Undergraduate and postgraduate pharmacovigilance education: A proposal for appropriate curriculum content

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Background: Adverse drug reactions (ADRs) are common, often preventable, and a leading cause of morbidity and mortality. Pharmacovigilance (PV) involves detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem. Education of healthcare professionals (HCPs) involved in drug prescription, dispensing and administration is essential to help prevent and mitigate both ADRs and medication errors and has to be focused on 3 pivotal aspects:

- **Awareness**: All medicines can produce adverse effects. ADRs should always be considered as part of the differential diagnosis if any new adverse condition, symptoms or signs appear after a drug administration or during or after pharmacological treatment.

- **Knowledge**: HCPs must have a sound understanding of the most frequently prescribed drugs and over-the-counter medications, factors that make patients more likely to benefit or more susceptible to harm, as well as of causes of medication errors.

- **Reporting**: HCPs should know how to report ADRs and the role of reporting on regulatory aspects and scientific knowledge.

Undergraduate curricula must provide, at a minimum, sufficient skills that warrant the appropriate and safe prescription/dispensing/administration of medications in clinical practice, focusing both on therapeutic effects and prevention of harm. Clinical appraisal skills must include ADRs as differential diagnosis, taking accurate medication history, basic individual causality assessment, identification and proper management of ADRs, and informing patients of possible ADRs.

Postgraduate periodic PV training should be mandatory as part of continuing education. Specialised postgraduate education should include advanced contents.

**KEYWORDS**
adverse drug reactions, basic and advanced contents, continuing education, medication errors university curricula, pharmacovigilance

**INTRODUCTION**

In the past decades, medical knowledge has advanced notably in all fields, particularly concerning medicines. The number of available pharmacological agents is continuously growing, and drugs are increasingly used. This progress has also led to worrying paradoxes: antimicrobial resistance threatens the effectiveness of anti-infective therapies and an epidemic of opioid abuse has emerged in the USA, 1 of the most developed and regulated countries. Serious adverse reactions—in most cases extensively...
described and often preventable—contribute to increasing mortality and hospitalisations.

Due to the extensive use of drug therapy, a large part of patient morbidity and mortality is currently drug related. However, drugs' beneficial effects are still perceived much above drug harms; this affects both prescribers and patients' expectations. Medicines are often overprescribed in clinical practice and overused within and outside clinical settings. In some countries, although drugs are regulated, their dispensing and sale is not controlled sufficiently, so that medicines can be bought with no medical prescription, often with no medical diagnosis or treatment surveillance.

Adverse drug reactions (ADR) have been defined as “any response to a medicinal product which is noxious and unintended”\(^\text{1}\); this definition now includes medication errors (MEs), off-label use, misuse and abuse. Adverse event, a term used both in the epidemiological assessment of drugs effects and pharmacovigilance (PV), is defined as "Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment."\(^\text{2,3}\)

The World Health Organization defined PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems".\(^\text{4}\) The main objective of PV is to prevent ADRs and their consequences. The importance of teaching PV to HCPs—who are responsible for the prescribing, dispensing, administration and monitoring of medicines—has been highlighted by a group of experts,\(^\text{5}\) and its main contents have been proposed for inclusion in curricula for the teaching of clinical pharmacology.\(^\text{6,7}\) Some years ago, an extensive core PV curriculum was presented, focusing on the different aspects of PV, with varying levels of complexity and completeness.\(^\text{8}\) However, there is still not a clear consensus concerning standards of PV teaching and what competencies healthcare students should have at graduation.\(^\text{9,9}\) A recently published article outlined the principles and objectives of the World Health Organization PV core curriculum for undergraduate education.\(^\text{9}\)

This paper aims to propose basic and advanced contents of PV be included in the under- and postgraduate curricula training of all clinical disciplines, not only in clinical pharmacology. It is based mainly on the experience of teaching PV in a university hospital. The contents have been selected considering the feasibility of their implementation in the context of saturated undergraduate curricula and the demands and workload of professional practice. Challenges in the application of this proposal are discussed. Recently, a Spanish approach to this topic has been published.\(^\text{10}\)

