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MICHIEL J. BAKKUM
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ONLINE COLLABORATION IN PHARMACOTHERAPY EDUCATION

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ISBN: 978-94-93278-89-9

DOI: https://doi.org/10.5463/thesis.1098

Layout and printing: Off Page, Amsterdam
Cover design: Nick Kailola

Financial support for the publication of this thesis was provided by: Research and Expertise Centre in Pharmacotherapy Education (RECIPE) and Stichting SBOH.

VRIJE UNIVERSITEIT

ONLINE COLLABORATION IN PHARMACOTHERAPY EDUCATION

ACADEMISCH PROEFSCHRIFT
ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. J.J.G. Geurts,
volgens besluit van de decaan
van de Faculteit der Geneeskunde
in het openbaar te verdedigen
op woensdag 14 mei 2025 om 11.45 uur
in de universiteit

door
Michiel Janniek Bakkum
geboren te Amsterdam

promotor:	prof.dr. M.A. van Agtmael
copromotoren:	dr. J. Tichelaar dr. M.C. Richir
promotiecommissie:	prof.dr. Y. Böttiger prof.dr. M. Okorie prof.dr. O. Horvat dr. E. Van Leeuwen prof.dr. R.A. Kusurkar dr. J.H. Bretschneider

Voor Marcella, Flip en mijn ouders

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GENERAL INTRODUCTION

1

THE PROBLEM

Doctors take the Hippocratic oath to prevent intentional harm and to mitigate the chances of unintended harm. Despite this, iatrogenic harm is the 14th primary contributor to morbidity and mortality globally, affecting 1 in 10 patients in high-income nations[1].

A significant portion of this harm stems from the adverse effects of medicines. The Hospital Admission Related to Medication (HARM) report from 2006 revealed that medication was implicated in 5.6% of acute hospital admissions in the Netherlands, amounting to 41,000 yearly hospitalizations[2,3]. Despite concerted efforts and interventions, such as HARM-Wrestling[4], to reduce these figures, the Vervolgonderzoek Medicatieveiligheid (VM) study found that the prevalence of medication-related hospital admissions was relatively stable between 2008 and 2013[5]. Specifically, the report revealed that 10.2% of acute hospital admissions among individuals aged 65 years and older were attributable to medication. While these data originate mainly from the Netherlands, they are remarkably consistent at an international level[6].

Not all of these hospital admissions, or the resulting adverse effects, can be prevented. If adverse effects arise despite diligent assessment of risks and benefits, along with precautionary measures and the absence of errors, then they are classified as unavoidable. Adverse effects that could potentially be avoided typically stem from errors in prescribing (such as dosing errors, inappropriate indications, drug interactions, etc.), dispensing (including patient mix-ups, incorrect deliveries, etc.), and administration (ranging from omissions to calculation mistakes). These errors are commonly attributed to the prescriber, pharmacy, and nurse or carer, respectively. Collectively, they account for 46% of the aforementioned hospital admissions (equivalent to 19,000 admissions and €85 million in medical expenses annually in the Netherlands) according to the HARM report[7].

Prescribing errors are responsible for the overwhelming majority of avoidable hospital admissions, accounting for 74.1% in the HARM study[3] and 96.75% in the VM study[5]. These errors stem from a variety of factors, such as high workloads punctuated by frequent interruptions, inadequate communication, insufficient supervision, unfamiliarity with or limited access to protocols, and deficits in knowledge and training[8]. A comprehensive systematic review that included 65 studies revealed that prescribing errors are present in a median of 7% of prescriptions, affecting a median of 50% of all hospital admissions[9].

The responsibility for prescribing errors primarily falls on junior doctors. This phenomenon can be attributed to two key factors. Firstly, because of their role as ward doctors, junior doctors tend to issue medication orders up to 14 times more often than their senior colleagues. At the same time, the chance of them making an error is also higher. In the UK EQUIP study, foundation year 1 and 2 doctors had error rates of 8.4% and 10.4%, respectively, compared with 5.9% among consultants[10]. Subsequent interviews with participants revealed that their errors were often triggered by work-related situations, such as busy rounds or difficulty in approaching supervisors, as well as a deficiency in knowledge and experience[11]. This pattern is consistent with findings from an international review study[12].

