Received: 25 June 2021 | Revised: 25 June 2021 | Accepted: 28 June 2021

DOI: 10.1002/psp4.12680

EDITORIAL

CPT: Pharmacometrics & Systems Pharmacology – Inception, Maturation, and Future Vision

INTRODUCTION

CPT: Pharmacometrics & Systems Pharmacology (PSP) is a cross-disciplinary journal which publishes research articles, reviews and tutorials that bridge various disciplines including pharmacometrics, systems pharmacology modeling, physiologically based pharmacokinetics (PBPK), translational research, model-based meta-analyses (MBMA) of clinical trials, computational pharmacology and bioinformatics. PSP was launched in September 2012, as the second journal of American Society for Clinical Pharmacology and Therapeutics (ASCPT), with the first being Clinical Pharmacology and Therapeutics (CPT). Since the launch of Clinical & Translational Science (CTS), PSP is now part of a family of three journals.

In June 2021, approaching its 9th anniversary, PSP was granted for the first time, an impact factor. We are proud to announce that the impact factor for 2020 is 4.054. Of note, the cite score of PSP was already increasing from 4.1 in 2015 to 6.3 in 2020, which is great news for both the journal and our scientific community. Hence, for the July 2021 issue, we introduce our first video-abstract, and in this editorial present our vision for the journal for the next ten years, and last, but certainly not least, present our new cover (Figure 1). It was selected by the Editor in Chief, associate editors and the ASCPT board members to illustrate the various aspects of PSP (molecules, equations, models, patients) and their interplay but also the cycling of the different components of model-informed drug development (MIDD) and development and application of models as they continue to evolve.

A JOURNEY THROUGH THE LAST DECADE

In the inaugural editorial of PSP,[1] the first Editor in Chief, Piet van der Graaf hoped that PSP would be a scientific foundation to provide the tools and methodologies for the development of quantitative concepts in pharmacology. PSP has certainly achieved this expectation and has become a leading source of learning for the growing fields of applied quantitative sciences in pharmacology. As recently expressed in response to our survey to the ASCPT Early Career Community members on which PSP content is most valuable to them; "There cannot be enough tutorials – these are great!". It is clear that tutorials are one of the best commodities we have in the PSP journal (59 published tutorials so far); indeed, after evaluating all articles, it was noted that according to their relative citation ratios, the top five most cited articles in PSP were tutorials (Table 1).

One of the early tutorials for the journal by Ron Keizer et al.[2] showed how to maximize workflow in commonly used software when performing nonlinear mixed effects (NLME) modelling and has been cited more than 400 times since 2013. The tutorial by Ryman et al.[3] on modeling pharmacokinetics of monoclonal antibodies has already been cited 284 times since 2017 and shows that PSP is providing knowledge on both accepted fundamentals in the field of pharmacometrics (PMX) while establishing good modeling practices for evolving research areas.

Our tutorials are not the only source of online discussion for PSP; while PMX tutorials are the most cited, our quantitative systems pharmacology (QSP) articles are the most talked about online, according to their Altmetric Attention Scores (Table 2). Original articles from PSP that have the highest attention scores reflecting topics important to the modeling and simulation community, include translational and detailed mechanistic modeling approaches.

Two and a half years after launching PSP, we decided to create 'virtual issues', which is indeed perfect for online journals, helping readers find all published articles in a specific area or topic of interest. Six virtual issues were first launched (Figure 2), with, of course, the Tutorials, but also PBPK Modelling, Pediatrics, Rare Diseases and Cancer. There are now 23 virtual issues, with the addition of more organ/diseases (e.g. Immunotherapy, Liver, Neuroscience, Infectious Diseases), specific populations (e.g. Pregnancy and Lactation), Safety Pharmacology and Precision Medicine,