2 | ADRs

ADRs are a substantial cause of hospitalisations, especially for the elderly and in acute care settings. From 5 to 7% of admissions in general adult populations are due to ADRs;\(^\text{11}\) in some countries, this percentage exceeds 10%.\(^\text{12}\) Hospitalizations related to adverse effects of medications are associated with widely used therapeutic groups: diuretics, coumarins, low doses of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs).\(^\text{13,14}\) A recent meta-analysis showed that warfarin, aspirin, renin-angiotensin system inhibitors and digoxin accounted for 60% of fatal ADRs.\(^\text{15}\)

ADRs are often preventable. ADRs' preventability is mostly related to type A ADRs—i.e. those that are related to pharmacological characteristics and depend on dose (or variations in bioavailability due to interactions or pharmacogenetic variants). A meta-analysis found that pooled preventable ADRs accounted for 45.11%; among the included studies, those focused on the elderly (63.31%) and all age groups (49.03%) showed higher percentages than the paediatric population (16.40%).\(^\text{15}\) ADRs can be fatal. In 1998, extrapolating hospital data to the national population, Lazarou and Pomeranz estimated that adverse effects of medications were the fourth most common cause of death in the USA.\(^\text{16}\) A population-based study estimated ADRs to be the seventh cause of death in Sweden, with 3% of total deaths, and 6.4% of fatalities in hospitals.\(^\text{14}\) A recently published meta-analysis showed that the mean fatal ADRs prevalence varied from 0.01% in paediatric patients to 0.44% in the elderly, with a wide range from 0 to 5.2%. The mean prevalence of fatal ADRs was higher than that reported in an earlier meta-analysis suggesting that ADRs remains a significant cause of mortality. Intracranial and gastrointestinal bleeding and renal failure accounted for more than 50% of fatal ADRs in the recent study.\(^\text{17}\) Some very rare, serious, fatal or life-threatening ADRs—e.g. hepatotoxicity or severe cutaneous ADRs—can occur with widely used medicines, such as antibiotics or NSAIDs.\(^\text{17}\)

Many causes contribute both to the increase in the number of drug-related hospitalisations and the number of drug-related deaths: the increased size of the exposed population, older populations, the increase in the number of available drugs and the larger number of medications administered to each patient.

Medical healthcare is increasingly complex. Specialisation and subspecialisation of medicine, both in diagnosis and prescribing, often lead to additive prescribing, unrecognised adverse drug reactions and dangerous interactions.

While some old and widely used drugs are not fully understood (either in pharmacokinetics or pharmacodynamics), new pharmacological developments extend the use of medicines to new areas (as an example, monoclonal biological agents are available for new indications).

The population is ageing worldwide, and older adults are more susceptible to ADRs, are more likely to have comorbidities and are at higher risk of drug–drug interactions because of polypharmacy.\(^\text{18}\) An increasing number of frail patients live in nursing homes.

Information about ADRs is often limited. In newly marketed drugs, initial drug labels contain limited information about serious ADRs, which may be significant causes of morbidity and mortality in general practice, particularly in severely ill patients.\(^\text{19}\) Some scientific publications do not report harms in a similar way to beneficial effects.\(^\text{20}\) In some settings, professionals may lack independent and science-based continuing education. Promotional information overestimates the benefits of drugs and emphasises positive study results but often omits or minimises the risks.\(^\text{21,22}\) The use of drugs such as
mood modifiers, availability of drugs without a medical prescription, and biased media or internet information addressed to patients can also influence expectations about drug benefits.

