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Review

# The Contribution of Clinical Pharmacologists in Precision Medicine: An Opportunity for Health Care Improvement

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## ARTICLE INFO

## ABSTRACT

Background: Clinical pharmacologists play an important role and have professional value in the field, especially regarding their role within precision medicine (PM) and personalized therapies.
Objective: In this work, we sought to stimulate debate on the role of clinical pharmacologists.
Methods: A literature review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, through electronic consultation of 2 databases, PubMed/Medline and Embase, and Google Scholar with manual research taking into account the peer-reviewed literature such as observational studies, reviews, original research articles, comments, mini-reviews, and opinion papers published in English between 2010 and February 2020. Titles and abstracts were screened by 1 author, and studies identified for full-text analysis and selected according to inclusion criteria were agreed on by 2 reviewers.
Results: We identified a total of 535 peer-reviewed articles and the number of full texts eligible for the project was 43. Several publications highlight the clinical value of pharmacologists in highly complex hospitals, where the strategies of PM are implemented. Although there are still no studies measuring the clinical efficiency and the efficacy of clinical pharmacology services, and the applicability of PM protocols, this review shows the considerable debate around the future mission of clinical pharmacology services as a bridging discipline capable of combining the complex knowledge and different professional skills needed to fully implement PM.
Conclusions: Various strategies have been conceived and planned to facilitate the transition from main-stream medicine to PM, which will enable patients to be treated more accurately, with significant advantages in terms of safety and effectiveness of treatments. Therefore, in the future, to ensure that the evolutionary process of medicine can involve as many patients and caregivers as possible, infrastructures capable of bringing together different multidisciplinary skills among health professionals will have to be implemented. Clinical pharmacologists could be the main drivers of this strategy because they already, with their multidisciplinary training, operate in a series of services in high-level hospitals, facilitating the clinical governance of the most challenging patients. The implementation of these strategies will lastly allow national health organizations to adequately address the management and therapeutic challenges related to the advent of new drugs and cell and gene therapies by facilitating the removal of economic and organizational barriers to ensure equitable access to PM. (Curr Ther Res Clin Exp. 2021; 82:XXX–XXX)

## Introduction

The greater availability of drugs and therapies has led to a progressive increase in the prevalence of polypharmacy, which ranges

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widely from between 10% to nearly 90% depending on the populations under study.[1] A rising number of adverse drug reactions (ADRs) has led to unplanned hospital admission or readmission of patients, with a drug–drug interaction suspected in 49% of cases.[2–5]

Important economic and social costs must be borne nowadays to cope with this situation. Therefore, significant efforts are being made to refine personalized, precise, predictive, and participatory therapeutic strategies that can be systematically defined as precision or personalized medicine (PM).[6]

This new scenario is emerging as an innovative way of treating citizens by combining all the health technologies available today. Consequently, through the use of artificial intelligence systems for the simultaneous processing of data from clinical research, diagnostic imaging, application of biomarkers, and genome analysis, in the future it will be easier to manage pathological conditions more precisely and also to identify the potential risk factors of a specific therapy.[7]