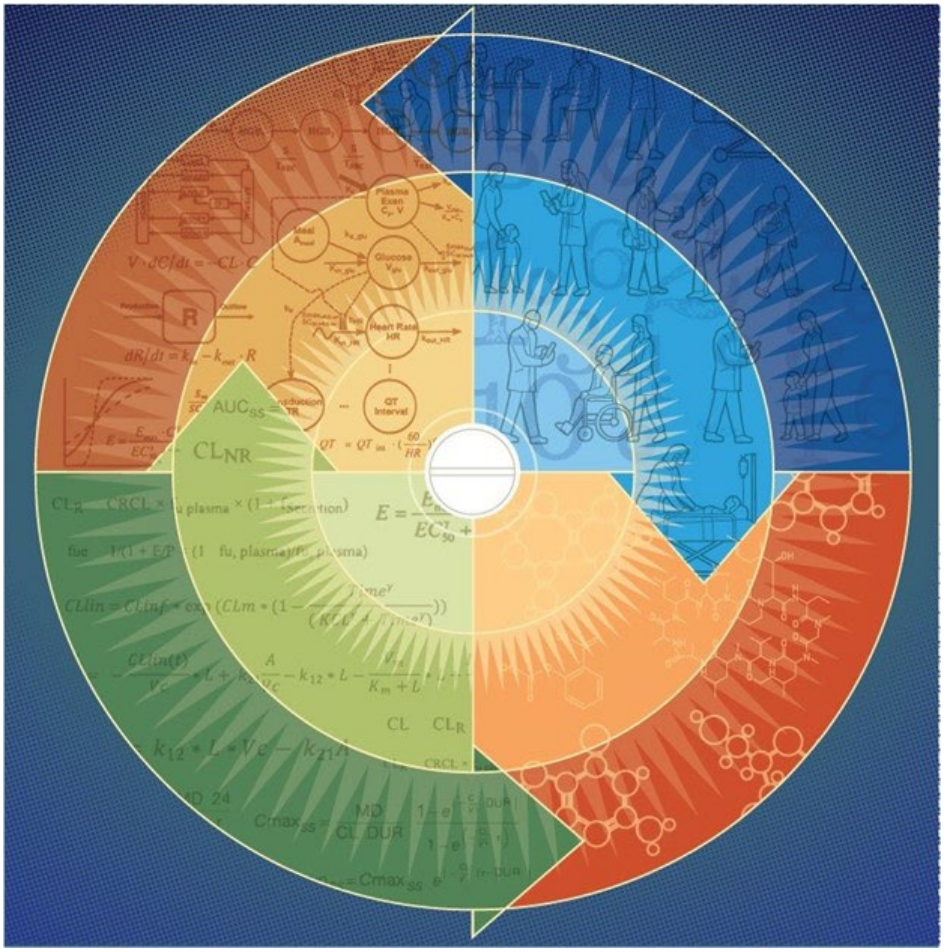

FIGURE 1 New Cover for CPT:PSP

and Regulatory MIDD. Since France Mentré became Editor in Chief, 4 new virtual issues have been launched including Methods and Software Tools, and the most recent one, 'Statistics and Pharmacometrics', that was launched simultaneously with the first special issue of PSP. The addition of new virtual issues with various themes, together with the growth of PSP, more than 750 articles published by March 2021 (including more than 500 original research articles), illustrate how the 'baby journal' PSP has now grown into a mature, diverse and truly international journal; hence the need to define a vision for the next ten years.

Pharmacometrics remains the mainstay of PSP as indicated in a crude analysis of articles published in the first 3 years of the journal (after launching) *versus* the last 3 years (Figure 3). Based on the article content, this approach appears to be trending towards becoming more mechanistic. Interestingly, the relative number of QSP articles (inclusive of Systems Biology) has decreased in this time-frame whilst the number specifically related to physiologically based pharmacokinetic modeling and simulation (PBPK) has increased significantly. This is probably a consequence of the increasing number of case studies whereby PBPK has had an impact on the drug label and rapid adoption by major regulatory bodies around the world. Today, CPT journals, including PSP, are the go-to journals for many product developers to publish PBPK cases. Meanwhile, through its regulatory model-informed drug development (MIDD) virtual issue, PSP has been the home of reporting perspectives and events from global regulators that are essential for the broader implementation of PBPK in research and development and regulations of both new and generic drug products.

The findings of our analysis were reflected in interviews with key opinion leaders (KOLs) in quantitative sciences, where they discussed milestone achievements of these quantitative approaches and also future perspectives – the challenges and opportunities. Overall, all agreed that regulatory and industry acceptance of PMX and also PBPK has grown and can now be considered "business as usual". This is evident by routine processes including quality control and assurance being standard practice and PMx analysis results becoming increasingly part of the label worldwide. The value of PMX on top of standard statistics and clinical pharmacology is recognized in drug development and clinical research, for example, by embedding these into pediatric licensing rules and the creation of research networks such as connect4children.org to support regulatory clinical trials in children. Such engagement should increase and modelers

TABLE 1 Top 10 published articles of PSP according to their relative citation ratio (RCR)

Rank	RCR	Title	Article type	First author	Year	PMID	Total citations[a]
1	17.75	Modeling and Simulation Workbench for NONMEM: Tutorial on Pirana, PsN, and Xpose	Tutorial	Keizer, RJ	2013	23836189	440
2	15.97	Basic Concepts in Population Modeling, Simulation, and Model-Based Drug Development Part 2: Introduction to Pharmacokinetic Modeling Methods	Tutorial	Mould, DR	2013	23887688	454
3	13.89	Pharmacokinetics of Monoclonal Antibodies	Tutorial	Ryman, JT	2017	28653357	283
4	13.88	Model Evaluation of Continuous Data Pharmacometric Models: Metrics and Graphics	Tutorial	Nguyen, THT.	2017	27884052	164
5	11.78	Application of Physiologically Based Pharmacokinetic (PBPK) Modeling to Support Dose Selection: Report of an FDA Public Workshop on PBPK	Tutorial	Wagner, C	2015	26225246	199
6	10.57	Basic Concepts in Physiologically Based Pharmacokinetic Modeling in Drug Discovery and Development	Review	Jones, HM	2013	23945604	336
7	9.86	Good Practices in Model-Informed Drug Discovery and Development: Practice, Application, and Documentation	White Paper	EFPIA MID3 Workgroup	2016	27069774	159
8	9.59	Basic Concepts in Population Modeling, Simulation, and Model-Based Drug Development	Tutorial	Mould, DR	2012	23835886	332
9	7.77	Predictive Performance of Physiologically Based Pharmacokinetic Models for the Effect of Food on Oral Drug Absorption: Current Status	Research Article	Li, M	2017	29168611	40
10	7.42	Applied Concepts in PBPK Modeling: How to Build a PBPK/PD Model	Tutorial	Kuepfer, L	2016	27653238	128

RCR, Relative citation ratio is a measure of scientific influence based on the number of citations of a paper relative to the citations received by NIH funded publications from the same area and year of publication (Digital Science. (2018) Dimensions [Software] available from https://app.dimensions.ai. Accessed on 06–22–2021, under license agreement.)

