Minimização do Risco




# Postgraduate level – Master in Regulation and Evaluation of Medicines and Health Products & other courses (FFUL)

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
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EN | PT



FACULTY ▾ EDUCATION ▾ RESEARCH ▾ INTERNATIONAL ▾ LIVING@ FF ▾ SERVICES AND PARTNERSHIPS ▾ MEDIA ▾



MASTER IN REGULATION AND EVALUATION OF MEDICINES AND HEALTH PRODUCTS

Aims	
Coordenation	
Study plan	
Accreditation	
Career Opportunities	
Schedule	
Fees and Tuition	
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### AIMS

This course aims to increase de knowledge on all the regulatory aspects, laws and directives, science based approaches on the Marketing authorisation in European Union for Medicinal Human Medicines and Veterinary Medicines. Furthermore, this course will include legislation in Health Products based on Medicinal Plants, Medical Devices as well as patent laws, price regulation and others.

This course will also guarantee the training of professionals that can work and solve complex issues in regulatory affairs and can contribute to optimize decision making process.

**Teaching Language**

The classes are per default lectured in Portuguese unless non-Portuguese speaking applicant is admitted. If a non-Portuguese speaking applicant is admitted, the great majority of lectures will be spoken in English. The large majority course contents and materials are written in English.



## PHARMACOVIGILANCE

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CURSO PÓS-GRADUADO DE ATUALIZAÇÃO EM FARMACOVIGILÂNCIA (7ª EDIÇÃO)

Objetivos	
Coordenação	
Programa	
Destinatários	
Propinas	
Avaliação	
Candidatura	
Contacto	

### OBJETIVOS

A Farmacovigilância é uma área científica que tem como objetivo detetar, avaliar, minimizar efeitos adversos associados à exposição a medicamentos. Faz parte da avaliação da relação benefício-risco do medicamento, e ao longo do seu ciclo de vida, fornece importantes metodologias e técnicas estatísticas para identificar e prevenir reacções adversas a medicamentos contribuindo assim para melhorar os indicadores de mortalidade evitável. A Farmacovigilância é uma das áreas científicas que dá suporte às atividades regulamentares na área do medicamento e dispositivos médicos. Um dos objetivos da Faculdade de Farmácia da Universidade de Lisboa é a disponibilização de cursos de 2º ciclo, conferentes e não conferentes de grau, que capacitem os profissionais, académicos e investigadores nesta área de conhecimento cuja perspectiva de abordagem a nível de redes colaborativas internacionais é cada vez mais consistente. Todos os agentes na área do medicamento, incluindo cidadãos têm um papel muito importante no Sistema de Notificação Espontânea, fonte primordial da Monitorização da Segurança dos Medicamentos. Este curso aborda todas estas vertentes e pretende ser um espaço de atualização e aperfeiçoamento desta área científica



# The role of Regional Pharmacovigilance Unit at FFUL

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✉ [uflss@ff.ulisboa.pt](mailto:uflss@ff.ulisboa.pt)

- ✓ Internships for students
- ✓ ‘Real-world’ examples
  - ✓ Case reports
  - ✓ Causality assessment, etc.
  - ✓ Case-studies
- ✓ Research (undergraduate and post-graduate students)





# Pharmacovigilance should be a Public Health priority.....

***Public health is ultimately a question of what kind of society we wish to live in.***

*Sweden 2004, National Health Plan*