A milestone in this new global strategy was set in 2015 by former US President Barack Obama with his All of US initiative. This government-funded action aimed to enroll at least 1 million patients in an intensive PM program (http://allofus.nih.gov), whereas a stronger and clearer position was adopted in the European Union (EU), where the European Council's conclusions on PM invite the EU member states and the EU Commission to "support access, as appropriate, according to national provisions, to clinically effective and financially sustainable personalised medicine by developing patient-centred policies including, as appropriate, patient em-
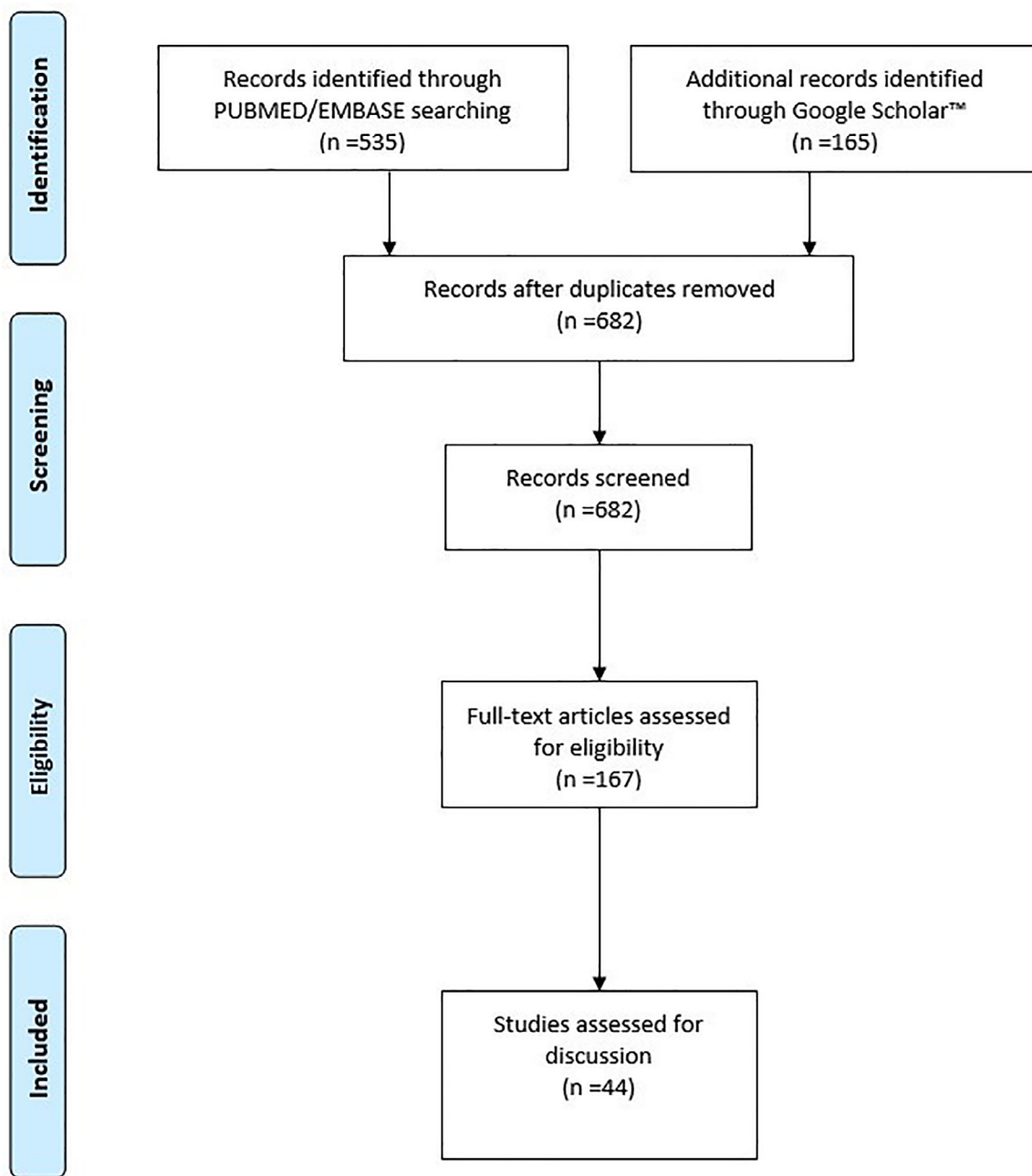


**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement flow diagram of the literature search and inclusion strategy for articles included in the review. Modified from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. *PLoS Med.* 2009;6(6):e1000097. For more information, visit http://www.prisma-statement.org.

powerment and the integration of patient perspectives in the development of regulation processes, in cooperation with patient organisations and other relevant stakeholders" and to "take personalised medicine into account in the broader context of the future framework for sustainable European Union collaboration on patient safety and quality of care."[8]

The adoption of PM practices in hospitals requires the interaction of different medical disciplines, including clinical pharmacology (CP). The American College of Clinical Pharmacology defines CP as the promotion of the rational use of medications in humans by studying their restorative effect, to amplify the effect of drugs, and reduce their side effects. Therefore, from this perspective, clinical pharmacologists bridge the gap between science and the practice of medicine through innovative research, development, and regulation of medications. CP pursues the optimal use of drugs by applying the provisions of personalized pharmacotherapy, taking into consideration the factors that have an influence on the interindividual variation of drug response.[9] The cultural domains that characterize CP, such as pharmacogenetics and pharmacogenomics, today become tools that are fundamental and indispensable to the critical development of future PM protocols and represent a substantial part of the link between the field of CP and the field of PM.