[a]According to Google scholar, accessed June 18th, 2021.

are becoming a natural part of design, decision-making, portfolio optimization, considering patient level data, real world data across all levels of drug development and clinical trials. Further, there has been some clear growth in the acceptance and use of PMX at the point of care as well and is now used in hospitals world-wide to actively optimize dosing for patients.[4,5] PBPK is increasingly used in drug development and is established in areas such as assessment of drug-drug-interactions. Ongoing and emerging areas of application include dose extrapolation in special populations, assessment of virtual bioequivalence and mechanistic absorption to address increasingly complex formulations. Over the past 5–10 years, global regulatory bodies have issued guidances or published best practice approaches for the application of PBPK in regulatory submissions.

Based on feedback from the KOLs, there were conflicting views on whether QSP has grown beyond an academic exercise. There are few examples of real application in drug development and progression appears to have been steady and relatively incremental rather than rapid. There are concerns about the uncertainty associated with the highly complex model structure and parameterization of QSP models and that this needs to be addressed in order to expand their use in drug development in the years ahead. As such, QSP is perceived to be a way of thinking "rather than a tool" in that it helps to bridge communication barriers that are seemingly greater than with other methodologies including PMX and PBPK. QSP is often seen in the light of “hypothesis generation” and has application in understanding the pharmacology of a drug for a disease and it's integration of mechanism into models throughout drug discovery and development may increase usability, understanding and extrapolation of models. Piet van der Graaf, founding Editor in Chief and a KOL in QSP, states that “Despite the fact that there will always be slow adaptors and non-believers in our industry, I think it is undeniable that mechanistic modelling has become an integral part of drug discovery and development (QSP) and regulatory decision making (PBPK), and its contribution and impact will continue to grow.[6,7] In my view, QSP and PBPK are better alternatives when it comes to extrapolation, which is done all the time in drug development. The choice is to either use a method that is based on best scientific principles,

TABLE 2 Top 10 Published articles of PSP according to their Altmetric Attention Score (AAS)

Rank	AAS	Title	Type	Authors	PubYear	PMID	Total citations[a]
1	124	A model qualification method for mechanistic physiological QSP models to support model-informed drug development	Tutorial	Friedrich, CM	2016	26933515	46
2	74	Quantitative Systems Pharmacology for Neuroscience Drug Discovery and Development: Current Status, Opportunities, and Challenges	White paper	Geerts, H	2019	31674729	13
3	67	Translational Pharmacokinetic-Pharmacodynamic Modeling and Simulation: Optimizing 5-Fluorouracil Dosing in Children With Pediatric Ependymoma	Research Article	Daryani, VM	2016	27104090	6
4	46	Mathematical modeling of the effects of CK2.3 on mineralization in osteoporotic bone	Research Article	Lisberg, A	2017	28181418	7
5	44	Capturing Drug Responses by Quantitative Promoter Activity Profiling	Research Article	Kajiyama, K	2013	24067440	3
6	43	Studying the Progression of Amyloid Pathology and Its Therapy Using Translational Longitudinal Model of Accumulation and Distribution of Amyloid Beta	Research Article	Karelina, T	2017	28913897	4
7	39	A Translational Systems Pharmacology Model for Aβ Kinetics in Mouse, Monkey, and Human	Research Article	Karelina, T	2017	28571112	5
8	32	Pharmacokinetics of Monoclonal Antibodies	Tutorial	Ryman, JT	2017	28653357	283
9	30	A Systematic Evaluation of Effect of Adherence Patterns on the Sample Size and Power of a Clinical Study	Research Article	Mallayasamy, S	2018	30291680	5
10	27	The Impact of Mathematical Modeling in Understanding the Mechanisms Underlying Neurodegeneration: Evolving Dimensions and Future Directions	Review	Lloret-Villas, A	2017	28063254	37

AAS: Altmetric attention score is an article-level score and collates metrics indicating the amount of online attention an article has received (J. Priem, D. Taraborelli, P. Groth, C. Neylon (2010), Altmetrics: A manifesto, 26 October 2010. http://altmetrics.org/manifesto).

[a]According to Google scholar, accessed June 18th, 2021.

uses all available information and knowledge and makes assumptions explicit, or to revert back to an approach that does none of these. An example is our work in predicting efficacy of COVID-19 vaccines in specific populations ahead of clinical trials, which was presented at the recent FDA workshop "Model Informed Drug Development Approaches for Immunogenicity Assessments"[8] and was submitted to regulatory agencies".