3 | THE ROLE OF UNDERGRADUATE EDUCATION

In most countries, the University has the fundamental purpose of ensuring that graduates have the necessary knowledge, skills and behaviour relevant for their chosen profession. In other nations, such as the UK, there is a licensing authority that says whether people are competent to practice, and there is a proposal for a licensing exam independent of the Universities.23 Universities also participate actively in collaboration with other institutions (professional and specialists’ associations, hospital centres, etc.), in specialists’ training and continuing education; and play a central role in the recertification of professionals. Besides, regulatory staff involved in production and marketing authorisation of drugs are often healthcare professionals (HCPs) that graduated from universities. Education of HCPs is carried out in 2 stages: undergraduate and postgraduate training. The training up to graduation must prepare future professionals to face very complex challenges in medical practice (diagnosis, prescribing and treatment monitoring), a continually growing number of drugs, characteristics of populations that change over time and potential bias of scientific drug information published under undisclosed conflicts of interests or open promotional aims. Postgraduate education comprises both specialisation and continuing education. Continuing professional development can be implemented as a mandatory update, or as a way to overcome shortcomings of previous undergraduate education and potential misconceptions acquired in clinical practice. Both in undergraduate and postgraduate training, teaching about ADRs and PV is fundamental.

4 | HCPS’ REPORTING AS A SOURCE OF PV INFORMATION

Due to the limitations of randomised clinical trials (RCTs)—namely selected population, a limited sample of subjects and time of observation—much of the evidence regarding ADRs of a medicinal product arise in the postmarketing phase, being collected in National PV systems or more massive international databases (such as EudraVigilance, FAERS and Vigibase). Observations of ADRs in clinical practice and during postmarketing use of drugs constitute 1 of the bases of PV: reports of new, rare and serious suspected ADRs where causation can be reasonably established in individuals are the basis for signal generation and has supported or contributed to many regulatory actions24–26; voluntary reports also can provide additional information on already identified ADRs. However, spontaneous reporting systems largely depend on the active participation of reporters: underreporting—significant in most countries and critical in some regions—makes it challenging to assess the burden of drug-related problems.27 Two decades ago, a more focused approach on patients as the central part of the healthcare and PV systems has led to the inclusion of patient reporting, to the search for adverse effects in social media and other strategies; enriching PV with the patient’s views—up to then, an unheard voice.27 However, patients may not link symptoms with their medicines, and HCPs—either physicians, community and hospital pharmacists, nurses among others—should have the technical expertise to describe and interpret adverse events and assess possible causality. HCPs are in contact with patients of all social status and cultural level, even those with the lower level of education—which prevents them from reporting—or with no access to the Internet and related technologies. In PV, the role of HCPs remains essential, not only for reporting but above all, for ADRs prevention, for prudent and safe prescribing and dispensing.

5 | HOW PHARMACOEPIDEMIOLOGICAL STUDIES CAN CONTRIBUTE TO PV TEACHING

It should be kept in mind that, for individuals present with some relatively frequent morbidities or risk factors, the assessment of drug causality in common conditions such as myocardial infarction or stroke can be challenging. These events—and many others conditions—probably will not be suspected as drug-induced, but the relationship with a drug can arise when the association is evaluated in a larger number of people. In the last 3 decades, RCTs, meta-analyses and formal pharmacoepidemiological studies (case–control and cohort studies) have noticeably increased their importance as a source of warning and support of regulatory actions.25 Recent RCTs, meta-analyses and observational studies provide many examples. NSAIDs had been associated with an increased occurrence of thrombotic events, especially for selective agents that inhibit cyclo-oxygenase 2. Nevertheless, assessing drug causality can be hard if myocardial infarction occurs in a patient having risk factors for coronary artery disease and who is treated with a selective cyclo-oxygenase 2 inhibitor or any other NSAID not inhibiting enough the synthesis of thromboxane A2 (included the widely used paracetamol).28 The VIGOR study assessed clinically important upper gastrointestinal events in patients treated with rofecoxib compared with naproxen; the results showed also an increased number of events of myocardial infarction in patients treated with rofecoxib.29 In spite of this published data, rofecoxib was marketed in 2004, but it was withdrawn by its manufacturer in September that year.28 The signal of adverse cardiovascular effects of rosiglitazone—an insulin-sensitizer supposed to have fewer adverse effects than insulin-secretagogues—arose since a meta-analysis found an increased number of myocardial infarction events in patients treated with rosiglitazone compared with placebo.30 Rimonabant was withdrawn from the European market as a result of the evidence raised by meta-analyses of RCTs (rimonabant was never marketed in the USA).31–33 The postauthorisation safety study SCOUT trial showed that patients treated with the appetite-suppressant sibutramine were at higher risk of thrombotic events.34–36 A valvular
condition—that can have weak clinical manifestations and be undiagnosed unless an echocardiogram is performed—was also hard to link with an appetite suppressant, such as the benfluorex: a case-control study revealed the causal association, which had been suggested by spontaneous and case-reports. These examples show that in many relevant safety issues affecting the vital prognostic of millions of people, the information from RCTs, meta-analyses and pharmacoepidemiological studies have been the source for detecting and or confirming the association between the drug and the adverse effect. Additionally, secondary databases of electronic health records are increasingly used for the assessment of effectiveness or safety of marketed drugs, adding confirmatory or complementary evidence to those from RCTs. Signal detection exercises in electronic health records have been proposed for newly introduced medicinal products on the market, in addition to the spontaneous reporting data. When teaching PV, particular emphasis should be put on the information provided by pharmacoepidemiology, which can be relevant for the causality assessment of individual cases of suspected ADRs, and HCPs should be encouraged to search for pharmacoepidemiological information when assessing individual cases.