The goal of the study was to review the literature on PM (also known as personalized medicine) to provide a perspective for CP.

## Methods

A review of the literature was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement,[10] through electronic consultation of 2 databases, PubMed/Medline and Embase, through manual research considering the peer-reviewed literature such as observational studies, reviews, original research articles, comments, minireviews, and opinion papers published in English between 2010 and February 2020, with the combination of the following Medical Subject Headings terms: *Pharmacology, Clinical/economics* OR *Pharmacology, Clinical/legislation and Jurisprudence* OR *Pharmacology, Clinical/methods* OR *Pharmacology, Clinical/organisation and administration* OR *Pharmacology, Clinical/standards* OR *Pharmacology, Clinical/statistics and numerical data* OR *Pharmacology, Clinical/trends* OR *Clinical Pharmacology, Precision Medicine* OR *Precision Medicine/organisation and administration*. The same research was performed using Google Scholar.

The criteria for inclusion were: the study reviewed the status of PM or personalized medicine in a context of optimization of health organization and administration and safety of therapy, optimization of costs, and hospital budgets; the study investigated the prospective or existing relationship of collaboration between different figures of health professionals in the fields of CP and PM.

The exclusion criteria were: noncompliance with the 2 inclusion criteria mentioned; articles for which full text was not available due to the fact that they were article abstracts and/or published posters, were not in English, or were grey literature.

### Data synthesis and analysis

Titles and abstracts were screened by 1 author (D.G.) and studies identified for full-text and selected according to inclusion criteria were agreed upon by the second (V.A.C.) and the third reviewer (F.S.). Each study was analyzed, and a summary of the findings was written. The results of this review process were compared, and any discrepancies were resolved by consensus following discussion.

## Results

### Identification and selection of studies

The literature selection and research strategy with the inclusion and exclusion criteria are shown in Figure 1. We identified a total of 535 peer-reviewed articles in the electronic databases, fixing a retrospective limit on date of publication to a 10-year range. Using Google Scholar as a research engine, we retrieved 165 additional records for a total of 700 records. The removal of duplicates reduced records to 682. After the screening, the number of full-text articles that were assessed for eligibility was 167. Finally, applying all the inclusion/exclusion criteria, the number of full texts eligible for the project was 44 (Figure 1).

### Characteristics of the included studies

The main characteristics of the included studies are presented in Table 1. They can be grouped as follows: review (n = 21); systematic review (n = 2); metanalysis (n = 1); research article (n = 3); observational study (n = 3); viewpoint (n = 3); commentary (n = 1); letter (n = 2); position paper (n = 1); report (n = 2); and focus, survey, and overview (n = 5).

### The Current Status of PM or Personalized Medicine

Synonyms such as *precision* or *personalized* are mentioned in current language use and literature to describe an identical model for health care delivery that relies heavily on data science, digital health, and disease evolution management. The European Commission in 2016, through the Horizon 2020 Advisory Group, defined instead personalized medicine as a medical model that uses characterization of individuals' phenotypes for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention (EU 2015/C 421/03). The term *precision* rather than *personalized* involves an evolution of contemporary medical practice toward more efficient and precise prevention, diagnosis, and therapeutic strategies, referring to an ecosystem that uses patients, digital health, genomics, and other molecular technologies as the common denominator.[11]

PM is therefore not only about drugs or medical products, but also about a better understanding of the biological mechanisms and environmental interactions that govern the health–disease process and its influence on the whole health continuum, from health research to patient care, an evolutionary rather than revolutionary approach that may take many years to develop and consolidate.[12]

The area of oncology is benefiting the most from this new approach: in 2018, out of the 41 new molecular entities approved by the Food and Drug Administration Center for Drug Evaluation and Research, 16 had oncologic indications.[13–15] The same year, the European Medicines Agency approved 84 drugs for commercialization, 23 of which had oncologic indications.[16]