These findings, which suggest a potential role for (undergraduate) pharmacotherapy education in preventing prescribing errors, precipitated a comprehensive European analysis of pharmacotherapy education. In his 2018 doctoral thesis, David Brinkman reported on how undergraduate medical education across Europe leaves medical students inadequately prepared, both subjectively and objectively, for the safe prescribing of medicines[13,14]. Through a standardized assessment, 895 final-year medical students from 17 institutions across 15 EU nations (including the UK at the time) were asked to make a (pharmaco)therapeutic plan for five distinct case scenarios. Alarmingly, nearly half of their proposed therapies (46.2%) were deemed inappropriate, and some were even harmful (15.2%) or potentially fatal (3.7%) for the patient. Moreover, the results of this skills examination correlated poorly with the results of a knowledge test. Interestingly, students from medical schools with a problem-based curriculum (defined in the subsequent section) outperformed their counterparts from medical schools with a conventional curriculum. In a subsequent study, Brinkman further demonstrated the considerable heterogeneity in pharmacotherapy curricula across Europe, particularly in terms of the number of contact hours (median of 68 hours, interquartile range of 35–100)[15]. Additionally, most pharmacotherapy courses adhered predominantly to traditional teaching methodologies. In the light of these findings, Brinkman concluded that there is an urgent need to improve and standardize pharmacotherapy education throughout Europe. In collaboration with the European Association for Clinical Pharmacology and Therapeutics' Education Working Group, he formulated 11 recommendations to facilitate the achievement of this objective (table 1).

The primary goal of the studies described in this thesis is to foster the widespread adoption of these recommendations, by utilizing the power of the internet and open education. Particular attention is given to recommendation #6, which centres on harnessing online learning resources and distributing them at a national and international level.

NETWORK OF TEACHERS IN PHARMACOTHERAPY (NOTIP)

Central to our endeavours to harmonize and improve European education in clinical pharmacology and therapeutics is the presence of the network of teachers in pharmacotherapy education. This network, established for research purposes through collaboration between the European Association for Clinical Pharmacology and Therapeutics and local national associations (as detailed by Brinkman[15]), has served as the principal pool of participants for the majority of the studies described in this thesis. Furthermore, this network was important for disseminating our initiatives.

Table 1. Recommendations of the European Association for Clinical Pharmacology and Therapeutics Education Working Group to improve and harmonize pharmacotherapy education

1	Clinical pharmacology and therapeutics should be a clear and visible programme throughout the entire medical curriculum, starting as early as possible, and should be emphasized in all clinical modules and attachments.
2	Prescribing should be trained in simulated and clinical environments, with emphasis on completing drug prescriptions, reviewing medication charts, and real responsibility for patient care.
3	Schools should formulate clear and specific learning objectives, preferably using a detailed list of core drugs ('student formulary') and diseases that students should be familiar with before graduation.
4	Schools should ensure that learning objectives are compatible with the learning environment and assessment activities.
5	The WHO 'Guide to Good Prescribing' should be used more intensively in order to teach and train rational prescribing.
6	Medical schools should utilize more online learning resources and preferably share these at national or international level.
7	Medical/pharmacy students and junior doctors should be engaged in 'near peer' education, supervised and trained by clinical pharmacologists and senior clinicians.
8	Clinical pharmacists and nurse prescribers should be given a greater role in the development and delivery of clinical pharmacology and therapeutics education.
9	Medical schools should implement a robust and separate clinical pharmacology and therapeutics assessment structure throughout the curriculum, with no compensatory mechanism (i.e. the possibility to get a sufficient score based on other subjects).
10	Medical schools should implement a valid and reliable final prescribing assessment at or near the end of the medical curriculum to assess whether graduates are able to prescribe safely and effectively.
11	Prescribing should be assessed in a simulated or clinical context, with emphasis on writing prescriptions, verifying the suitability of the treatment choice, giving information to patients, and drug monitoring.