6 | THE TEACHING OF PV IN UNDERGRADUATE MEDICAL CURRICULA

Prescribing is a very complex task and should always involve an accurate diagnostic—underpinned by a thorough knowledge of the pathophysiology of the patient's problem—and a sound understanding of pharmaceutical, pharmacokinetic, and pharmacodynamic properties of the prescribed drug. Newly qualified doctors are not allowed to perform high-risk practical procedures, although they are enabled to prescribe many powerful medications from the first day of practice. Safety education remains largely absent from pre-service training in many settings, and the majority of medical students do not feel well prepared for prescribing. In low- and middle-income settings, errors due to inadequate knowledge or skills are mentioned as a cause of safety incidents in primary care. In high-income settings, many studies highlighted the lack of proper prescribing skills. A cross-sectional survey among 900 final-year students in Europe revealed poor knowledge of drug interactions and contraindications; students also chose inappropriate therapies for common diseases or made prescribing errors. A systematic review of 25 articles describing final-year medical students' competencies and 47 papers evaluating skills, showed that students lacked preparation, confidence in their abilities and knowledge, specifically in terms of the prescription of antimicrobials and PV. Students should be trained in how to look for information about interactions and how to avoid them. Phase 1 interaction studies performed on healthy volunteers usually do not report severe clinical manifestations due to variations in plasma drug concentration, although they are possible in older people with comorbidities and polypharmacy.

MEs, including prescribing errors, can cause ADRs that can be very serious. Six out of 15 recommendations from an expert consensus for reducing the risks of MEs refer to education and training. Prescribing errors are more frequent in physicians in the first and second years after graduation, although physicians' competencies for prescribing might improve after 6 months of clinical practice. Clinical practice can correct (or not) MEs caused by shortcomings in undergraduate training but at the expense of patients' safety. Prescribing errors account for 40% of all MEs from the use of low doses of methotrexate collected in 4 Danish databases. One study reported that 10% of hospital admissions in hospitals in the UK were due to prescribing errors, mostly related to the low level of training in clinical pharmacological received by physicians. In a study conducted in Australia, less than half the graduates responded that they felt they were adequately trained to prescribe, and most indicated that they wanted to have more training in pharmacology during their career. Almost all final-year medical students (96%) who received an educational supplementation in various aspects of drug therapy, including pharmacological interactions, considered that this education helped them avoid MEs.

Health care undergraduate curricula must guarantee that all new graduates have a sound knowledge of basic and clinical therapeutics, of the most commonly prescribed medications and ADRs, as well common MEs and how to avoid them. PV should be taught across all healthcare disciplines and should be included both in undergraduate and continuing education. This crucial aspect of medical healthcare merits discussion in order to reach a consensus on the minimum competencies that HCP must have, and how this can be achieved.