The approval of these new treatments has in fact been facilitated by the contextual development and application of PM procedures, in particular the simultaneous advancement and refinement, discovery, and analysis of the clinical value of those prognostic biomarkers that are associated with outcome independent of treatment, in combination with the characterization of predictive biomarkers that are associated with the effects of the treatment.[17]

The traditional development process, in which drugs are evaluated for safety in Phase I, efficacy in Phase II, and finally against standard therapy in a randomized clinical trial in Phase III, is grad-

**Table 1**

Selected papers, publication year, design, relevant topics and outcomes of the studies included in the review.

| Author | Publication year | Study design | Relevant topics and outcomes |
|---|---|---|---|
| Pirmohamed M, et al[3] | 2004 | Prospective observational | Current burden of ADRs through a prospective analysis of all admissions to hospital. Outcome: Prevalence of admissions due to an ADR, length of stay, avoidability, and outcome |
| Forster AJ[4] | 2003 | Prospective cohort | Incidence, severity, preventability, and ameliorability of AE affecting patients after discharge from the hospital and to develop strategies for improving patient safety |
| Bonnet ZD, et al[5] | 2013 | Ancillary | Study from a 6-mo, prospective, randomized, parallel-group, open-label trial to assess the effect of an intervention on drug-related problem related readmission rates in older adults |
| Schleidgen S, et al.[6] | 2013 | Systematic review | How PM is actually used in scientific practice using the key words *individualized medicine*, *individualised medicine*, *personalized medicine*, and *personalized medicine* |
| Ginsburg GS, et al[11] | 2018 | Narrative review | PM and the stakeholder community in the context of clinical care and that optimize the tools and information used to deliver improved patient outcomes. |
| Ramaswami R, et al[12] | 2018 | Review | Areas of promise demonstrated by PM, discussing the limitations of each of these areas from a population health perspective, and how it is possible approaching PM in a manner that is congruent with the core aims of public health |
| Bhangoo MS, et al[13] | 2019 | Review | Authors highlight the preclinical development, recent clinical studies, and future directions of larotrectinib in patients with NTRK fusion-positive tumors with new PM approaches |
| Pagliuca M, et al. [14] | 2019 | Review | Systemic treatments regarded as most likely to have an impact in clinical practice and diagnostic tools that have been paving the way for the development of PM |
| Kaplon H, et al[15] | 2019 | Review | Last monoclonal antibodies documenting progress made with these and other antibodies to watch in the next installment of article series |
| European Medicines Agency[16] | 2019 | Review | Challenges and opportunities of conducting clinical trials in precision oncology and PM with AI and the collaboration of health care providers with pharmaceutical and biotechnical companies, scientific organizations, and governmental regulatory agencies |
| Fountzilas E, et al[17] | 2018 | Expert commentary | PM implementation and bioinformatics infrastructure to support optimization of treatment selection AI will facilitate accurate utilization of sequencing data to perform algorithm analysis with a crucial role in curing cancer |
| Jiang F, et al[18] | 2017 | Survey | Survey on the current status of AI applications in health care and discuss its future on PM applications |
| Dolley S[19] | 2018 | Review | Review article to identify the precision public health and PM use cases where big data has added value, identify classes of value that big data may bring, and outline the risks inherent in using big data in precision public health efforts |
| Garralda E, et al[20] | 2019 | Review | Review about the main challenges and opportunities that innovative PM trial designs may provide for a more efficient drug development process, which may ultimately help ensure that PM becomes a reality for patients New clinical trial designs are helping optimize early drug development |
| Weber JS, et al[21] | 2017 | Focus | Focus on the important issues in the design and conduct of PM Phase I clinical trials in oncology |
| Harrington JA, et al[22] | 2017 | Overview | Current concepts in Phase I clinical trials, highlighting issues and opportunities to improve their meaningfulness. The particular challenge of how to design combination trials is addressed, with focus on the potential of new adaptive PM and model-based designs |
| Padhy BM, et al[23] | 2011 | Review | Drug repositioning as a strategy involving exploration of drugs that have already been approved for treatment of other diseases and/or whose targets have already been discovered. |
| Vicini P, et al[24] | 2017 | Review | Examples of intersectional blind spots across the disciplines of quantitative pharmacology and translational science and offer a roadmap aimed at enhancing the caliber of clinical pharmacodynamic research in the development of oncology therapeutics |
| Reinharth D[25] | 2001 | Viewpoint | Viewpoint on "start low, go slow" approach and the necessity of flexible, individualized prescribing and PM |
| Benetos A, et al[26] | 2019 | Review | PM controlled trials necessary for the most frail older subjects to gain stronger evidence regarding the benefits of the various therapeutic strategies such as arterial hypertension and particularly systolic hypertension, which is constantly rising worldwide |
| Guilleminault L, et al[27] | 2017 | Review | Various asthma phenotypes, personalization of the patient's diagnosis, biological therapies, patient education, and a new approach to curative medicine in the coming years for PM, focused on subjects at risk |
| Vogenberg FR, et al[28] | 2018 | Viewpoint | Information technology and efforts to transform the health care experience to more positively use a mostly unchanged delivery system and supply chain |
| Lazarou J, et al[29] | 1998 | Meta-analysis | ADRs as an important clinical issue |
| Clinical Pharmacology WHO Position Paper[30] | 2012 | Position paper | Roles of clinical pharmacology in health care, teaching, and research was composed and edited by representatives of the International Union of Basic and Clinical Pharmacology, WHO, and CIOMS. |

