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REVIEW ARTICLE

Appraising the visibility, relevance and impacts of clinical pharmacology

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Aims: Clinical pharmacology (CP) used to be a strong medical and scientific field, but during the last three decades it seems to have lost some of its appeal. We reviewed the visibility, relevance and impact of CP and clinical pharmacologists across the globe and suggest ways to strengthen the discipline to address future pharmacotherapeutic challenges.

Methods: Literature consultations and multiple survey approaches through personal contacts with leading experts from high-income countries, Asia and Africa and with CP scientific journal editors with presentation, discussion and recommendations at a workshop (World Congress in Basic and Clinical Pharmacology, Glasgow 2023).

Results: Historically, CP has been a leading discipline for the advancement of knowledge and practice of rational principles for human drug use. However, currently there is variable visibility and impact between countries in research, education and clinical services. The workshop participants agreed that CP continues to be an open transdisciplinary subject to address challenges of drug development with affordable access to essential medicines and rational use of new advanced therapies as well as essential medicines. Medical specialisation programmes in clinical pharmacology and therapeutics should be the norm and become attractive through introducing board programmes for accreditation of specialists building on models existing in some European countries, India, Nigeria and South Africa.

Conclusions: Clinical pharmacologists should collaborate across countries and disseminate success stories, demonstrating their essential contributions to medical science and patient care. A *white book* with comprehensive global representation on the future role, structure and impact of the discipline should be developed.

KEYWORDS
clinical pharmacology, global impact, policy making, rational use of medicines, specialization, therapeutics

1 | INTRODUCTION

There were efforts by a consortium of the International Union of Basic and Clinical Pharmacology (IUPHAR), the World Health Organization (WHO) and the Council for International Organization of Medical Sciences to set the scene and role for clinical pharmacology (CP) in healthcare, academia, research and industry through the publication of the CP *white book* in the early decades of the 21st century.[1] The recommendations were built on a pioneering report by WHO in 1970.[2] The CP *white book* aimed at enabling decision makers in governments and healthcare ministries as well as chief executives and directors of primary and secondary care systems and pharma industries to comprehend the benefits that CP- and CP and therapeutics (CPT)-trained physicians can bring to health, healthcare services and society.

While these efforts have resulted in varied levels of success, there are gaps in the visibility and perceived relevance of CP across the world. A major observation that seems consistent globally is the relatively few numbers of medical graduates enrolling in a career as clinical pharmacologists compared to other medical specialties. This has been interpreted as likely to be due to low priority of clinical services by CP leaders historically.[1] Similar to many areas of science and medicine, CP seems to be in a perpetual existential crisis about its identity and its role in science, health care and in society. What is CP, who practices it, what are the characteristics of a clinical pharmacologist and for what is CP important? In other words, what would be the possible impact on the world should clinical pharmacologists disappear, or might things improve if there were sufficient numbers of them, and, if so, what would these be and how many clinical pharmacologists would be needed?

The above questions need to be answered, if we are to convincingly advocate for CP, as a medical profession, as a science, as an educational subject, and as an essential part of healthcare services and drug development. A major challenge is that CP varies around the world in concept, perception, defined scope and practice, and a global strategy to strengthen the field therefore needs regional tailoring. By contrast, numerous ground-breaking discoveries and drug therapies have in recent decades provided society with a variety of new types of expensive medicines based on molecular and genomic breakthroughs highlighting the necessity of CP in a world hit by multiple existential crises such as pandemics.[3,4]

To develop such a strategy, the Global Health Pharmacology and Therapeutics Committee of IUPHAR in partnership with the *British Journal of Clinical Pharmacology*, organized a workshop at the World Congress of Basic and Clinical Pharmacology (WCP 2023) in Glasgow in July 2023. Various aspects of CP were discussed for high-income countries (HICs), for Asia and for Africa, as well as the role of scientific journals in dissemination and strengthening of CP research and other society activities. This workshop report summarizes the presentations, the discussions and the conclusions from the workshop on the role and organization of CP across the globe, aimed to guide a global strengthening of CP.

2 | DEFINITION OF CP

CP is defined differently between contexts and countries. The British Pharmacological Society (BPS) uses the definition: "*Clinical pharmacology encompasses all aspects of the relationship between drugs and humans. It is the only medical specialty in the National Health Service (NHS) focusing on the safe, effective, and economic use of medicines. It is a diverse discipline that both sustains and advances best healthcare practically*." Clinical pharmacologists are "*clinicians with training in Clinical Pharmacology and Therapeutics (CPT). Their core goal is to improve patient care through the safe and effective use of medicines*."[5] As such, CP is practiced by holders of Bachelor of Medicine and Bachelor of Surgery degrees (MBBS or MBChB) in the UK and by doctors of medicine (MDs) in, for example, Denmark, Germany, India, Nigeria, Norway, South Africa and Sweden after completion of specific clinical training programmes.[1]

The American Society for Clinical Pharmacology and Therapeutics (ASCPT) also defines CP *as the study of drugs in humans. CP is underpinned by the basic science of pharmacology, with added focus on the application of pharmacological principles and methods in the real world including but not limited to the discovery of new target molecules and the effects of drug usage in whole populations*. In contrast to the BPS definition of a Clinical Pharmacologist, the ASCPT recognizes clinical pharmacologists as physicians, pharmacists, and scientists whose focus is developing and understanding new drug therapies.[6] This definition is more on involvement in academia, industry and government than with prominent roles in health care. Tasks include the study of biomarkers, pharmacokinetics, drug metabolism and genetics, clinical trials, development and implementation of regulatory guidelines, drug utilization research on local and global scales, patient care, experimental studies and investigation of adverse reactions and interactions.

The CP *white book* defined CP to involve all aspects of the relationship between drugs and humans and clinical pharmacologists in the professional sense referred to those physicians who are specialists in CPT.[1] Such physicians must have undergone several years of postgraduate training in many aspects of the relationship between drugs and humans involving teaching, research and health care. The primary goal is to improve patient care, directly or indirectly, promoting the safer and more effective use of drugs and developing better medicines.[1]

3 | EMERGING OPPORTUNITIES TO STRENGTHEN CP IN HICS

CP has changed the practice of medicine with visionary leadership, breakthrough research addressing major public health problems, and by applying new concepts and unique technologies in HICs.[1,7] Major therapeutic advances include the placebo-controlled trial, therapeutic drug monitoring, the WHO Essential Medicines Lists, and critical drug evaluation.[1,2,7] Today, these pioneering CP concepts are integrated into most clinical disciplines and considered as core characteristics of research and practice across disciplines. Thereby knowledge and

appreciation about the critical role of CP in developing and introducing these concepts and methods have become less clear.[1,7]

CP is inherently a translational discipline but with few CP-accredited specialist physicians in most HICs and with geographically variable Janus-like faces in research, teaching and clinical services. The structure, architecture and role of CP in each country depends on national priorities. CP needs as a discipline to demonstrate a shared core identity across countries to become a reliable partner in research, teaching and clinical services. For all these tasks we have 1 common ground: we are trained, practice and master *critical drug evaluation*.[1] If we can demonstrate similarities across nations, the future might be brighter.

Today CP has a golden opportunity in HICs to strengthen its contributions in all its 3 core fields. Mankind is entering a molecular and digital era in curative medicine and in health prevention with challenging costs for provision of new diagnostics, vaccines and medicines, challenges to uphold ubiquitous access to innovations, and burning needs to balance false drug information and automatic algorithms in social media.[8–10] Physicians and healthcare will have access to new types of medicines replacing the classical small molecular drugs. In 2022, about 40% of new medicines approved by the Food and Drug Administration through its Center for Drug Evaluation and Research were protein based.[8] In addition, the Food and Drug Administration through other branches increasingly approve cell as well as gene therapies and medicines based on RNA-technologies.[8] In research and medical practice, we will need to rely on transdisciplinary collaboration as diverse technologies are needed to develop, produce and use such medicines. CP can play a key role with its bridging perspectives between science and clinical medicine and with its expertise in clinical trial study design and in critical drug evaluation.[1] Transdisciplinary perspectives are also needed to ensure access to essential medicines for all globally.[1,2,11,12]

4 | GLOBAL CHALLENGES: ASIAN AND AFRICAN PERSPECTIVES

Asia (48 countries and 60% of the world's population) is usually poorly represented among consortia of international CP groups. Asia had only 1 of 19 members in the CP *white book* editorial group.[1]

Asia is not a uniform continent economically. Half of Asia's countries are classified as high- and upper/middle-income economies while the other half are low- and low/middle-income countries.[13] Life expectancy has improved remarkably but it ranges widely, with 84.3 years in Japan and 63.2 years in Afghanistan. While the infant mortality rate (deaths per 1000 live births) decreased from 205 to 11 in East Asia, it dropped from 244 to 44 in South Asia from 1960 to 2018.[14,15]

In countries such as India, CP as a discipline started in the 1960s,[16] most often triggered by visiting professors and by training fellowships of Indian medical doctors in the UK, Europe and the USA. Further development of the discipline in the subsequent decades as well as career opportunities in Asian countries were affected by various socioeconomic, local and global factors.