These recommendations were previously published by Brinkman et al. (CC BY-NC-ND 4.0)[15]

PEDAGOGICAL THEORIES

Traditionally, the pharmacology education given in medical schools has primarily centred on the drugs used. Students typically delve into fundamental aspects, ranging from molecular and cellular basics to clinical aspects such as indications, pharmacokinetics and dynamics, side effects, and drug interactions. This pedagogical approach commonly makes use of textbooks and lectures and is known as traditional teaching. In stark contrast, in real-world clinical settings, prescribing health care professionals use a patient-centric methodology when deciding on suitable medications for individual patients. In 1994 the World Health Organization's (WHO) Guide to Good Prescribing introduced a structured six-step framework that fosters rational, patient-centred prescribing practices (figure 1)[16]. This process involves the intricate task of balancing clinical pharmacological insights with the distinctive needs of each patient, all within the context of shared decision-making.

This nuanced competency flourishes in an experiential learning – learning through doing – setting. According to the principles of experiential learning theory, learning is most effective when a student is given tangible, relevant hands-on activities. This process is complemented by reflection and integration of the experience with pre-existing knowledge. Students then apply their newly acquired insights, solidifying their understanding[17].

Experiential learning remains a cornerstone of medical education. Nonetheless, during internships, the focus is often more on diagnostics than therapeutics[18]. Hence, students have limited opportunities to participate in authentic prescribing scenarios, so that they often mimic their teachers rather than think for themselves[19]. In recognition of this limitation, students are often given medical case scenarios to supplement their real-life experience, thereby generating an inclusive and comprehensive educational approach. This is the essence of problem-based learning, which can be considered a form of experiential learning[20]. In problem-based learning, teachers shift from being authoritative "Sages on the Stage" to adopting the role of supportive "Guides on the Side". They guide