**Table 1** (*continued*)

| Author | Publication year | Study design | Relevant topics and outcomes |
|---|---|---|---|
| Eugene AR, et al[31] | 2018 | Research article | Study to identify the most frequently reported medications and associated side effects in adolescent patients in an effort to prioritize clinical pharmacology consultation efforts for hospitals seeking to improve patient safety |
| Harder B, et al[32] | 2017 | Review | Methodologies and improvements on hospital services and standards in their ratings |
| Borobia AM, et al[33] | 2018 | Report | Experience in integrating pharmacogenetic testing and the feasibility of their implementing in clinical practice within a national health system |
| Van der Wouden CH, et al[34] | 2017 | Overview | Overview pre-emptive pharmacogenomic testing for prevention of ADRs and the influence on patient outcomes and cost-effectiveness |
| Breckenridge A, et al[35] | 2006 | Letter to editor | Letter to support the future of clinical pharmacology as detailed expertise on the mechanism of action of drugs, dose response, AEs, disposition, as well as knowledge of their use in medical practice |
| Responsible Use of Medicines Report[36] | 2012 | Report | Prioritizing working together to address inappropriate medication use over the next decade, to ensure the quality, economic, and political systems are put in place to improve medication safety for patients |
| Nimmesgern E, et al[37] | 2017 | Review | PM as a promising new concept for dealing with challenges of health and health systems |
| Rosenman MB, et al[38] | 2017 | Viewpoint | Implementation guide development process to provide insight for prioritizing development of future resources and support the value of collaborative efforts to create resources for genomic/PM implementation |
| Oprea TI, et al[39] | 2015 | Review | Concept of the hypothesis-driven or observational-based expansion of the therapeutic application in drug repurposing and PM |
| Delavan B, et al[40] | 2018 | Focus | Means of utilizing accumulated genomic data for accelerating and facilitating drug repositioning for rare diseases |
| Li YY, et al[41] | 2012 | Review | Current state of research in PM/drug repositioning, focusing on recent large-scale efforts to systematically find repositioning candidates and elucidate individual disease mechanisms in cancer |
| Tobinick EL[42] | 2009 | Review | Drug repositioning as a rational approach, including a cross-disciplinary focus on the elucidation of the mechanisms of disease and targeted therapeutic agents |
| Light DW, et al[43] | 2011 | Research article | This article takes apart the most detailed and authoritative study of research and development costs to show how high estimates have been constructed by industry-supported economists, and to show how much lower actual costs may be |
| Smith RB[44] | 2011 | Review | Repositioning of drug products that provide effective and long-lasting product exclusivity even where the underlying API, and the original formulations, indications, and methods of use are off-patent |
| Tiriveedhi V, et al[45] | 2018 | Review | The pricing of targeted medicines continues to be a major area of contention in health care economics. In this article, authors discuss the various factors influencing pricing decisions, and consider evolving economic trends in PM |
| Pritchard DE, et al[46] | 2017 | Research article | Research article on setting a list of common challenges through a series of group discussions, surveys, and interviews, and convened a national summit to discuss solutions for overcoming these challenges |
| Janković SM, et al[47] | 2016 | Letter to editor | Letter to the editor where authors describe clinical pharmacologists and the necessity to have more important role within the health care systems where their services are available |
| Grisafi D, et al[48] | 2018 | Systematic review | Several significant differences across European countries among the organizational models of CP services in hospitals because current European legislation |
| Brinkman DJ, et al[49] | 2018 | Review | The need to update both WHO publications by evaluating their use and influence, including new (theoretical) insights and demands on PM |
| McGrath S, et al[50] | 2016 | Review | Review to identify main areas that require attention in PM, increasing the number of professionals with the necessary expertise to correctly interpret the genomics profiles of their patients, and several strategies that involve medical curriculum reforms, specialist training, and ongoing physician training |