In the 1960s, there was a huge upsurge of new drug development and some Asian countries were looked upon as potential markets as well as providing golden opportunities for clinical trials.[17] However, soon the cost of new medicines became a significant barrier to access, resulting in development locally of generics, special formulations and targeted drug delivery products such as liposome compounds. Opportunity for clinical trials of new drugs and hence jobs for CP in industry declined.[18,19] Availability of low-cost generics generated a huge public health boom. However, it also caused inappropriate use of drugs with problems of antimicrobial resistance and preventable adverse drug reactions, which in turn stimulated the development of CP in academia and hospitals in Asia.

African countries, particularly those south of the Sahara, have high rates of morbidity and mortality from infectious diseases, neglected tropical diseases, and an increasing burden of noncommunicable diseases. The rising multimorbidity burden provokes challenges related to polypharmacy and rational use of medicines (RUM) on largely uncontrolled drug markets.[20,21] Furthermore, black African populations are the most genetically diverse on earth; factors including disease phenotypes and polymorphic drug metabolizing enzymes make it imperative that drugs are studied in the populations for their use.[22,23] However, most drug development, from early phase development through clinical trials takes place in HICs, with the assumption that findings can be directly extrapolated to African populations. Furthermore, there are key gaps in training and career opportunities in CP with few medically licensed clinical pharmacologists, which further perpetuates inequity.

The last 2 decades have seen a paradigm shift with a push for globalization with the World Trade Organization-initiated Trade-Related Aspects of Intellectual Rights agreements stimulating countries and companies to invest in development of generics and biosimilars. In addition, the revolution in pharmacogenetics with personalized medicine, increasing prevalence of lifestyle diseases and ageing population have affected development and use of medicines.

5 | SURVEY OF CP PRESENCE AND ACTIVITY GLOBALLY

By selecting representatives from several continents to the WCP2023 workshop, we aimed to initiate a global debate. Each WCP workshop only allows a limited number of speakers, so a selection was made by the organizers (L.L.G. and O.O.O.) who invited speakers with a track record for representing their region or area of expertise. Speakers were instructed to present a summary of success stories, challenges and opportunities and suggest ways forward from their different continent perspectives and the scientific publishing sphere. The representatives were L.L.G. (HICs), N.A.K. (Asia), C.W. (Africa) and S.C. (scientific journals). They worked within their networks to gain a range of current and future perspectives on CP role, impact and emerging challenges across the globe.

For HIC, a nonrandom group of personally identified CP leaders in Australia, Europe and North America were contacted ($n = 35$, 23 responded) via e-mail during Spring 2023. The HIC mini-survey

(Appendix 1) consisted of open questions about CP's role, presence and activities in their countries and regions. The respondents were asked to list perceived breakthrough CP contributions in (A) research, (B) teaching and (C) clinical services. They were also invited to assess the potential value of increased international CP collaboration for strengthening the roles of CP in each of these areas.

To capture the status of CP in Asia 40 experts with training/experience/residence in Asian countries) and the WHO were contacted by email or by telephone. They were asked about their perspectives and information on development of CP including training programmes in Asia and asked to list discerned success stories, opportunities and challenges and suggest ways forward in Asia (Appendix 2). In total, 25 experts from China, India, Indonesia, Japan, Malaysia, Singapore, South Korea, Sri Lanka, UK and USA with experience of Asian countries responded. These responses, information from a literature search and personal experience (N.A.K.) form the CP narrative for Asia.

Opinions about CP role and potential in Africa were collected from 10 persons who had completed their training relatively recently. This largely limited the target group to colleagues who had trained in Nigeria and South Africa, which are the only African countries with formal CPT training programmes for MDs; 1 individual who trained formally in haematology but is recognized as a Clinical Pharmacologist from Uganda was also included. Many clinicians who are active clinically and in research within the discipline have not undergone such formal training. Colleagues were identified through personal networks (C.W., O.O.O.) and were asked about the challenges and opportunities within CP, together with any advice they would give to a junior colleague seeking to enter the field (Appendix 3). Due to the strong training programme in South Africa, there was high representation from this country.

6 | SUMMARY OF SURVEY FINDINGS OF CP PRESENCE, IMPACT AND CHALLENGES GLOBALLY

6.1 | HICs

The following research topics were listed as breakthroughs in HICs: (i) pharmacogenomics; (ii) advanced therapies based on biologics, RNA-technologies and cell therapies; (iii) pharmacoepidemiology; (iv) functional human studies in vivo of drug transporters, such as variability in drug transport across the blood brain barrier; and (v) groundbreaking trials (e.g., for hypertension and HIV). Perceived educational breakthroughs included: (i) prescribing safety assessment (PSA) procedures; and (ii) trans-European teaching models. Listed breakthrough health-care services included: (i) comprehensive approaches for selection, training and monitoring of adherence to recommendations of essential and new expensive medicines; (ii) CP-guided multidisciplinary expert consultations for personalized care of complex therapies and geriatric care of fragile old patients; and (iii) design and implementation of drug knowledge data base services in clinical practice, for students and the public.

Most respondents from HICs considered that increased collaboration, in particular in teaching and clinical services, would help to strengthen CP in their own countries. There was a strong voice about the necessity to harmonize the CPT training for specialists across countries. Several initiatives in Europe of cross-country CPT curricula development and exchange of residents between institutions training medical specialists in CPT were mentioned.

CP research has made progress with new sophisticated ways to study the mechanisms for variability in drug response in humans in vivo.[24,25] Today, progress in radionuclide science and in imaging technologies allows us to explore and understand interindividual variability in drug transport across membranes, for example, the blood–brain barrier.[24,25] These conceptual in vivo studies on about 18–30% decrease of C^{11}-metoclopramide transfer rate from brain to plasma in old as compared to young subjects were rated as breakthrough research. Since this radionuclide is a substrate for P-glycoprotein (P-gp) these research results indicate that P-gp activity in the blood brain barrier decreases by age, a likely explanation for the high risk of tardive dyskinesia during metoclopramide therapy of elderly patients.[25] The research group has also demonstrated that inhibition of P-gp activity affects regional drug distribution across the blood–brain barrier with effects on neuroefficacy and toxicity of P-gp substrates.[26] These remarkable studies were possible due to progress in radionuclide chemistry and with the introduction of positron emission tomography to quantitate changes in transport capacity across membranes in animal and man.

The AMBORA (Medication Safety with Oral Antitumor Drugs) trial design and its findings that major endpoints, mostly severe adverse effects, were reduced to half with pharmacological and pharmaceutical expert consultations during treatment with oral anticancer agents was also rated as breakthrough research.[27] A multisite randomized control trial in Germany to confirm their findings is under way. Several respondents rated the PSA of young MDs' knowledge in CP and skills to prescribe medicines as an innovative teaching project and important for improving the quality of drug therapy.[28] This initiative has spread from UK across Europe and to Africa recently.

Various initiatives on innovative clinical services were listed. One of those was the *Wise List* in the Stockholm metropolitan region issued by its Drug and Therapeutics Committee—a limited number of essential medicines (Figure 1). The concept has maintained trust and support in the region by involving drug experts and colleagues as well as prescribers and the public in the selection of medicines.[11,29] The *Wise List* has achieved 90% adherence to recommendations in primary care after 15 years and saves 10% of the annual drug budget in the region. A key to its success as a cost-effective prescribing model is the multifaceted approach combining continuous medical education, decision support and follow-up of adherence and acceptance (Figure 1). The *Wise List* model to achieve cost-effective prescribing has been adapted globally.[30]

In recent decades, a multitude of groups directed by or collaborating with CP have designed, developed and implemented knowledge bases and decision support systems as part of individualized (precision) medicine programmes.[31–33] The advantage of knowledge bases