Last but certainly not least, it was interesting to note that the contributions of other disciplines, including bioinformatics and computational pharmacology, to the makeup of the journal in terms of research articles, have declined. However, this trend is likely to reverse over the next 10 years with the emerging interest in machine learning (ML), artificial intelligence (AI) and real-world data analyses.

LOOKING AHEAD TO THE NEXT DECADE

Looking ahead to the next decade, as also illustrated by the new cover (Figure 1), a future vision of PSP is proposed (Figure 4), encompassing (i) perspectives from pertinent ASCPT networks/communities and readership, including feedback from

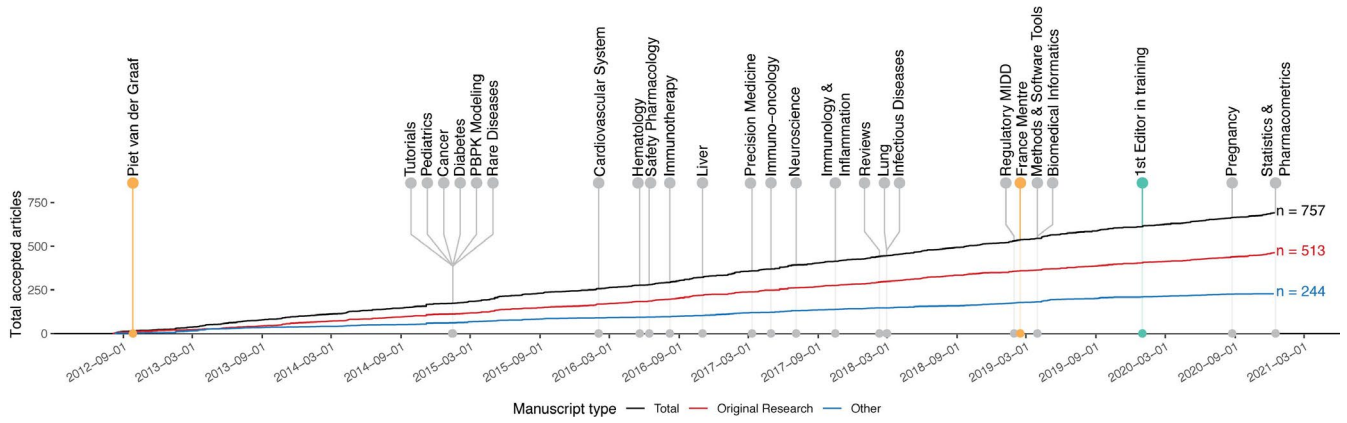

FIGURE 2 Timeline of CPT:PSP's accepted articles and special issues and major events. Launching of virtual issues (grey), Change in Editor in Chief (yellow), Initiation of the Editor in training program (green)

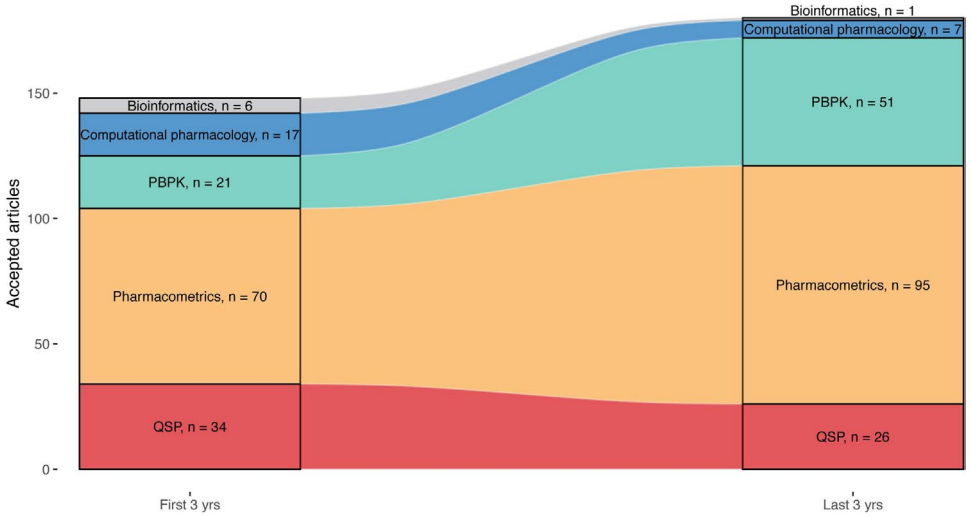

FIGURE 3 Change in article's fields of research in CPT:PSP from the first 3 years (2012–2015) to the last three years (2019–2021)

early career scientists, (ii) interviews with key opinion leaders (KOLs), and (iii) discussions within the journal's editorial team reflecting on efforts and advances in the disciplines over the preceding decade as well as emerging trends over the next 10 years.