ADR = adverse drug reaction; AE = adverse event; AI = artificial intelligence; API = XXXXXX; CIOMS = Council for International Organizations of Medical Sciences; CP = clinical pharmacology; NTRK = XXXXXXX; PM = precision medicine; WHO = World Health Organization.

ually adapting to the implementation of new PM tools such as big data science, the discovery of biomarkers, and artificial intelligence.[18,19]

Currently, Phase I dose-escalation trials are very often followed by adaptive studies with basket and umbrella designs that aim to optimize the process of codevelopment of the biomarker drugs. Consequently, to respond to this growing complexity of clinical trials, new structures are in progress for stronger and faster collaboration between all stakeholders in drug development and management.[20–22]

Another particularly interesting aspect of the use of PM approaches to studying individual diseases is the fact that drugs can be repositioned for these diseases, with wide-ranging implications for diagnosis and treatment. Both PM and drug repositioning are particularly relevant for rare diseases, for which it is challenging to conduct clinical research for due to their low prevalence and the high costs they entail. They are also important for disease subtypes that are resistant to treatment or that have no treatment options.[23]

These achievements currently make it possible to predict the effectiveness of the treatment with good approximation, but also to facilitate application of the paradigm of the 3 Rs: The right dose for the right patient at the right time. The PM approach is expected to exert a beneficial influence by reducing the critical issues and problems posed by a traditional therapeutic approach in all medical care, not necessarily limited to the context of patients with cancer.[24]

Among the most interesting areas of application of these approaches is medical therapy in elderly patients because it is closely influenced by the impairment of physiological conditions alongside the well-known changes in the pharmacokinetic/pharmacodynamic profile of drugs. Moreover, multidrug therapy, common in these patients, favors the onset of ADRs and often unpredictable drug–drug interactions, leading physicians to use start low, go slow recommendations as a widespread precaution in routine clinical care.[25] These empirical dosing approaches may lead to an increase in mortality, as is evident from overtreatment of hypertension and diabetes mellitus in older adults,[26] with similar considerations that may be valid also in the wide panorama of those respiratory diseases that have an important influence on quality of life in the elderly population.[27]

## Discussion

At present, the policy trend in health services is to maintain their economic and organizational sustainability by reviewing spending and adequacy while improving the quality and safety of therapies offered to patients.[28] Significant efforts are made, with the support of CP, to reduce causes of death and number of days of hospitalization, particularly by reducing the number and the severity of ADRs and medication errors, and by preferring drugs targeted at specific populations of patients selected according to the well-known 3 R paradigm.[29]

The role of CP has been well described in the Council for International Organizations of Medical Sciences/World Health Organization/International Union of Basic and Clinical Pharmacology booklet:[30] The rational use of medicines both for individual patients and for patient populations ensures that clinical pharmacologists are experts in the critical evaluation of old and new therapies. The situation is sometimes paradoxical when public hospitals are prevented from sustaining the costs of clinical pharmacologists, which would translate into better hospital service and commitment to the use of precision dosing in patient treatment and research into daily patient care, with cost savings for the hospital budget.[31]