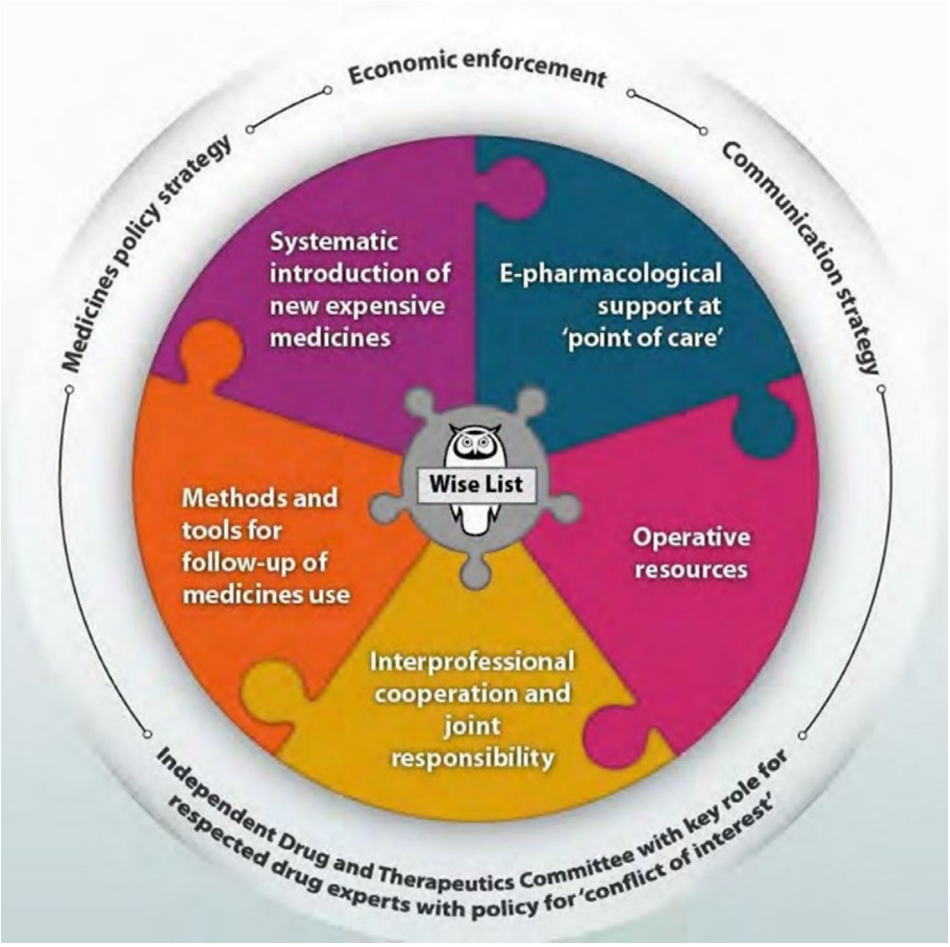

FIGURE 1 Stockholm model for wise use of medicines (Figure reprinted from[29]). The Stockholm (2.3 million people) model for wise use of medicines is built on application of a multifaceted interventional philosophy.[11,29] Pillars include collaborations between colleagues, 200 recommendations of essential medicines (wise list) by trusted experts at the drug and therapeutics committee, and strict handling of conflict of interests. The outer circle presents key organizational strategies. The jigsaw puzzle shows key elements deemed vital for achieving a wise use of medicines (reflective drug therapy for optimal patient value) with the wise list as the most exposed channel of knowledge. Operative resources include an annual budget for staff and financing of costs for key elements for success (continuous medical education, support of experts, infrastructure for follow-up, programme for handling new expensive medicines and e-pharmacological services). Stockholm model saves about 10% of drug budget (100 million USD of total costs of 1 billion USD 2022).[29]

developed and maintained by independent clinical pharmacologists, pharmacists and clinical colleagues is the possibility to deliver precise and up-dated knowledge through variable routes into desk and mobile computers, websites, telephones, teaching tools and above all to decision support applications in medical record systems. Across HICs this area was seen as important for access to trusted drug information and for CP presence. Knowledge base expertise was given priority for global collaboration to maintain high standards of the contents of the knowledge bases.[33]

6.2 | Asia

Discussion with experts and a literature search highlighted some illustrative success stories in which CP endeavours have provided cost-effective solutions for local, but also for some global, healthcare challenges.

Traditional medicines, used for centuries, in Asian countries have contributed to modern therapeutics such as preparations of reserpine from Rauwolfia serpentina from India to treat hypertension.[7] The Nobel Prize winning discoveries of artemisinin therapy from China has revolutionized treatment of malaria globally and ivermectin isolated from soil organisms producing avermectin compounds, originally in Japan, had provided effective cure for river blindness and filariasis.[34,35] CP in Asia has worked closely with the WHO Tropical Disease Research Program and with industry to develop and pursue clinical trials to document efficacy and safety of new drugs and combinations to treat diseases such as malaria, filariasis and visceral leishmaniasis.[36–38] Clinical trials in Asia as well as in Africa have been crucial for the development of effective, safe and practical dosage schedules suitable for public health programmes. The demonstration of a single-dose efficacy of ivermectin to control filariasis was an accidental finding while comparing it with diethylcarbamazine therapy.[39,40] CP has also contributed in the development and in clinical trials of vaccines and new drugs.[41,42]

There are other important CP success stories on the RUM in public health and tropical diseases. In Bangladesh, the essential medicines list helped remove unnecessary products. In India, cohort event monitoring as part of the conditional access programme for the TB drug bedaquiline, helped identify preventable side effects[41] (e.g., managing diarrhoea and vomiting in tropical climate with proper oral rehydration salts, avoiding electrolyte imbalance and QT prolongation).[41] WHO pharmacovigilance programmes, involving many clinical pharmacologists, have provided a sense of confidence for safe use of medicines among stakeholders of public health programmes. A recent success story is the identification of ophthalmic side effects of miltefosine (for leishmaniasis and a post kala azar dermal form affecting the poorest of poor) and a procedure for issuing risk management guidance.[43]

Besides success stories, development of CP can be assessed/judged by the availability of university courses. In Asia, CP university courses are available as part of medical and pharmacy training curricula (Table 1). In Indonesia CP training is provided as a 3-year medical specialty course. In India CP is a medical subspeciality course of 3 years, after MD in Pharmacology. This MD pharmacology course is a 3-year training programme exclusively for medical graduates with its syllabus comprising different Clinical Pharmacology and Therapeutics components. In Vietnam, CP is part of Clinical Pharmacy training and in West Asia Clinical Pharmacy is dominant for CP training.

The roles and responsibilities of clinical pharmacologists have been described in a recent training curriculum in the UK.[44] The schedule includes development of skills to assess, advice and manage adverse drug reactions (ADRs), overdose toxicity, and complex prescribing and deprescribing in multimorbidity and polypharmacy patients including understanding and applying personalized medicine approach. Clinical pharmacologists are active in public health, hospitals, academia, industry and in regulatory agencies. They assist with pharmacovigilance expertise and help to appraise and synthesize evidence in antimicrobial stewardship programmes. They contribute to essential medicines lists, chair drugs and therapeutic committees, and assist in the procurement of medicines. Besides practicing medicine, CP specialists also educate and train the next generation of prescribers and patients in the use of medicines. CPT syllabi in a country such as India are similar but emphasis on providing direct patient care is limited due to shortage of trained manpower.[45] In decades to come, one can expect increasing opportunities and need of clinical pharmacologists in Asia (Table 2).

In Asian countries, the interdependence of many factors such as local ecosystems, frequent use of traditional medicines, lack of qualified professionals, locally prevalent diseases, remote rural areas, and the need for rapid response with medicines during disasters all require a unique set of knowledge, skills and attitude. CP is needed for early phase clinical trials to support discovery and development. In public health, pharmacovigilance is essential as drugs and vaccines increasingly are introduced with fewer data and will be used in large populations varying widely in race, ethnicity, health care systems and the use of traditional medicines. The COVID-19 pandemic illustrated the need for clinical trials to support policy.[46] Indonesia has, by government decree mandated establishment of CP teams in every hospital (starting from referral hospital; personal communication, Wawaimuli Arozal). Other countries can be encouraged to follow this example. Lifestyle diseases, an ageing population, special needs in rural areas (e.g., snake bite), and remote and difficult to reach terrains of population also provide opportunities. Such skills and knowledge are probably best grown locally requiring access to locally trained clinical pharmacologists.

TABLE 2 Clinical pharmacology (CP) in Asia: needs, opportunities, challenges and the way forward.

Needs	• Generating and incorporating evidence into patient care, strengthening drug development, policy work, disaster management considering incorporating the variability of population (e.g. genetics, diseases, beliefs) and health ecosystem diversity (e.g. traditional medicines, access and quality) • Serve policy bodies and healthcare organizations with evidence-based decisions on recommendations and risks of medicines as well as on reimbursements and funding issues
Opportunities	• Asia's improving economy, increasing insurance coverage
Challenges	• Inadequate manpower • Role of CP not defined
Way forward	• Research and training/human resource development needs based and modular • Advocacy for incorporating CP with specified roles in healthcare

TABLE 1 Examples of provided clinical pharmacology courses in Asia.