Integral in shaping PSP's future vision is actively soliciting and synthesizing timely feedback from ASCPT's networks and communities, which constitute PSP's core readership. We surveyed 16 participants representing the membership/leadership within the Quantitative Pharmacology Network (QPN) and Early Career Communities (ECC). As a potential testament to the broad coverage of current research content featured in PSP, it was encouraging that all survey respondents answered favorably (Yes) to the question, "Do you think that current research relating to your community is reflected in PSP publications?". Another point of unanimity related to the importance and value of the Tutorials published in PSP. Further, respondents provided a wealth of topic areas to serve as potential future Tutorials, such as PK-PD concepts and modeling approaches for novel drug modalities (e.g., cell- and gene-based therapies), approaches integrating bioinformatics (*omics*) analyses with QSP modeling, guidelines for QSP model validation/qualification, model-based preclinical to clinical integration of large data sets/streams, and techniques connecting machine learning with pharmacometrics and QSP.

The vital importance of an 'Open' approach to science and access to published data and mathematical models has become well-recognized.[9,10] As an important step in maintaining reproducibility, rigor, and integrity in published pharmacometrics and systems pharmacology models, submission of relevant model code to supplement Original Research articles is required for publication in CPT:PSP. It was interesting to find that early career respondents placed greater value on the importance of code sharing and data; all early career participants supported this practice, whereas 30% (3/10) mid-to-late career respondents indicated 'Providing model code' as a potential discouraging factor for submitting to the journal. Despite this, we do not intend to change our stand-point and will continue the drive towards Open Source.

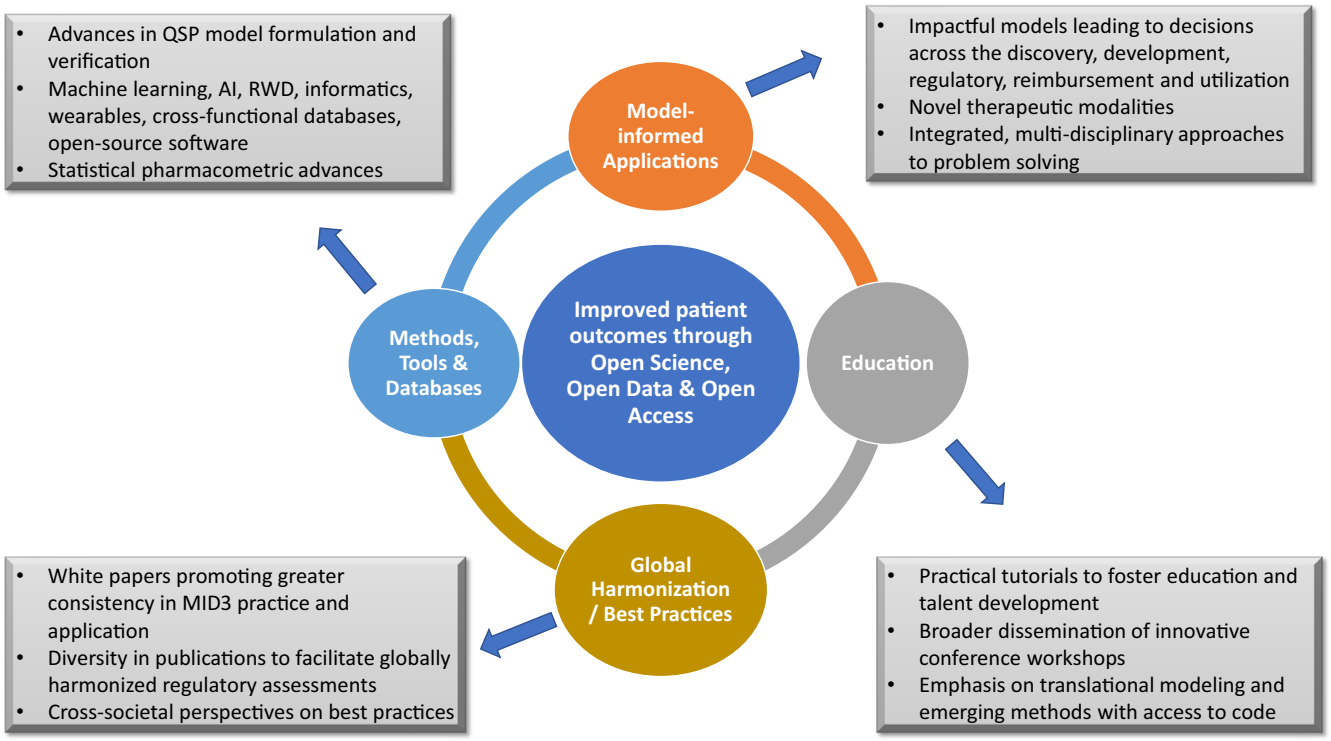

FIGURE 4 Pharmacometrics and Systems Pharmacology Journal Vision. CPT: Pharmacometrics and Systems Pharmacology (CPT:PSP) welcomes contributions in Pharmacometrics and Systems Pharmacology and research bridging across related quantitative disciplines with the overall objective of improving global health on a foundation of open science, open data and open access. The journal aims to be a holistic source for impactful model-informed applications, educational endeavors, harmonization/best practices and new methods and tools. QSP, Quantitative Systems Pharmacology; MID3, model-informed drug discovery and development; AI, artificial intelligence; RWD, real world data

As MIDD approaches become routine in pharma R&D and regulatory decision making, manuscripts submitted from product developers account for a significant percentage of submissions. To accommodate the shift of the focus from scientific innovation to impact on development and regulatory decision making, as well as to facilitate rapid and timely dissemination of original work in a condensed matter (impactful examples of model-informed applications), we also asked the communities about a new potential article category for the journal: original research presented as short case reports of MIDD applications. All respondents showed appreciable interest with 50% 'Extremely interested', 30% Very interested, and 20% 'Somewhat interested'. The editorial team is assessing the concept, content, and format of this article type, with details forthcoming.