7 | OBJECTIVES OF A PV EDUCATION PROGRAMME

An undergraduate teaching and continuing education programme for PV should provide 3 pivotal axes:

7.1 | Awareness of adverse effects

- All medicines have adverse effects. There are no 100% safe medications.
- ADRs can be manifest soon after the drug administration or a long time after treatment.
- The severity of ADRs may differ between individuals.
- Some ADRs are listed in product information, but others are not.
- Some patients are especially vulnerable to ADRs due to their pathology, age, sex or functional status. This susceptibility can change during the patient's life.
- Some individuals are genetically susceptible to specific adverse effects.
- ADRs can present as any new adverse symptoms or condition in a patient treated with a pharmacological agent, or as a worsening of the patient's condition; this can complicate or obscure the identification of an ADR.
| Undergraduate education/continued education | Postgraduate specific training |
|------------------------------------------|-------------------------------|
| **Basic principles** | | |
| All medications have adverse effects and can cause hypersensitivity reactions and organ-specific lesions, irrespective of their frequency of use. There are no 100% safe medications | Define an adverse effect of medications and identify other problems related to the use of medications | Investigation of rare or unreported side effects |
| | Know the frequency of adverse effects of medications in the population and their impact on public health | | |
| | Know the most frequent classifications of adverse drug reactions, and be able to identify them. | | |
| **Drug hypersensitivity** | | |
| Gell–Coombs classification applied to drugs | Know Gell–Coombs classification applied to drug hypersensitivity | Importance of proper and prompt diagnosis |
| | Identify an anaphylactic reaction and to know how to treat it. Recommendations to patient and caregivers. | To identify the time to onset, relationship with changes in doses and intermittent administration. |
| | Know the risk factors for allergy/anaphylaxis | | |
| | Know that allergy or anaphylactic reaction is possible without a known antecedent of prior exposure to the agent | | |
| | Know most commonly causative medications | | |
| | Types and modes of presentation of delayed hypersensitivity | | |
| | Rare serious cutaneous drug reactions: Most causative agents, time to onset, symptoms and signs. | | |
| **Pharmacogenetics** | | |
| Definition, concepts | Pharmacogenetic causes of drug-disposition variability | Epidemiology of pharmacogenetic variants in local population |
| | Metabolizing enzymes that can present with pharmacogenetic variants, and drugs metabolized. | | |
| | Pharmacogenetic basis of variability in drug response focused on pharmacodynamics. | | |
| | Pharmacogenetic basis of hypersensitivity ADRs | | |
| **ADRs: Identification and assessment** | | |
| Basic principles of causality assessment | Taking accurate medication histories: these must include current prescription and over-the-counter drugs and significant past drugs (long periods of treatment and/or hazardous drugs, or potential for delayed ADRs) | Therapeutic decisions based on clinical and laboratory data (renal and liver failure, RIN, cytology) and on pharmacokinetic data |
| Recording and assessing current and past ADRs | Evaluation of new symptoms and signs | Therapeutic decisions in a complex risk/benefit context |
| WHO algorithm and Naranjo scale for causality assessment | | |
| **ADRs prevention** | | |
| Patient factors that increase susceptibility to adverse reactions | | |
| Factors of the patient in therapeutic decision-making. | | |
| Drug-dose adjustment in renal, hepatic impairment and in cardiac failure. | | |
Very rare, fatal or life-threatening ADRs can occur with very frequently used drugs, such as antibiotics, NSAIDs or anticonvulsants. Students and graduates should be advised not to overprescribe.