Specialty	Course type	Country(s)	Duration (years)
Medicine	Diploma	• Myanmar	1
	Degree	• China • Indonesia • Kazakhstan • Nepal	3
		• Armenia • Korea	4
Medical subspecialty	Degree	• India • Sri Lanka	3
Clinical Pharmacology Oriented Medical Pharmacology (CPOP)	Degree	• Iran • Türkiye	4
Master of Science (MSc)	Degree	• China • Iraq	3
Others			
As part of Pharmacy course		• Vietnam	

Maturity of medicines regulatory system in a country is influenced by CP and indicates the impact of the discipline. The WHO applies a bench marking tool to assess and compare medicine regulatory systems in different countries. The tool evaluates input, focuses on resources and functioning leading to output and outcome that impacts public health. WHO reported that India, China, Thailand, Indonesia and Vietnam have a stable regulatory authority, the Republic of Korea and Singapore have an authority at an advanced level, while Japan is at the highest quality level of regulation. This is reassuring but many other countries could do better and might benefit from support.[47]

Another indicator of growth of CP is pharmacovigilance. The WHO international monitoring programme for pharmacovigilance resides in Uppsala, Sweden. Currently most Asian countries are members with 16 joining after 2010.[48] Unfortunately, the number of ADRs per million population reported by many Asian countries is low.[48] A major reason for low reporting rates refers to lack of knowledge and competence in CP principles.

Asia is now on a growth trajectory that is expected to take a substantial share in world economy. The trade landscape is changing rapidly with initiatives for harmonization of legislation and the marketing approval process. A good example is the regional comprehensive and economic partnership among 15 Asia-Pacific countries.[49] There is also a growing global need for multiregional clinical trials for unmet medical needs at both a global and a local level. Global and regional collaboration is essential for e.g. the development of orphan drugs as well as of drugs for unmet needs and appropriate drug schedules suitable for mass administration.[50] All this augurs well for the future for CP in Asia.

6.3 | Africa

The discussions with African representatives focused primarily on the challenges inherent in raising a skilled, sustainable workforce with appropriate capabilities to lead CP initiatives in a range of resource-constrained settings. A key strength of CP is its diversity, but this can also make the discipline somewhat intangible. A South African working group led by Eric Decloedt used a modified Delphi methodology to define the *entrustable professional activities* of clinical pharmacologists (personal communication). These include the ability to assess a patient's status through clinical history and examination and interpretation of laboratory investigations in order to make a clinical judgement and decide on appropriate management in a range of presentations including adverse drug events, acute toxicology and those with complex prescribing needs or where a personalized pharmacotherapeutic decision is necessary. Furthermore, incorporating these elements of rational clinical decision making, additional domains include guiding formulary recommendations at local, regional and national levels, and providing input into regulatory drug committees and task forces.

Respondents were unanimous in naming mentorship as having been key to their own professional development. Drawing together the perspectives of the African group of colleagues, we also considered the question of *What would have helped you in your career*? and *What do you wish you had known*? Responses are summarized in the word cloud (Figure 2). Similarly, the ability to develop an area of personal interest and expertise was noted as a strength and concluded well by Clifford Banda: "*Skills in Clinical Pharmacology and Therapeutics are diverse (and in many training centres, the program may sometimes not be thoroughly structured to impart them all). However, the breadth of the skillsets in the discipline offers a unique opportunity to shape and pivot one's career in a direction that best suits their personality, and in line with what they are passionate about*."

Whilst the diverse opportunities and possibilities to carve out a unique career niche were seen as a major strength of the discipline in the African context, the same features also were named as a major challenge to overcome. Figure 3 displays a word cloud drawn in response to the question, *What have been the greatest barriers or hindrances?* The lack of clear training paths, funded opportunities and clear role models are potential deterrents to young physicians who are considering their choice of the specialty. Clear guidance on the options, the opportunities available and being able to link with others through networks were suggested by African colleagues as ways to overcome barriers.

7 | ROLE OF CP JOURNALS

CP is a broad field that is practiced by various, often differently trained healthcare professionals and scientists and encompasses patient care, education, research and therapeutics. In addition, globally, there are substantial differences in *who's doing what* as well as in *training*. Consequently, advocating for CP and strengthening the field is a challenge.

Despite CP inherently being dispersed, it is quite well organized around the world with professional societies such European Association of Clinical Pharmacology and Therapeutics, ASCPT, American College of Clinical Pharmacology, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, the BPS, and the overarching IUPHAR. Most of the CP societies around the world publish one or multiple journals with a special emphasis on CP, and these journals are a powerful tool to disseminate CP research as well as other information relevant for patient care, education and drug development presented as review and methods papers, and guidelines. These journals are therefore in a unique position to strengthen CP and advocate for it and the role of clinical pharmacologists in healthcare.

However, it is good to realise that CP journals are not the only option for authors to publish their manuscripts. Most papers with CP in it are published somewhere else, in high-impact journals such as *New England Journal of Medicine*, *The Lancet*, *Journal of the American Medical Association* or *Nature* or in one of their more specialised subjournals. If either rejected by one of these journals or not appropriate, then a paper can be submitted to disease- and organ-specific journals such as *Journal of Clinical Endocrinology and Metabolism*, American Association for Cancer journals, *Antimicrobial Agents and*

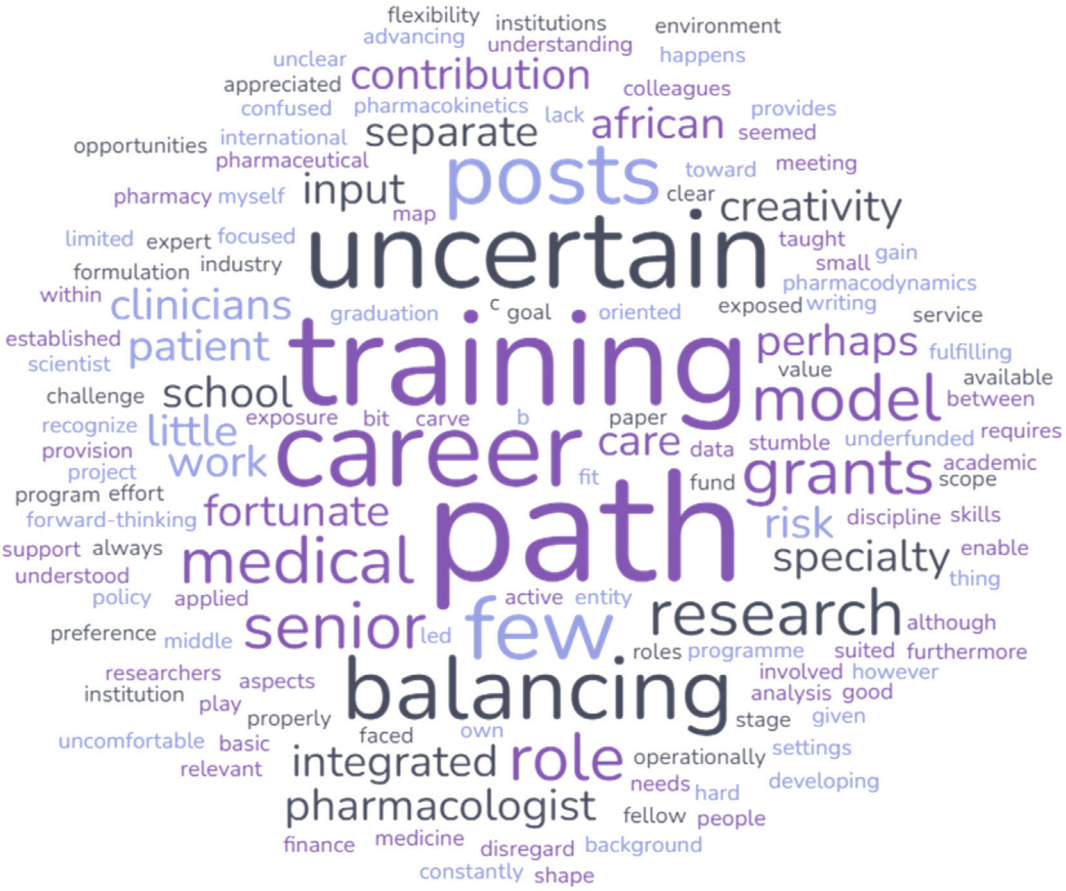

FIGURE 2 Word cloud of "*What would have helped you in your career?*" and "*What do you wish you had known?*" mentioned in various email discussions by a group of clinical pharmacologists in a few African countries and who had recently completed specialist training (cf. methods).

Chemotherapy or *Journal of Clinical Oncology*, all with impact factors usually higher than CP journals. Of course, most of these also have their own cascade journals. Society CP journals, and their cascade journals, are usually next on the ladder, but again they are only one of the options for publishing in CP literature. There are also various well-respected peer-reviewed CP journals such as *Clinical Pharmacokinetics and Drugs* that are not published by a professional society. By contrast, there are several other journals that range from not-so-respected to predatory journals that are usually easy to publish in as long as a publication fee is paid for, a practice that is sometimes mistaken for the growing Open Access component of respected peer-reviewed journals. The important point is that authors have choices and that any journal must find the balance between being strict and realizing that there is only so much it can ask from authors before they move on and submit their work to another journal. Given this publishing landscape it is important to realize that messages in CP journals have limited impact. Collaboration between societies and their journals therefore seems key to increase visibility of and advocate for CP as a whole.