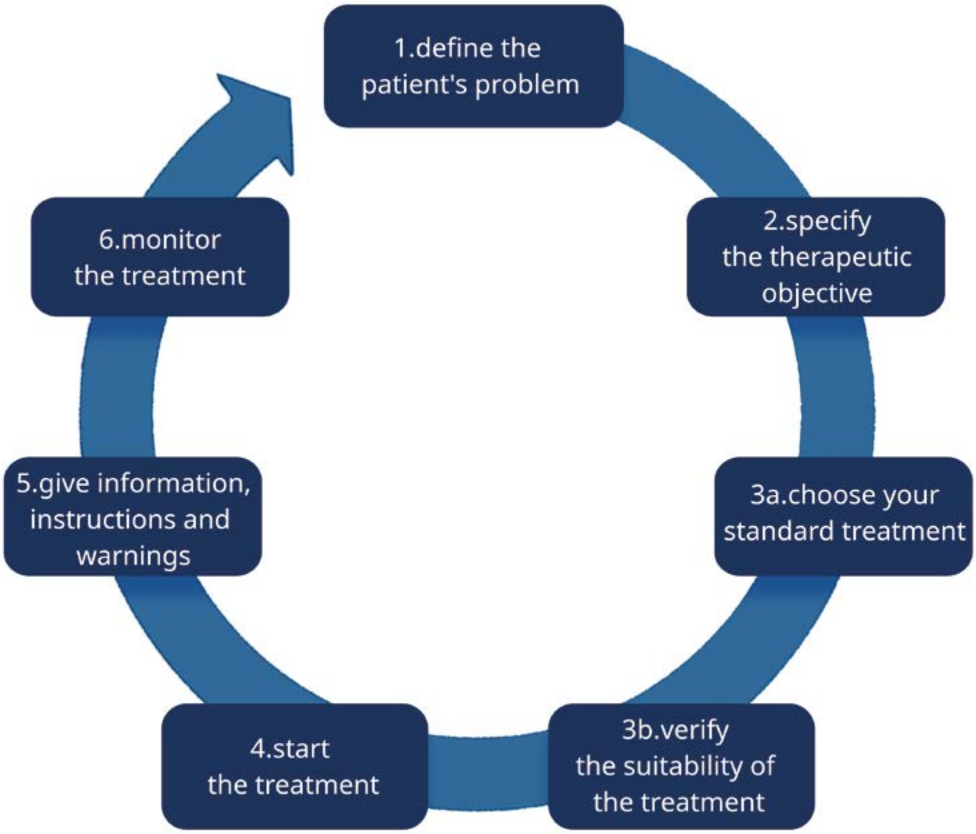


Figure 1. World Health Organization Guide to Good Prescribing six step method

small groups of students, preferably with diverse perspectives, in collaboratively solving problems through discussion and the exchange of information. This approach should not be confused with Team-Based Learning, which is a term reserved for a specific instructional strategy whereby teams work independently and the teacher assumes a more traditional role [20]. However, some elements of Team-Based Learning, such as a readiness assurance test, may also be incorporated into problem-based teaching lessons. In addition to the Guide to Good Prescribing, the Teacher's Guide to Good Prescribing was introduced in 2001[21]. This supplementary resource outlines how cases can be tailored to introduce differences in patient age, medical history, and other factors, thereby adjusting the complexity of the case history. While the guide encourages the development of cases based on drugs for which students already have treatment scripts (or "p-drugs"), subsequent research showed that teaching using the six-step methodology resulted in a transfer effect when addressing new clinical problems[22]. Supplemented by WHO-organized training courses for teachers, the guides have significantly facilitated the widespread adoption of problem-based teaching within the global clinical pharmacology and therapeutics education community. However, there is still room for broader implementation, as elaborated above. Closely tied to problem-based learning is the concept of context-based learning, which aims to reproduce problems that students may encounter as authentically and realistically as feasible[23-25]. This approach improves the relevance of the scenarios, effectively boosting student motivation. An important way to increase realism is through interprofessional education, whereby students from various health disciplines collaborate in problem-based learning settings (or, even better, real-life clinical situations)[26]. This collaborative approach allows students to glean insights into each other's discipline-related perspective, an insight which will prove valuable for future collaborative endeavours[27-29]. In prescribing education, interprofessional education often involves collaborative learning among medical, pharmacy, and/or nursing students.

The essence of these learning theories can largely be understood in the context of the self-determination theory, which poses that individuals possess three fundamental psychological needs that, when fulfilled, contribute to their optimal development and functioning[30]. These essential needs encompass autonomy, competence, and relatedness[31]. *Autonomy* entails the requirement for individuals to exercise control over their actions and decisions, a crucial element intrinsic to problem-based learning. In this framework, students are granted considerable freedom in how they approach problem-solving, thereby fostering a sense of autonomy. *Competence* pertains to the necessity of feeling proficient in performing tasks, another important facet of problem-based teaching. By adjusting problems to a student's level of competence, this approach nurtures a sense of capability. Furthermore, context-based learning presents familiar clinical issues that students may have previously mastered or will likely face in the future, which increases their sense of responsibility. Lastly, the concept of *relatedness* encompasses the need for social connections and is manifested in the team dynamics inherent to problem-based learning and interprofessional education. These collaborative assignments provide nurture the essential social connections that support the fulfilment of this need .

ONLINE AND OPEN EDUCATION

Today, a significant proportion of clinical pharmacology and therapeutics education is delivered via the internet. Educational materials range from relatively straightforward e-learning modules to podcast series, educational videos, and highly interactive serious games. Prior to the COVID-19 pandemic, online education was primarily confined to self-study. However, the disruptions caused by the pandemic have forced us to conduct virtually all aspects of education to online. While many of us have experienced the drawbacks of Zoom lectures and similar platforms, it is undeniable that they also offer tangible advantages. In fact, our experiences during the pandemic have brought about lasting changes in the way we approach teaching at Pharmacotherapy section of Amsterdam UMC.