It is important to note that hospitals offering training programs in CP or where CP services are operational are often ranked at the top in global reports.[32] There could be a meaningful contribution from clinical pharmacologists because they are vital for supporting the widespread application of what PM entails; that is, the development of precision drugs, rational and safe treatment of patients, participation in regulatory matters, health technology assessment, and the implementation of pharmacogenomics.[33–35]

The advent of PM as a new clinical approach to treatment requires customization in the management of the complexity of diseases and related therapies, limiting the use of blockbuster medications and managing polypharmacy appropriately to the advantage of a more targeted and appropriate treatment. In addition to clinical benefits, there are also economic advantages, with savings up to 0.3% of the overall health budget due to a reduction in the number of drugs prescribed, the identification of vulnerable patients, and a more collaborative role between pharmacologists, physicians, and patients.[36] In this review, we illustrate the reasons why, to achieve this evolution, it is essential for different professionals to work together in the health sector: Clinical pharmacologists remain among the main drivers of this process.

The future will therefore require greater understanding and speed in the interpretation of available information from multiple sources, such as electronic health records and other relevant data sources, which are growing in volume and variety. Lower data collection costs, the emergence of new computational methods, and the promotion of professional skills are expected to be necessary pillars for the success of PM.[37] Similarly, although the costs of most of the genetic testing needed to characterize a patient's

genome continue to decrease (www.genome.gov), pharmaceutical companies are confronted with the volatility of the economic value of already approved drugs, which could have new therapeutic indications if prescribed within the context of what we call PM.[38,39] Drug repositioning, which aims to find new uses for existing drugs, is certainly among the most interesting and controversial aspects among those related to PM from a pharmacologic and regulatory perspective, and is currently considered as a concrete action[40] able to accelerate the process of drug development. In fact, it must be taken into account that only 11% of the drugs studied in clinical trials are definitively approved, with an actual cost of drug development that is much higher than the estimates published,[41] and that the average time from bench to hospital has risen from 10 to 17 years.[42]

This approach to improving productivity is therefore rapidly increasing in popularity as a result of the advent of PM, because the premise of repositioning is that the reuse of drugs that have previously passed clinical trials minimizes the risk of failure of further clinical trials at an advanced stage; for example, due to toxicity, thus leading to faster drug approval. The implementation of PM also considers the fact that stratification of patients and diseases into molecular subtypes and treatment with specific medicines will surely improve the effectiveness of the drug.[43]

The repositioning of medicines opens up a considerable regulatory and assessment front in a scenario that is already very complex for European and US regulatory authorities, which will have to monitor and control purchase and reimbursement procedures, adapting their existing systems for monitoring and containing health expenditure, known as managed entry agreements.[44] Cost containment will thus be the key for the future of PM. Innovative cost-effectiveness strategies and novel health care economic models involving hospitals, pharmaceutical industries, and reimbursement agencies are needed for the adoption of PM in patient care.[45]

Without doubt, the multidisciplinary approach constitutes an added value as a means of developing, implementing, and evaluating interventions to promote a more accurate use of health resources. It is therefore essential to identify the necessary actions and analyze the strategies that allow their transfer to clinical practice in an informed and ordered manner, ensuring quality of care through a complete integration of the new model, designed to encompass the entire structure of the health system. This requires endorsing the participation of all the stakeholders involved, through an appropriate regulatory framework with ethical standards that promote innovation while contributing to the sustainability of the system.[46]

According to the Council for International Organizations of Medical Sciences/World Health Organization/International Union of Basic and Clinical Pharmacology statement, some of these stakeholders are indeed medical doctors specialized in CP who already provide and support protocols of PM with regard to pharmacogenetic consultations.[47] Today, there are already several agreements and good practices of collaboration between physicians, pharmacists, and biologists, although academic training for graduates of medical schools specializing and training in CP remains limited to some universities, and in some cases programs vary significantly between countries.[48,49] Numerous limitations could prevent the application and consolidation of PM in the hospital of the future: certainly, for example, the lack of sufficiently trained doctors in the use of pharmacogenomics, including many specialists in CP, and also the lack of appropriate clinical studies of PM with new and improved regulatory aspects in the potential care of patients on the basis of PM protocols.[50]