Publishing interesting and high-quality CP papers is what several US East Coast CP journal Editors-in-Chief unanimously mentioned when asked what the most important thing is that CP society journals can do to improve the visibility of and advocate for CP and improve the quality of CP research. While acknowledging the limited impact of CP society journals, several other steps were mentioned that journals can take to improve CP. Expanding the editorial boards with sufficiently broad and deep expertise being one of them. CP includes drug development (phase 1–4), pharmacokinetics/pharmacodynamics/pharmacogenomics, computational modelling and simulation, drug safety, regulatory science, prescribing/deprescribing, therapeutic drug monitoring, pharmacoepidemiology, education, omics-based drug discovery and development, novel therapeutic modalities, precision medicine, big data, and artificial intelligence. Some of these areas are well-established while others are more novel and in continuous flux requiring adaptive expertise in the editorial boards. Another important step that CP journals could take for the discipline as a whole is to increase its diversity. Increasing diversity on the editorial boards, authors, patients, subjects and readership, will improve recognition and application of the publications. On a global scale this is a challenge as diversity in North America, for example, has a different meaning from diversity elsewhere such as South America, Africa, the UK or Australasia, to name but a few. A third aspect that most CP journals can improve is its editorial processes, making it easier for authors to submit their papers and shortening the turnaround times, while maintaining highest levels of quality assurance for the content. Finding good reviewers is pivotal for this, but it is an increasing challenge, not

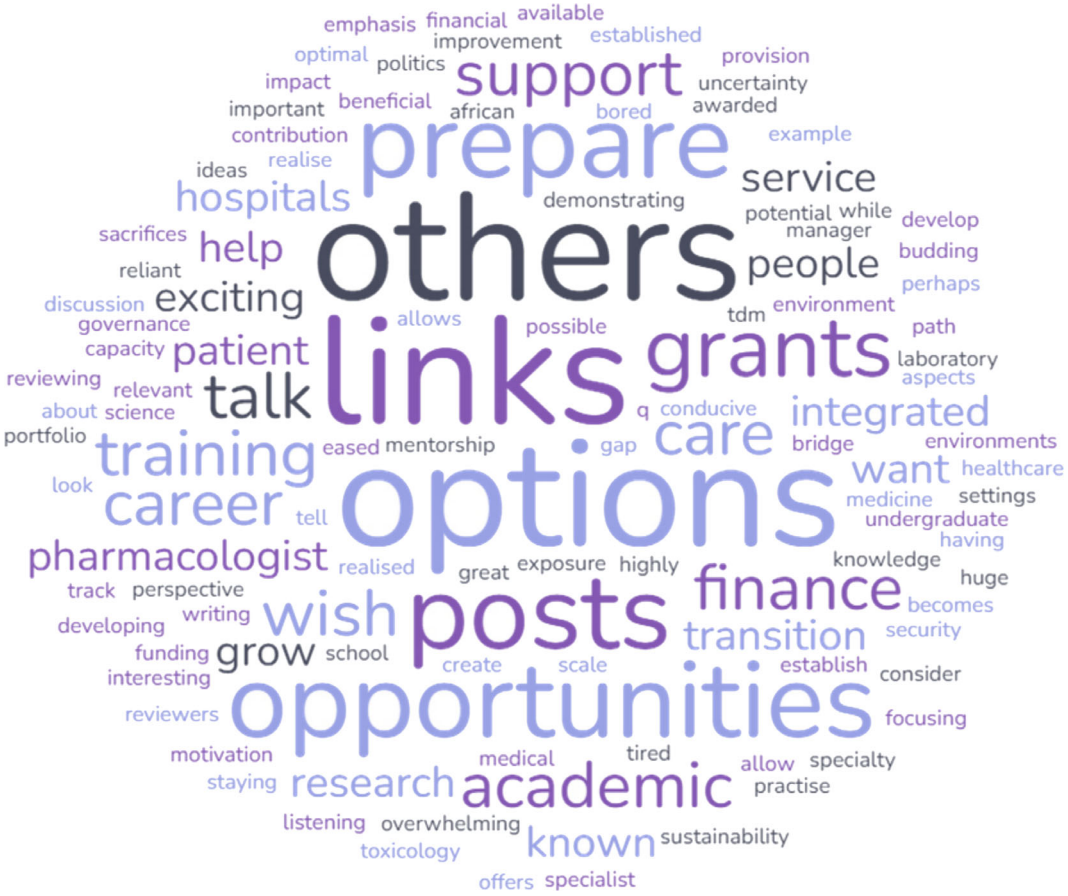

FIGURE 3 Word cloud of "*Barriers and hindrances for Clinical Pharmacologists (CPT specialists)*" mentioned in various email discussions by a group of clinical pharmacologists in a few African countries and who had recently completed specialist training (cf. methods).

exactly helped by the tens of daily emails most potential reviewers get with invitations to review, prepare a special issue, or join an editorial board. In that sense it is good to hear that publishing in nonreputable journals is now actively discouraged by most promotion committees in most western academic institutions, including those that have CP groups.

Other actions that CP journals can undertake include alignment with their societies as well as with other journals. An active commissioning strategy is also relevant to increase visibility. In general, publication of expert reviews from world authorities, themed issues, guidelines and methods papers are most guaranteed to be frequently cited and thereby improve the visibility of the journal, its other papers included, and with that the entire field of CP. With the widening of the therapeutic armamentarium with cell, protein-based and gene therapies CP journals are well positioned to publish basic papers on these therapies as well as models for their introduction and follow-ups in healthcare.

There is a powerful role for social media to advocate for the journals, its content, as well as CP in general. It is an area that currently remains largely untapped by most CP journals, or at least not exploited to its fullest extent. However, social media is also largely driven by novelty, which does not always pair well with scientific publications. So, while the use of social media is powerful, it should probably be complementary. The quality of our publications remains CP's biggest advocate, and ensuring this simply takes time, like rising of dough or aging of good wine.

8 | RARE BIRDS ACROSS CONTINENTS

CP specialists in research, teaching and clinical services are *rare birds*. Still the contributions to advancement in all these areas are impressive. With the rapidly expanding introduction of new types of medicines clinical pharmacologists have all the possibilities to contribute provided they continue to combine research, teaching and clinical services and strengthen their competence in cross-disciplinary collaboration with both biology oriented basic and clinical expertise as well as with society-oriented research fields. The shortage of clinical pharmacologists and the expected vast expanse of knowledge and expertise create both challenges and opportunities.[51] In all settings, there is a void to be filled. The BPS has vividly and successfully argued for the value of more clinical pharmacologists in NHS calculating that £1 invested will give £6 back and increase quality of use of medicines.[52] This is achieved by an increase of the number of clinical pharmacologists working multiprofessionally managing multimorbidity and complex polypharmacy; implementation of a national pharmacogenomics

programme and developing capability in clinical research across NHS. The UK has 150 CPT specialists while 400 would be a more appropriate number,[52] which would still be fewer than 6 per million inhabitants. This is a relatively high ambition considering that 20 out of 31 countries reported fewer than 5 positions/million inhabitants in CP in a European survey from 2010.[53] One of the main challenges in Asia with respect to CP is that there are not enough clinical pharmacologists. For example, in Indonesia there are no more than 40 medically qualified persons with CPT board certification. Globally, however, professional and government leadership organisations have not specified the total number needed of specialists trained in CPT. In Africa, CPT specialists are concentrated to South Africa, a country that could be a role model for initiating specialist programmes for physicians.

There are about 100 times more clinical pharmacists compared to clinical pharmacologists in UK. Because of shortages of CPT specialists, there is task shifting to pharmacists. Not trained as a medical doctor, pharmacists are however unable to fulfil some roles and responsibilities (e.g., causality assessment and management of ADRs/adverse events).[54] Another gap to close is that clinical pharmacologists rarely collaborate with public health departments despite the numerous contributions CP has made to pharmacoepidemiology and pharmacovigilance.

Probably the most significant challenge for CP services for patients is that they are not specifically costed like for other medical specialties, such as cardiology. There is often no procedure as in surgery or oncology, there is no diagnostic test such as imaging or laboratory tests that clinical pharmacologists can charge for, such as radiology and pathology do, and there is often no reimbursement for consultancies like those provided by infectious disease specialists. Furthermore, while medicine management is often mandatory by national and international quality accreditation organizations, this is mostly done by pharmacists.