Discussions with KOLs surfaced several insights and opportunities. The future challenge across our fields is "integration". Integration of PMX, PBPK and QSP with big data and ML, but also integration with other fields and knowledge, e.g. pharmacogenetics, clinical laboratory data, health data, economics, pharmacoepidemiology, toxicology, biopharmaceutics and statistics. PSP can help with this integration through (i) special themed issues that bring multiple disciplines together (e.g. as highlighted in the special themed issue Statistics and Pharmacometrics), (ii) providing access to data and models for re-usability, adaptability, and applicability (a unique feature of the journal), (iii) highlighting the application of the science and its impact at point-of care or in MIDD and (iv) fostering the next generation of talent with tutorials on "how-to" and best practices, (v) placing greater emphasis on examples that integrate PBPK with QSP, MBMA with QSP, QSP with PMX, pharmacoeconomics with PMX and other collaborations. PSP also plans to update the current journal scope to clarify that it welcomes translational and preclinical modeling submissions, understanding fully that earlier integration of quantitative tools are needed in drug discovery and early development. While big data and AI/ML are the "buzz" words, and these approaches are well positioned to rapidly increase with time, the integration of the core areas is still largely lacking and needs fostering. Increase of data is inevitable; however the quality of data of well-designed trials currently still outweighs big noisy 'real world' data. Agreement on a recognized standard of data entry and collection is needed e.g. electronic health records could be an initial step forward to improve the quality of big data. AI and ML together with big data may be useful in identifying early signals or help sort and search the large amount of knowledge using Natural Language Processing.

Further challenges and opportunities for the future of our science are:

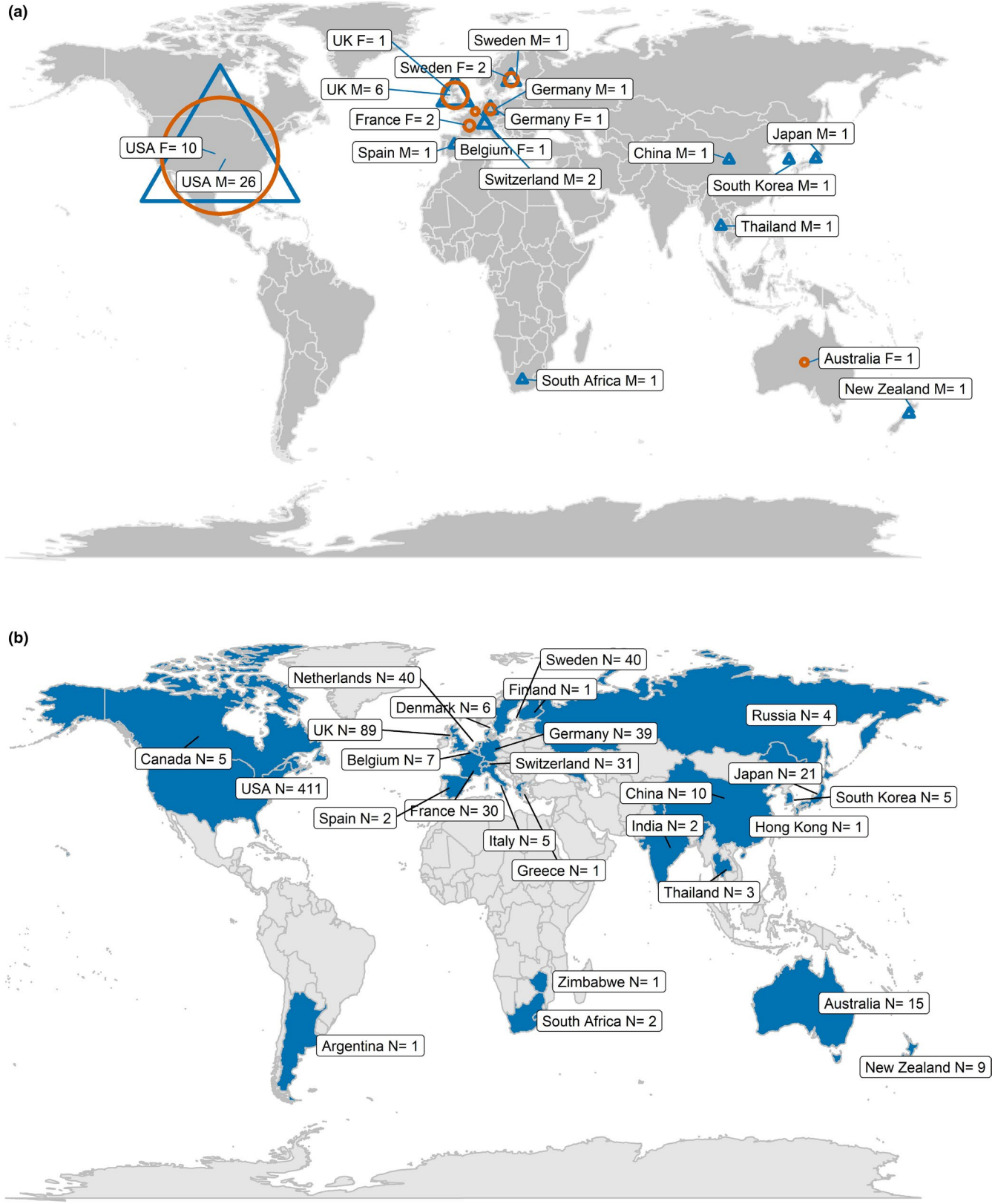

FIGURE 5 Country location of the (a) Members of the Editorial Leadership team, including Editor in Chief, Associate Editors, Editorial Board and Scientific Advisory Board in 2021 and (b) corresponding authors of all articles published in CPT:PSP. (a) M = number of Males; F = number of Females; colors represent the sex of the members, blue representing males; size of the symboles represent the total number of members per country). (b) N = number of articles with corresponding authors from that country; note that Hong Kong, illustrated separately, is a Special Administrative Region of the People's Republic of China; proportions of articles published by continent: North and South America: 53.4%, Europe: 37.3%, Asia: 5.9%, Oceania: 3.1%, Africa: 0.3%

- to increase the credibility of models, as larger models and more data are not necessarily better,
- to increase utilization of PMX at the point of care by increasing strong evidence from outcome-based research and embrace model-based precision dosing paradigms,
- to increase data sharing, development and use of open-source software, establish further technology standards, and
- to integrate quantitative methods and training in undergraduate curriculums.

Another common vision among KOLs was to increase and improve communication within and outside our community, to find and establish a common ground with e.g. statisticians. The general population is more aware of modelling and quantitative sciences now; as opportunities increase for more mainstream outreach, development of talented scientists with a quantitative mindset and opportunities for pharmacometricians to take on leadership roles outside the "core" area will enable MIDD to be more impactful.

Additional themes pertinent to the journal's future vision emerged from discussions within the editorial team, reflecting upon experiences gained from manuscripts submitted to PSP, individual research interests, and the recently published strategic vision, 'Pharmacometrics and Systems Pharmacology 2030'.[11]

Foremost was the paramount importance of Open Science, Open Data and Open Access to ensure re-usability, reproducibility, integrity and adaptability of models, tools and databases. This was considered the foundation upon which the journal could articulate a clear vision. Built on this core identity and the benefits to authors in being Gold Open Access, PSP will continue working towards being the first choice for articles on best practices, standards and how-to (tutorials, white papers) and be a preferred forum for discussions and community interactions (perspectives). Equally important is the continued emphasis on showcasing impactful examples (original research articles, case reports) of successful application of PMX/PKPD/PBPK/QSP to support decision-making, including novel therapeutic modalities (e.g. CAR-T, AAV, siRNA). Here, the team sought to clarify that impactful examples do not automatically imply complex or novel modeling methods. A well-performed population pharmacokinetic analysis of a novel therapeutic leading to impactful decisions was seen as valuable to the community.

Future areas of high potential that the team considered relatively untapped included the application of pharmacometric models for pivotal/registrational clinical outcome data, model-based probabilities of success to inform design and go/no-go decisions at all stages of drug development, machine learning and analyses of health databases and/or other unstructured data sources (e.g. wearables), pharmacometric/pharmacoeconomic models that address important gaps in clinical evidence to inform reimbursement decisions and precision dosing at the bedside. Based on the very positive feedback on the themed issue of Statistics and Pharmacometrics, the editorial team is planning several new themed issues and welcomes suggestions from readers.

The editorial team agrees with feedback from several KOLs that original research showcasing end-to-end model applications[12] and/or integrated modeling approaches (QSP + PMX) will be well received by the community. Hypothesis-generating QSP models with demonstrated utility (e.g. inform target/molecule selection/optimization) are also highly encouraged. The continued expansion of PBPK-based applications, particularly to support decisions for special/rare populations and untestable clinical scenarios, will remain a core component of PSP's future.

Finally, the past decade has witnessed increasing gender and geographic diversity in contributions from the community (Figure 5b). This is also reflected in the composition of the editorial team (Figure 5a), with colleagues having a wide range of research interests, viewpoints, backgrounds and experiences. The journal will continue to strongly encourage diversity in the leadership team, authorship and subject matter in publications, including an increased emphasis on research contributions from authors located in low and middle-income (LMI) countries. In support of this, PSP's publisher, Wiley offers fee waivers and discounts to corresponding authors based in LMI countries.[13]

CONCLUDING REMARKS

PSP aspires to be the premier journal for pharmacometrics and systems pharmacology by having the right balance of articles that showcase impactful model-informed applications, promote educational endeavors, facilitate global harmonization and best practices, and advance new methodologies and tools. Encouraged by feedback from the community in terms of progress achieved since its inception in 2012, as well as opportunities for the future, PSP is well-positioned to keep pace with science and innovation, serve the global community of pharmacometricians and systems pharmacologists and continue to be a bridge to support emerging quantitative disciplines. The editorial team is committed to continuous improvement and welcomes feedback from the community across all aspects of the journal.