CP services, promoting cross-disciplinary interaction, notably between specialists in genetics and statistical methodologies, specialists in bio and public health informatics, epidemiology, and
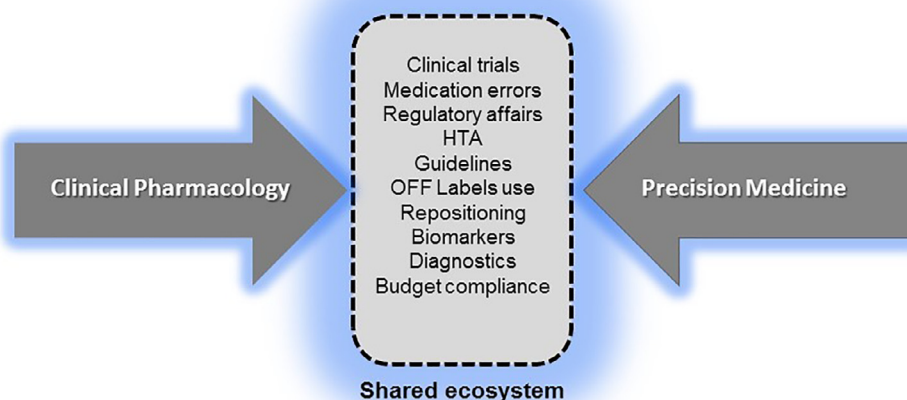
**Figure 2.** Clinical pharmacology and precision medicine share an ecosystem of common clinical and care activities, representing a strategic opportunity for the efficient functioning and governance of future health systems. HTA = Health Technology Assessment.

health professionals, may ensure better understanding of the available data, more efficient integration and interpretation of information from multiple sources, and appropriate decision making on treatment options. Clinical pharmacologists are among the main drivers of these services, capable of performing a renewed task, facilitating, and implementing the provision of PM strategies, with a set of good practices that can bring together complex knowledge acquired in the field of clinical trials, in the prevention of medication errors, in the participation in regulatory affairs in national agencies, and in the setting up of guidelines and health technology assessments as well as in the various professional competences involved in PM processes (Figure 2).

With the intention of giving a summary overview of the experiences made on the subject, we applied the Preferred Reporting Items for Systematic Reviews and Meta-Analyses methodology for systematic reviews, and although there are some limits due to the complexity of the research issue and the lack of consolidated literature, we believe that our work can be classified as a narrative review. To date, we are not in possession of peer review publications that demonstrate, through the measurement of performance indicators, the improvement of quality of care, clinical research, and patient management in hospitals through the interaction between CP and PM: The different outcomes described in this review have in fact a common limitation, namely the lack of quantitative assessment allowing for an objective comparison between the various realities.

Various strategies have now been conceived and planned to facilitate the transition from mainstream medicine to PM, which will enable patients to be treated more accurately, with significant advantages in terms of safety, the effectiveness of treatments, their duration and, lastly, the reduction of costs for society in terms of quality of life improvement.

Therefore, in the future, to ensure that the evolutionary process of medicine can involve as many patients and caregivers as possible, infrastructures capable of bringing together different multidisciplinary skills among health professionals will have to be implemented.

Clinical pharmacologists should be among the main drivers of this strategy because they already, with their multidisciplinary training, operate in a series of services in high-level hospitals, facilitating the clinical governance of the most challenging patients, namely those in pediatric, polytherapy, and elderly populations.

The implementation of these strategies will finally allow national health organizations to adequately address the management and therapeutic challenges related to the advent of new drugs and cell and gene therapies by facilitating the removal of economic and organizational barriers to ensure equitable access to PM.

## Conclusions

Currently, interesting organisational models, especially in high-level hospitals, are those in which PM services are part of an ecosystem in which the different competencies of clinical pharmacologists converge in departments specialised in medicines management and governance, focusing their activities on the implementation of clinical therapeutic appropriateness, evaluation, clinical research and teaching. Ultimately, the aim is not to create new bureaucratic structures, but to streamline the transition of patient care into the new era of PM.

## Acknowledgments

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