9 | RECOMMENDATIONS ON THE WAY FORWARD

The participants at the workshop concluded that the diversity of CP with professionals having complementary expertise, working as a team is a strength but to address challenges in research, education and clinical services, the discipline needs to adapt to local needs making a difference and thereby ensuring funding. Broader needs requiring global collaboration are to be on the agenda, i.e. antibiotic resistance and drug development since these challenges and opportunities affect locally across borders and require global strategies. To expand into healthcare services will require access to quite a number of physicians trained in CPT, clinical pharmacologists. The international character of CP with research and access to strong journals and scientific meetings can help CP to provide up-to-date knowledge and services locally/regionally by promoting awareness of successes stories. At the workshop, 5 key strategies were identified to increase the visibility, relevance and impact of CP:

9.1 | Strengthen the translational nature of CP

CP should keep its vision that the discipline "*involves all aspects of the relationship between drugs and humans*" and be prepared to address research, educational and service aspects on both classical and emerging complex and advanced drug therapies. CP's bridging role with insights from basic to clinical research, in regulatory affairs and with expertise in personalized use of medicines as well as on society-oriented evaluations of value and safety of medicines should be developed. In future, CP research, education and healthcare services will continue to gain from teamwork with different professions, such as nurses, pharmacists, chemists, computer scientists, clinical laboratory specialists and statisticians.

9.2 | Address the needs for optimal use of essential medicines globally

Globally, the most important assets of clinical pharmacologists might be their expertise in promoting rational use of medicine and their expertise in critical drug evaluation applied to selection and monitoring of use of essential medicines as well as of new complex therapies. Training and maintenance of critical drug evaluation skills are critical since this competence was considered by the participants of the workshop as a *door opener* ensuring scientifically based and independent selection of medicines to ensure cost-effective use of limited financial resources. Both CP societies and scientific journals help update and train skills in critical drug evaluation, pharmacoepidemiology and pharmacoeconomics.

The CP societies can enhance the visibility of the specialty and promote its relevance in healthcare through educational activities in partnerships with public institutions such as governments, multilateral organisations and societies. A good example of such an initiative was the Drug and Therapeutics Committee workshop organized by the Nigerian Society for Clinical Pharmacology and Therapeutics in partnership with IUPHAR and the Nigerian country office of the World Health Organization in November 2019. The majority of 50 participants were from health services and administrative and regulatory bodies representing 14 out of the 36 states of the federation of Nigeria and its Capital Territory in Abuja.[55]

9.3 | Board certification programmes for clinical pharmacologists and online educational initiatives

The participants at the workshop noticed that structured training programmes for physicians to become clinical pharmacologists exist in some parts of the world aiming for board certification in CPT. This has been successful in Europe with an increasing number of countries establishing board certification programmes for clinical pharmacologists after fulfilling requirements of defined clinical curricula.[56] Those curricula need to train a specialist to be able to address variability in drug response in individuals and populations and guide clinical

colleagues based on critical drug evaluation skills and knowledge and insights in clinical, laboratory and epidemiological methods. With well-trained clinical pharmacologists and also participating in cross-country curricula courses and exchange programmes between institutions CP can become indispensable in health care and thereby strengthen its resources. Board certification programmes for clinical pharmacologists such as those in Europe should be introduced across continents, preferably as joint actions across countries by our regional CP associations. To gain support for widespread specialization programmes in CPT, awareness programmes towards healthcare officials on how much is to be saved by increased use of generics and biosimilars and systematic introduction and follow-up of new costly therapies as demonstrated with the Wise List in Stockholm[29] (Figure 1) and with the BPS proposal of increased number of NHS clinical pharmacologists in the UK[52] can be helpful.

Online CP courses are a powerful tool for education in clinical pharmacological principles with ample opportunities for collaboration across borders and can speed up cross-country board certification programmes of clinical pharmacologists. The online prescribing skills course developed by the Indian Council of Medical Research is an innovative example of the possibilities with online training courses.[57] The course consists of 50 video lectures, case scenarios, demonstration videos, assignments for prescribing tests, analysing quality of prescribing and providing feedback. Over 15 000 medical interns and practicing physicians enrolled with excellent feedback on contents, quality, relevance and usefulness. The online training is convenient, scalable and with opportunities for incorporating interactive elements and continuous assessments. The earlier mentioned PSA of the BPS is another excellent example of an online prescribing skills course.[28]

9.4 | CP with its societies to invest in public goods including essential drug information

The Guide to Pharmacology on drug targets published by IUPHAR and BPS has been a success story and helped to simplify drug development worldwide.[58] In a similar way, it would be an optimal time to share knowledge bases on medicines developed in different countries and settings as public goods available at point of care through a variety of electronic pathways for healthcare staff, patients, and for educational and research purposes.[32,33] The contents of the databases should be easily searched using artificial intelligence tools. CP experts on knowledge bases and management should, through CP societies, raise funding for sharing, coordination and access of trusted drug information. This initiative will strengthen CP's role as a bridging science between knowledge and practice.

9.5 | *White book on Clinical Pharmacology* advocating for the discipline is a priority

The participants at the workshop agreed that rapid progress in science, needs of training of health care professionals in CP concepts and principles and of CP expertise in health care, industry and at regulatory agencies urged for a thoroughly updated edition of the CP *white book* published 2012.[1,59] With the remarkable progress and introduction of gene and cell therapies and RNA-based compounds and complex drug markets appearing globally, the needs of independent and solid CP competence to guide colleagues and healthcare institutions on the RUM will explode. It is logical that IUPHAR in partnership with WHO and Council for International Organization of Medical Sciences initiate a working group for design and development of a CP *white book* relevant for the 21st century with solid representation from all continents.

9.6 | Limitations

The current manuscript describes the findings presented during a symposium, which was part of the 2023 meeting of the International Union of Pharmacology, organised by the BPS. It is a compilation of the symposium's presentations supplemented with literature data and describes the state of CP in various regions of the world. One of the limitations of this paper is that it includes interviews with colleagues but that these interviews are far from extensive. In addition, not all regions in the world are covered. This paper therefore does not fully describe all CP around the world. However, it does describe several key aspects and major impact of CP in a varied range of regions, so we think it forms a good basis for the development of the discipline.

9.7 | Final remarks

CP has contributed remarkably well to discoveries and knowledge on drug therapy and on its rational practice in public health and clinical medicine in recent years. Breakthroughs in molecular and clinical medicine combined with data revolution as well as unmet access to affordable and cost-effective drug therapies for millions of people will require more effective use of limited resources based on solid scientific and clinical knowledge. CP is a discipline well-positioned and used to working transdisciplinary and should nationally, regionally and globally speed up the work with a *White book for CP* for the 21st century building on increased cross-country collaboration and exchange.

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Design of work by contribution of all authors. Draft of initial region-specific contributions on HIC, Asia and Africa by L.L.G., N.A.K. and C.W., respectively and on scientific journals by S.C. O.O.O. drafted the first complete version of the paper followed by input by all authors. L.L.G. and S.C. revised and restructured the paper with input from all authors and with final editing and corrections by L.L.G. and authorization of the submitted paper by all authors.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to report.

DATA AVAILABILITY STATEMENT

Not applicable for this paper.