### 7.2 Knowledge of (commonly) used medications

- To prevent known ADRs and those that can be produced by pharmacokinetic or pharmacodynamic interactions, undergraduate training must provide a sound understanding of drugs that the professional can prescribe or dispense, and the most commonly prescribed or used agents, including those prescribed by specialists (e.g. antidepressants) and OTC drugs. Information on ADRs and metabolism of more common herbal remedies should also be advisable.
- HCPs must know how to identify and manage known ADRs. For previously unreported suspected ADRs, HCPs should be aware that they can make clinical decisions (to change, reduce or withdraw the pharmacological agent) based on the individual-case causality assessment of the suspected ADR.
- HCPs should be aware of the most frequent MEs related to some products and how to avoid them.

### 7.3 Reporting through spontaneous reporting systems

- HCPs must know how suspected ADRs reporting can contribute to regulatory aspects and scientific knowledge. Information contained in ADR reports can provide a basis to signal generation, and, as a consequence, can support regulation if a signal is confirmed. Regulators may require modification of the patient information leaflets, warnings or specific security information, changes of the marketing authorisation conditions, or withdrawal from the market.
- Both reports of adverse drug effects and formal PV studies contribute to scientific knowledge about relationships between the presentation of symptoms, signs or diseases and exposure to drugs, and can provide elements for the generation of hypothesis about the mechanism of adverse reactions, which in turn can contribute to their prevention.
- HCPs should be able to identify MEs and how to report them.

### 8 ADDITIONAL TARGETS FOR A PV EDUCATION PROGRAMME

Other targets for a PV education programme include raising critical awareness and promoting active attitudes to avoiding polypharmacy and over-prescription, optimising the use of antimicrobials to prevent drug-resistant infections and deprescribing safely if an ADR is suspected. Future HCPs should be trained in the identification of the ADR and the causative agent and in avoiding prescribing cascades.

Students should develop skills in how to reach effective and open communication with patients, both to elicit and record an accurate medication history and to provide proper and clear advice when prescribing.
Students should be able to identify and utilise sources of reliable scientific information and ask specialised PV or regulatory centres for information. Future HCPs should know how the quality and legitimacy of medicinal products are controlled and tracked since the current approach to security of the medicines also refers to the reliability of origin of the product and the integrity of the quality of the product throughout the entire distribution chain.55,56

Tables 1–4 present a proposal of PV basic and advanced contents for undergraduate, continuing education and postgraduate levels. Contents encompass detection, evaluation, prevention and handling of adverse drug reactions, reporting and communication, interactions, and MEs. This proposal does not include specific training in regulatory aspects, detection and evaluation of signals and pharmacoepidemiological studies.

| TABLE 2 | Minimum contents on adverse drug reaction (ADR) reporting and communication in undergraduate and postgraduate curricula |
|----------|----------------------------------------------------------------------------------|
| **Sources of information of ADRs Of adverse effects** | **Regulatory information:** Development of drugs. Basics of the marketing authorization. Postmarket surveillance. WHO website. Regulatory websites **Other sources:** Independent websites |
| **Pharmacovigilance systems** | To be familiar with the national pharmacovigilance (PV) system To know how to report (yellow cards, via the internet, by telephone etc.): To PV centres, to the national regulatory authority. Create awareness about the importance Of notification of adverse effects by Of the health professional. To know the minimum necessary elements that a report must contain to be assessable. |
| **Communication** | Training in reporting a suspected ADR with all necessary and relevant data, including free text. Protection of the patient’s identity. Medication history focused on ADR, medications administered, administration time, Dose, route. How to communicate to the patient the risk of possible ADRs. |
| | **Postgraduate specific training** |
| **Sources of information of ADRs Of adverse effects** | How regulatory requirements have evolved. National regulation. Other countries/regions regulations. Data search in bibliography, databases, information of product. Search of information in regulatory websites, other institutions and organizations. |
| **Pharmacovigilance systems** | To know international PV systems To search in PV databases publicly available. Analysis of clinical cases, detection of reactions, adverse and training. In notification. Design and interpretation, of PV or PE studies. |
| **Communication** | Training in writing ADRs case or case-series Training in the survey of data, discuss |
| | Communication strategies to patients and to society. |