ACKNOWLEDGEMENTS

The authors acknowledge the following leaders for graciously sharing their perspectives in support of this editorial: David D'Argenio, Paolo Denti, Jin Yan Jin, Kristin Karlsson, Mats Karlsson, Ron Keizer, Richard Lalonde, Peter Milligan, Joseph Standing, Piet van der Graaf and Sandra Visser.

Karen Rowland Yeo[1]*
Stefanie Hennig[2]*
Sriram Krishnaswami[3]*
Natasha Strydom[4]†

Vivaswath S. Ayyar[5]†
Jonathan French[6]
Vikram Sinha[7]
Eric Sobie[8]
Ping Zhao[9]
Lena E. Friberg[10]‡
France Mentré[11]‡

[1]*Certara UK Ltd (Simcyp Division), Sheffield, UK*
[2]*Certara, Inc, Princeton, NJ, USA*
[3]*Pfizer, Groton, CT, USA*
[4]*Department of Bioengineering and Therapeutic Sciences, School of Pharmacy, University of California, San Francisco, CA, USA*
[5]*Janssen Research & Development, LLC, Spring House, PA, USA*
[6]*Metrum Research Group, Tariffville, CT, USA*
[7]*Takeda, Cambridge, MA, USA*
[8]*Department of Pharmacological Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA*
[9]*Bill & Melinda Gates Foundation, Seattle, WA, USA*
[10]*Department of Pharmacy, Uppsala University, Uppsala, Sweden*
[11]*IAME, INSERM, Université de Paris, Paris, France*

Correspondence
France Mentré, Université de Paris, IAME, INSERM, F-75018 Paris, France.
Email: france.mentre@inserm.fr

*Co first authors.
†Co second authors.
‡Co last authors.

ORCID

Stefanie Hennig https://orcid.org/0000-0001-5972-3711
Natasha Strydom https://orcid.org/0000-0002-0929-0783
Jonathan French https://orcid.org/0000-0001-9649-169X
Lena E. Friberg https://orcid.org/0000-0002-2979-679X
France Mentré https://orcid.org/0000-0002-7045-1275

REFERENCES

1. van der Graaf PH. Pharmacometrics and/or Systems Pharmacology. *CPT Pharmacometrics Syst Pharmacol*. 2019;8:331-332.
2. Keizer RJ, Karlsson MO, Hooker A. Modeling and simulation workbench for NONMEM: Tutorial on Pirana, PsN, and Xpose. *CPT Pharmacometrics Syst Pharmacol*. 2013;2:e50.
3. Ryman JT, Meibohm B. Pharmacokinetics of monoclonal antibodies. *CPT Pharmacometrics Syst Pharmacol*. 2017;6:576-588.
4. Shukla P, Goswami S, Keizer RJ, et al. Assessment of a model-informed precision dosing platform use in routine clinical care for personalized Busulfan therapy in the pediatric hematopoietic cell transplantation (HCT) population. *Front Pharmacol*. 2020;11.
5. Mizuno T, Dong M, Taylor ZL, Ramsey LB, Vinks AA. Clinical implementation of pharmacogenetics and model-informed precision dosing to improve patient care. *Br J Clin Pharmacol*. 2020:1-9. https://doi.org/10.1111/bcp.14426
6. Zineh I. Quantitative systems pharmacology: a regulatory perspective on translation. *CPT Pharmacometrics Syst Pharmacol*. 2019;8:336-339.
7. Bai JPF, et al. FDA-Industry Scientific Exchange on assessing quantitative systems pharmacology models in clinical drug development: a meeting report, summary of challenges/gaps, and future perspective. *AAPS J*. 2021;23:60.
8. https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/model-informed-drug-development-approaches-immunogenicity-assessments-06092021-06092021
9. Kirouac DC, Cicali B, Schmidt S. Reproducibility of quantitative systems pharmacology models: current challenges and future opportunities. *CPT Pharmacometrics Syst Pharmacol*. 2019;8:205-210.
10. Cucurull-Sanchez L, Chappell MJ, Chelliah V, et al. Best practices to maximize the use and reuse of quantitative and systems pharmacology models: recommendations from the United Kingdom quantitative and systems pharmacology network. *CPT Pharmacometrics Syst Pharmacol*. 2019;8:259-272.
11. Mentré F, Friberg LE, Duffull S, et al. Pharmacometrics and systems pharmacology 2030. *Clin Pharmacol Ther*. 2020;107:76-78.
12. Fediuk DJ, Nucci G, Dawra VK, et al. End-to-end application of model-informed drug development for ertugliflozin, a novel sodium-glucose cotransporter 2 inhibitor. *CPT Pharmacometrics Syst Pharmacol*. 2021;10:529-542.
13. https://authorservices.wiley.com/open-research/open-access/for-authors/waivers-and-discounts.html