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REFERENCES

1. Clinical pharmacology in health care, teaching and research. A joint report by WHO, IUPHAR AND CIOMS. Published 2012. Accessed August 22, 2024. https://cioms.ch/publications/product-category/earlier-publications/
2. Clinical pharmacology scope, organization, training. Report of a WHO studygroup. *World Health Organ Tech Rep Ser*. 1970;446:5-21. PMID: 4987611.3
3. Gustafsson LL. Strengthening Global Health research. *Glob Health Action*. 2023;16(1):2290638. doi:10.1080/16549716.2023.2290638
4. Choi Y, Vinks AA, van der Graaf PH. Novel therapeutic modalities: the future is now. *Clin Pharmacol Ther*. 2023;114(3):493-496. doi:10.1002/cpt.2996
5. What is clinical pharmacology? British Pharmacological Society. Accessed August 15, 2024. https://www.bps.ac.uk/about/about-pharmacology/what-is-clinical-pharmacology
6. What is Clinical Pharmacology? ASCPT. Accessed August 15, 2024. https://www.ascpt.org/Resources/Knowledge-Center/What-is-Clinical-Pharmacology
7. Dollery CT. The scientific contribution of clinical pharmacology. *Eur J Clin Pharmacol*. 2008;64(2):99-106. doi:10.1007/s00228-007-0420-3
8. Mullard A. 2022 FDA approvals. *Nat Rev Drug Discov*. 2023;22(2):83-88. doi:10.1038/d41573-023-00001-3
9. Rome BN, Egilman ACKA. Trends in prescription drug launch prices, 2008-2021. *Jama*. 2022;327(21):2145-2147. doi:10.1001/jama.2022.5542
10. Ceylan G, Anderson IAWW. Sharing of misinformation is habitual, not just lazy or biased. *Proc Natl Acad Sci U S A*. 2023;120(4):e2216614120. doi:10.1073/pnas.2216614120
11. Gustafsson LL, Wettermark B, Godman B, et al. The'wise list'- a comprehensive concept to select, communicate and achieve adherence to recommendations of essential drugs in ambulatory care in Stockholm. *Basic Clin Pharmacol Toxicol*. 2011;108(4):224-233. doi:10.1111/j.1742-7843.2011.00682.x
12. Martin JH, Henry D, Gray J, et al. Achieving the World Health Organization's vision for clinical pharmacology. *Br J Clin Pharmacol*. 2016;81(2):223-227. doi:10.1111/bcp.12803
13. Methodology, definitions and country groupings. Updated January 9, 2024. SDG Gateway, Asia Pacific. Accessed August 24, 2024. https://data.unescap.org/stories/escap-database
14. Mortality rate, infant (per 1,000 live births). World Bank Open Data. World Bank Group. World Bank Gender Data Portal. Accessed August 22, 2024. https://liveprod.worldbank.org/en/indicator/sp-dyn-imrt-in
15. UNDP Human Development Reports. *2023-2024 human development report*. UNDP. Accessed August 24, 2024. https://hdr.undp.org
16. Kshirsagar NA, Bacchav SS, & Kulkarni LA. Clinical pharmacology training in India: status and need. *Ind J Pharmacol*. 2013;45(5):429-433. doi:10.4103/0253-7613.117718
17. Differding E. The drug iscovery and development industry in India:two decades of proprietary small-molecule R&D. *ChemMedChem*. 2017;12(11):786-818. doi:10.1002/cmdc.201700043
18. Kshirsagar N, Kumar V. Clinical pharmacology: prospects and development in India. *Indian J Pharmacol*. 2011;43(5):489-491. doi:10.4103/0253-7613.84946
19. Kshirsagar NA. History of Clinical Pharmacology in India: a brief account. In: Patil PN, Gulati OD, Balaraman R, Goyal RK, eds. *Topics in the history of pharmacology*. 1st ed. BS Shah Prakashan; 2005:148-169.
20. Alhuneafat L, Al Ta'ani O, Jabri A, et al. Cardiovascular disease burden in the Middle East and North Africa region. *Curr Probl Cardiol*. 2024;49(3):102341. doi:10.1016/j.cpcardiol.2023.102341
21. Sorato MM, Davari M, Kebriaeezadeh A. Improving access to medicines to reduce marketing and use of substandard and falsified medicines in Africa: scoping review. *J Med Access*. 2024;8:27550834241236600. doi:10.1177/27550834241236598
22. Dandara C, Swart M, Mpeta B, Wonkam A, Masimirembwa C. Cytochrome P450 pharmacogenetics in African populations: implications for public health. *Expert Opin Drug Metab Toxicol*. 2014;10(6):769-785. doi:10.1517/17425255.2014.894020
23. Rajman I, Knapp L, Morgan T, Masimirembwa C. African genetic diversity: implications for cytochrome P450-mediated drug metabolism and drug development. *EBioMedicine*. 2017:17:67-74. doi:10.1016/j.ebiom.2017.02.017
24. Breuil L, Ziani N, Leterrier S, et al. Impact of C,ytochrome induction or inhibition on the plasma and brain kinetics [^{11}C]-metoclopramide, a PET probe for P-glycoprotein function at the blood-brain barrier. *Pharmaceutics*. 2022;14(12):2650. doi:10.3390/pharmaceutics14122650
25. Bauer M, Bamminger K, Pichler V, et al. Impaired clearance from the brain increases the brain exposure to metoclopramide in elderly

subjects. *Clin Pharmacol Ther*. 2021;109(3):754-761. doi:10.1002/cpt.2052

26. Eyal S, Ke B, Muzi M, et al. Regional P-glycoprotein activity and inhibition at the human blood-brain barrier as imaged by positron emission tomography. *Clin Pharmacol Ther*. 2010;87(5):579-585. doi:10.1038/clpt.2010.11
27. Dürr P, Schlichtig K, Kelz C, et al. The randomized AMBORA trial: impact of pharmaco-cological/pharmaceutical care on medication safety and patient-reported outcomes during treatment with new oral anticancer agents. *J Clin Oncol*. 2021;39(18):1983-1994. doi:10.1200/JCO.20.03088
28. Maxwell SRJ, Coleman JJ, Bollington L, Taylor C, Webb DJ. Prescribing safety sssessment 2016: delivery of a national prescribing assessment to 7343 UK final-year medical students. *Br J Clin Pharmacol*. 2017;83(10):2249-2258. doi:10.1111/bcp.13319
29. Eriksen J, Gustafsson LL, Ateva K, et al. High adherence to the "wise list" treatment recommendations in Stockholm: a 15-year retrospective review of a multifaceted approach promoting rational use of medicines. *BMJ Open*. 2017;7(4):e014345. doi:10.1136/bmjopen-2016-014345
30. Wirtz VJ, Hogerzeil HV, Gray AL, et al. Essential medicines for universal health coverage. *Lancet*. 2017;389(10067):403-476. doi:10.1016/S0140-6736(16)31599-9
31. Sheikh A, Coleman J, Chuter A, et al. *Electronic prescribing systems in hospitals to improve medication safety: a multimethod research programme*. National Institute for Health and Care Research; 2022. PMID: 36223444
32. Maxwell S, Eichler HG, Bucsics A, Haefeli WE, Gustafsson LL, e-SPC Consortium. E-SPC consortium. E-SPC - delivering drug information in the 21st century: developing new approaches to deliver drug information to prescribers. *Br J Clin Pharmacol*. 2012;73(1):12-15. doi:10.1111/j.1365-2125.2011.03981.x
33. Hoffmann M, Vander Stichele R, Bates DW, et al. Guiding principles for the use of knowledge bases and real-world data in clinical decision support systems: report by an international expert workshop at Karolinska Institutet. *Expert Rev Clin Pharmacol*. 2020;13(9):925-934. doi:10.1080/17512433.2020.1805314
34. Ma N, Zhang Z, Liao F, Jiang T, Tu Y. The birth of artemisinin. *Pharmacol Ther*. 2020;216:107658. doi:10.1016/j.pharmthera.2020.107658
35. Crump A. The advent of ivermectin: people, partnerships, and principles. *Trends Parasitol*. 2014;30(9):423-425. doi:10.1016/j.pt.2014.07.001
36. Kshirsagar NA, Gogtay NJ, Moorthy NS, et al. A randomized, double-blind, parallel-group, comparative safety, and efficacy trial of oral co-artemether versus oral chloroquine in the treatment of acute uncomplicated *plasmodium falciparum* malaria in adults in India. *Am J Trop Med Hyg*. 2000;62(3):402-408. doi:10.4269/ajtmh.2000.62.402
37. Kshirsagar NA, Gogtay NJ, Garg BS, et al. Efficacy and tolerability of treatment with single doses of diethylcarbamazine (DEC) and DEC plus albendazole (ABZ) for three consecutive years in lymphatic filariasis: a field study in India. *Parasitol Res*. 2017;116(10):2683-2694. doi:10.1007/s00436-017-5577-9
38. Karbwang J, Na-Bangchang K. The role of clinical pharmacology in chemotherapy of multidrug-resistant *plasmodium falciparum*. *J Clin Pharmacol*. 2020;60(7):830-847. doi:10.1002/jcph.1589
39. Kazura J, Greenberg J, Perry R, Weil G, Day K, Alpers M. Comparison of single-dose diethylcarbamazine and ivermectin for treatment of bancroftian filariasis in Papua New Guinea. *Am J Trop Med Hyg*. 1993;49(6):804-811. doi:10.4269/ajtmh.1993.49.804
40. Ottesen EA, Vijayasekaran V, Kumaraswami V, et al. A controlled trial of ivermectin and diethylcarbamazine in lymphatic filariasis. *N Engl J Med*. 1990;322(16):1113-1117. doi:10.1056/NEJM199004193221604
41. Salhotra VS, Sachdeva KS, Kshirsagar N, et al. Effectiveness and safety of bedaquiline under conditional access program for treatment of drug-resistant tuberculosis in India: an interim analysis. *Indian J Tuberc*. 2020;67(1):29-37. doi:10.1016/j.ijtb.2019.10.002
42. Kansagra KA, Parmar D, Jani RH, et al. Phase I clinical study of ZYAN1, a novel prolyl-hydroxylase (PHD) inhibitor to evaluate the safety, tolerability, and pharmacokinetics following oral administration in healthy volunteers. *Clin Pharmacokinet*. 2018;57(1):87-102. doi:10.1007/s40262-017-0551-3
43. Advisory committee on safety of medicinal products (ACSoMP): measures to minimize the risk of ocular adverse events with miltefosine. World Health Organization Published March 20, 2023. Accessed August 27, 2024. https://cdn.who.int/media/docs/default-source/medicines/pharmacovigilance/miltefosine-2023.pdf?sfvrsn=13e0c48c_3
44. Training Clinical Pharmacology and Therapeutics. Joint Royal College of Physicians Training Board (JRCPTB). Accessed August 27, 2024. https://www.thefederation.uk/training/specialities/clinical-pharmacology-and-therapeutics
45. Guidelines for competency based postgraduate training programme for DM in Clinical Pharmacology. Indian National Medical Commission: Postgraduate Medical Education Board. August 4, 2022. Accessed August 27, 2024. https://www.nmc.org.in/wp-content/uploads/2022/revised/DM_in_Clinical_Pharmacology.pdf
46. Park JJH, Mogg R, Smith GE, et al. How COVID-19 has fundamentally changed clinical research in global health. *Lancet Glob Health*. 2021;9(5):e711-e720. doi:10.1016/S2214-109X(20)30542-8
47. List of National Regulatory authorities (NRAs) operating at maturity level 3 (ML3) and maturity level 4 (ML4). (as benchmarked against WHO Global Benchmarkinbg Tool (GBT) (in alphabetical order). Technical document, June 13, 3024. World Health Organization (WHO). Accessed August 27, 2024. https://www.who.int/publications/m/item/list-of-nrs-operating.ml3-and-ml4
48. The WHO Program for international drug monitoring. World Health Organization Accessed August 27, 2024.https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance/networks/pidm
49. Jakovljevic M, Wu W, Merrick J, Cerda A, Varjacic M, Sugahara T. Asian innovation in pharmaceutical and medical device industry - beyond tomorrow. *J Med Econ*. 2021;24(suppl 1):42-50. doi:10.1080/13696998.2021.2013675
50. Venkatakrishnan K, Gupta N, Smith PF, et al. Asia-inclusive clinical research and development enabled by translational science and quantitative clinical pharmacology: toward a culture that challenges the status quo. *Clin Pharmacol Ther*. 2023;113(2):298-309. doi:10.1002/cpt.2591
51. Dollery CT. Clinical pharmacology – the first 75 years and a view of the future. *Br J Clin Pharmacol*. 2006;61(6):650-665. doi:10.1111/j.1365-2125.2006.02672.x
52. British Pharmacological Society. Spending review: invest in clinical pharmacology to support our NHS workforce. Published 2021. Accessed April 2, 2024. https://www.bps.ac.uk/about/policy-positions-and-statements/consultation-responses/articles/2021/spending-review-2021
53. Orme F, Sjoqvist F. Clinical pharmacology in European health care-outcome of a questionnaire study in 31 countries. *Eur J Clin Pharmacol*. 2013;69(9):1635-1639. doi:10.1007/s00228-013-1519-3
54. Burckart GJ. Clinical pharmacology and clinical pharmacy: a marriage of necessity. *Eur J Hosp Pharm*. 2012;19(1):19-21. doi:10.1136/ejhpharm-2011-000002
55. Ogunleye OO, Fadare JO, Ogundele SO, et al. The IUPHAR subcommittee on Global Health pharmacology and therapeutics and the Nigerian Society for Clinical Pharmacology and Therapeutics (NSCPT) held a drugs and therapeutics committee (DTC) workshop in Lagos, Nigeria. Pharmacology International number 94, January 2024, page