9 | THE TEACHING AND LEARNING OF PV AND LOCAL HEALTHCARE SYSTEMS

The learning of adverse effects and how to prevent them should be adapted to the local healthcare system while providing updated and unbiased information. Trainers should pay attention to regional population characteristics and health needs and resources availability. For instance, pharmacogenetic variability varies among regions and can affect enzymes regulating drug metabolism, receptors for drug response and immune reactions. Some pharmacogenetic tests that can predict the possibility of developing ADRs are not available or affordable in some countries. If this is the case, teaching can be focused on the frequency of pharmacogenetic variants in different populations and recommendations not to prescribe such agents if not strictly necessary, or, if prescribed, to monitor their effects closely.
**TABLE 3** Minimum contents on pharmacological interactions in undergraduate and postgraduate curricula

|                          | Undergraduate curricula/continued education | Postgraduate specific training |
|--------------------------|---------------------------------------------|-------------------------------|
| **General concepts of drug–drug interactions and food–drug interactions** | Interactions with therapeutic objective and interaction causing ADRs Pharmacokinetic mechanisms: identification of pharmacokinetic characteristics that can favour interactions. | Deeper knowledge about transporters, metabolism, elimination. Interactions caused by parent drug and by metabolites |
|                          | Interactions between systemic and topical or locally administered medications. Role of transporters on interactions Elimination. Dose-adjustment according to renal function. Nephrotoxicity. Interactions due to decreased elimination. Pharmacodynamic interactions | To identify patient characteristics that favour clinical manifestation of adverse interactions and/or serious outcomes |
|                          | Epidemiology. Potential of interactions with polymedication | Evaluation of information contained in label or summary of product characteristics |
|                          | Interaction in patients with pharmacogenetic variants | Consultation and evaluation of information contained in package inserts or summary of product characteristics in order to prevent adverse reactions due to interactions. Continued updates regarding variations in marketing authorisations, e.g. changes to indications, new contraindications Drug-dosing adjustment in order to prevent and handling ADRs caused because of interactions |
| **Prevention and handling of ADRs due to interactions** | Prevention and handling of ADRs due to interactions Consultation and evaluation of information contained in package inserts or summary of product characteristics in order to prevent adverse reactions due to interactions. Continued updates regarding variations in marketing authorisations, e.g. changes to indications, new contraindications Drug-dosing adjustment in order to prevent and handling ADRs caused because of interactions | Evaluation of information contained in label or summary of product characteristics |

**10 | INCLUSION IN CURRICULA**

Health sciences curricula for undergraduate education are usually saturated, and this makes it challenging to incorporate recent advances. In medicine, clinical pharmacology curricula must include PV contents. Also, every postgraduate clinical training programme should incorporate training in PV. In pharmacy, pharmacists should have an awareness of when ADRs occurred, and be able to advise on ADRs and motivate patients to report them. Engaging clinicians—and not only clinical pharmacologists and pharmacists—in PV training can provide sustainable strategies for PV teaching.

**11 | POSTGRADUATE EDUCATION**

If not used or rehearsed, knowledge and skills are lost, the estimated half-life of learning is about 2 years. The importance of postgraduate education in clinical pharmacology and therapeutics has been highlighted at least 4 decades ago. Since then, there has been a lack of coordinated and mandatory training specifically addressed to improve graduates’ prescribing skills, maximising drug use benefits, and minimising harms.

Two professional cohorts can benefit from postgraduate education. For professionals whose degree curriculum did not provide the minimum training in PV, a supplementary PV education can offer the essential contents for achieving professional competence in terms of safe and effective prescribing, dispensing and administration of medications, prompt recognition of possible adverse effects of drugs and how these ADRs can be managed and reported. For professionals who have received adequate primary training in PV, learning should include complementary more advanced contents and more complex problems.

In both cases, the learners’ clinical experience is an advantage—and also a challenge—for developing specific materials and enriching discussion. Postgraduate education allows multidisciplinary interactions and exchange of experiences among physicians, pharmacists, nurses, dentists etc., despite the challenges posed by different levels of knowledge. Interdisciplinary audiences should be considered when planning postgraduate PV training.