1-9. Accessed September 4, 2024. www.iuphar.org/publications/pharmacology-international-newsletters/
56. Sjoqvist F. Development of clinical pharmacology as a medical Speciality in Europe-the roles of WHO, IUPHAR and EACPT. *Basic Clin Pharmacol Toxicol*. 2014;115(2):172-178. doi:10.1111/bcpt.12278
57. Kshirsagar NA, Kaul R, Kumar V. ICMR National Virtual Centre for clinical pharmacology with network of rational use of Medicines & Product Development Centres. *Indian J Med Res*. 2021:154(5):665-668. doi:10.4103/ijmr.IJMR_1857_19
58. Harding SD, Armstrong JF, Faccenda E, et al. The IUPHAR/BPS guide to PHARMACOLOGY in 2024. *Nuclei Acids Res*. 2024;52(D1):D1428-D1449. doi:10.1093/nar/gkad944
59. Birkett D, Brøsen K, Cascorbi I, et al. Clinical pharmacology in research, teaching and health care: considerations by IUPHAR, the International Union of Basic and Clinical Pharmacology. *Basic Clin Pharmacol Toxicol*. 2010;107(1):531-559. doi:10.1111/j.1742-7843.2010.00602.x PMID: 20590536

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APPENDIX 1: E-mail survey to colleagues in Australia-Europe-North America

Workshop on "*Appraising the Visibility, Relevance and Impacts of Clinical Pharmacology Globally*" at World Congress in Pharmacology and Clinical Pharmacology July 2023.

My name is Lars L Gustafsson. I am professor and senior consultant in clinical pharmacology at Karolinska Institutet in Stockholm, Sweden—see CV.

I hope you have a chance to give me some help. I will speak and chair the Workshop *Appraising the Visibility, Relevance and Impacts of Clinical Pharmacology Globally* at World Congress in Pharmacology and Clinical Pharmacology in Glasgow July 2023 (cf. enclosure). I want to ensure that my talk is concordant with views of leaders in clinical pharmacology in rich countries (Europe, USA, Canada and Australia—Asian and African perspectives will be covered by others).

I will talk about *Emerging chances to strengthen clinical pharmacology in resource-rich countries* and will build my presentation on the concept that a combined research-teaching-service approach strengthens clinical pharmacology nationally and globally (Enclosed Clinical Pharmacology Strategic Document from 2012).

I would appreciate if you can answer a few questions that will help me to give a fair and forward fair picture about the emerging chances in clinical pharmacology in rich countries.

1. What is the 2 best examples of breakthroughs in clinical pharmacology in rich countries the last 10 years within:
   a. Research
   b. Teaching
   c. Clinical service
   d. Regulatory science/drug industry

2. What is the best example (local or national) of breakthrough in clinical pharmacology in your country during the last 10 years within:
   e. Research
   f. Teaching
   g. Clinical service
   h. Regulatory science/drug industry

3. What is in your mind the most promising project/initiative in your country (regional or nationally) that can become a breakthrough during the next few years within
   a. Research
   b. Teaching
   c. Clinical service
   d. Regulatory science/drug industry

4. Can the establishment of international task force groups within various fields/areas from different countries strengthen the impact of clinical pharmacology within research, teaching, clinical services and regulatory science/drug industry (for example coordinated by IUPHAR-International Union of Basic and Clinical Pharmacology)?
5. Any other comments

I appreciate if you can answer no later than May 20, 2023.
Thank you for your interest and help
Greetings
Lars

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APPENDIX 2: E-mail/telephonic survey to colleagues in Asia

Dear ----

Greetings, I hope you are all well and I hope to meet you again some day.

I am writing to you to request information and help from you about clinical pharmacology in your country/Asian region, with respect to its:

1. development, historical aspects

2. training, courses, where conducted—university, academic institutions

3. careers, in academic, research, industry, government, regulatory, pharmacovigilance, toxicology etc,

4. opportunities, challenges

5. future vision

6. CP in relation to traditional medicine, pharmacy, pharmaceutical medicine

I have to give a talk on Clinical Pharmacology Asian Perspective at the WCP 2023 in the workshop on Appraising the visibility, relevance and impacts of Clinical Pharmacology globally.

Your own/your societies/experts' perspectives will be very important

You can also highlight some of the achievements and outstanding work done, and perhaps provide names of prominent clinical pharmacologists, as well as publications.

I look forward to hearing from you, contributions will be duly acknowledged.

Best wishes

Nilima

Dr Mrs Nilima A. Kshirsagar, MD, PhD, FNAMS, FAMS, FACCP USA, FRCP UK, GFMD, IFAPP

Member WHO committees ACSoMP, Drug Statistics Methodology, MPAG

Former National Chair, Emeritus Scientist, Chairperson SAG BMS, Member SAB, ICMR

Member DTAB, Chairperson FDC Subcommittee, Govt of India

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APPENDIX 3: Email survey to colleagues in Africa

Email to colleagues within Africa—used a *snowball* method whereby the colleagues initially contacted made suggestions of other individuals to invite.

Dear Colleague (Individual names redacted),

Through different committee roles, I find myself giving a talk in Glasgow in July at the world conference on pharmacology on clinical pharmacology careers: barriers and opportunities etc. in Africa.

I wondered if I could enlist you to provide me with some guidance/information.

I thought to focus on medically qualified clinical pharmacology because there seems to be a particular gap there. OK, there are many gaps, drug development and so forth, but I have 20 min and think it is better to focus in a bit. Of course there will be a slide on Pharmacometrics Africa!

I thought it would be good to showcase a couple of 'case studies' of people who have overcome obstacles, and any examples of best institutional practice.

I also wondered about putting a quick survey together to ask African clinical pharmacologists some of their experiences i.e.:

1. What has helped you most in your career?
2. What has hindered?
3. If there was 'one thing' that you could have that would have helped, what would it be/have been?
4. Anything else relevant.

I thought I would start by asking the small group of you, as you are clearly doing well!

What kind of talk would you have wanted a few years ago?

Would want now?

What do you wish you had known?

Are there any useful resources or publications on this you have come across (careers in Africa …)?

Thank you for spitting out any thoughts!

And also, please advise who else I should reach out to. I want to be able to present on behalf of many of us, not just give my view.

The talk is in July—so clearly no huge rush on this!

Catriona