**12 | MODALITY OF TEACHING**

Often, learners are only engaged and motivated if contents provide a guide to their concerns and patients’ problems. Therefore, each audience needs an adaptive approach and tailored content. Didactic lectures must take into account the practical issues that the students
face daily and should also give the room to retrieve the perspective learners have about this specific content. Problem-based learning is the most appropriate way to address a topic; when possible, examples should arise from the learners’ environment (hospital, primary care). For graduated doctors, pharmacists and nurses in training, clinical rounds offer the opportunity to refresh pharmacological concepts and diagnostic skills.

Adaptive design of the contents of teaching based on issues that are brought up spontaneously from the audience favours the interest of the participants and improves the learning outcome. However, some students are used to a more traditional mode of teaching, prefer less participation and welcome structured contents that they have to learn more passively. These preferences should be elicited and taken into account.

In undergraduate education, pharmacists and physicians usually have separate classes. Postgraduate training offers the possibility of gathering both perspectives in multidisciplinary courses. This interaction favours professional collaboration, which can also be fostered through the development of specific task in hospitals or clinical practice. An elective module for 3rd and 4th-year medical students, with a multi- and interprofessional group of faculty (family physicians, internists and paediatricians, nurse practitioners, a pharmacist) and held in designated ambulatory practice sites showed encouraging results.

### ATTITUDE TOWARDS ADRS

Both experienced and in-training physicians and other HCPs, such nurses and hospital pharmacists, often see and accept ADRs as natural consequences of pharmacological therapies, even if the reactions are
The frequency and seriousness of medicines-related harms occurred in clinical practice depend on how medicines are prescribed and used. Universities should promote and teach the principles of therapeutic and medicinal safety surveillance during clinical practice. Contents and modality of PV teaching should always be selected considering the healthcare needs and resources of the community to which the University belongs. Curricula must include the main aspects of PV (understanding, preventing, recognising, managing and reporting ADRs) and the importance of accurate and thorough medication histories, taking into account both current and past drugs, past ADRs and delayed adverse effects. ADRs should always be considered as a differential diagnosis in a patient previously exposed to drugs. All future HCPs should be taught how to avoid preventable ADRs and MEs, when to suspect an ADR and how to report it. In undergraduate medical education, required clinical skills and proper training in rational and safe prescribing should be included in all disciplines addressing drug therapies, and not only in clinical pharmacology curriculum. For graduates, continuing education in PV—to raise awareness and to provide independent scientific information about ADRs and MEs—should be mandatory for periodic recertification.

This proposal of basic and advanced contents is expected to be enriched by comments and experiences from teachers, HCPs and students, to build a further consensus about the minimum competencies that HCP must have, and how this objective can be reached and put in practice.

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15 | CONCLUSION

The frequency and seriousness of medicines-related harms occurred in clinical practice depend on how medicines are prescribed and used. Universities should promote and teach the principles of therapeutic and medicinal safety surveillance during clinical practice. Contents and modality of PV teaching should always be selected considering the healthcare needs and resources of the community to which the University belongs. Curricula must include the main aspects of PV (understanding, preventing, recognising, managing and reporting ADRs) and the importance of accurate and thorough medication histories, taking into account both current and past drugs, past ADRs and delayed adverse effects. ADRs should always be considered as a differential diagnosis in a patient previously exposed to drugs. All future HCPs should be taught how to avoid preventable ADRs and MEs, when to suspect an ADR and how to report it. In undergraduate medical education, required clinical skills and proper training in rational and safe prescribing should be included in all disciplines addressing drug therapies, and not only in clinical pharmacology curriculum. For graduates, continuing education in PV—to raise awareness and to provide independent scientific information about ADRs and MEs—should be mandatory for periodic recertification.

This proposal of basic and advanced contents is expected to be enriched by comments and experiences from teachers, HCPs and students, to build a further consensus about the minimum competencies that HCP must have, and how this objective can be reached and put in practice.

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