In pursuit of the objective to improve and standardize European clinical pharmacology and therapeutics education, the most promising aspects of online education lie in its capacity to reach a vast number of students, including those geographically distant, and the potential to widely disseminate educational materials that are adaptable to diverse educational systems, after a single investment of time and resources. Regrettably, at present, these capabilities remain significantly underutilized.

Open Education is a movement with the overarching objective of dismantling the barriers that stand in the way of formal education and of making knowledge accessible to all,[32] thereby improving societal participation and inclusivity. This movement is closely aligned with the Open Science movement, which is best known for its work in facilitating access to scientific research through open access publishing and, more recently, open data sharing. The term "open" encompasses freedom from financial constraints, as well as liberation from other limitations such as copyright, geographical boundaries (as open materials are typically available online), and admission requirements. The removal of these barriers is believed to not only enhance accessibility but also to raise the standard of education and promote collaboration. By rendering source data transparent, open education and open science initiatives contribute to the verifiability of quality. Moreover, by encouraging others to build on these data, these initiatives improve quality and advance the collective body of knowledge[33].

While some advocate complete openness, the term "open educational resource" typically encompasses materials that do not quite reach the utmost level of openness. For instance, it is common practice to allow the free re-use of educational materials, provided proper credit is given to the original creator, and the material is not used for commercial purposes. Unfortunately, international copyright laws exhibit significant disparities and generally do not offer such nuanced licensing options. In response to this legal complexity and in pursuit of promoting openness, the Creative Commons organization offers an international alternative that creators can use to indicate their willingness to relinquish a portion of their intellectual property rights. [33] These licenses are made up of a combination of four different conditions (Figure 2), resulting in six possible licenses, each representing a different degree of openness[34].

With the exception of chapter 8, which remains under the publisher's copyright, this thesis is available under the open access license CC BY 4.0 for chapters 1, 4, 6, 9, 11 and 12 or CC BY NC 4.0 for chapters 2, 3, 5, 7 and 10.

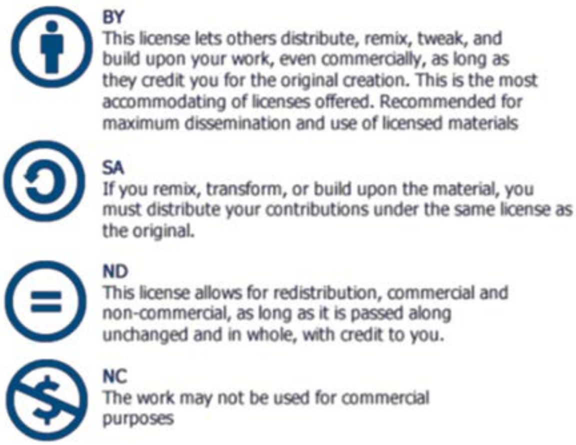


Figure 2. Explanation of the four Conditions of Creative Commons Licenses

AIMS AND OUTLINE OF THIS THESIS

Aim 1: To investigate the current use of digital resources for clinical pharmacology and therapeutics education and to assess their impact.

Chapter 2 Presents a systematic literature review examining the effects of digital educational resources in teaching safe and effective prescribing.

Chapter 3 Explores how European clinical pharmacology and therapeutics teachers incorporate digital education into their curricula, offering an overview and characterization of the available resources.

Aim 2: To facilitate the harmonization and improvement of European clinical pharmacology and therapeutics education by fostering collaboration and resource sharing among teachers.

Chapter 4 Explores the attitudes of European clinical pharmacology and therapeutics teachers towards sharing digital resources, and translates the barriers and benefits of sharing into a framework for the European Open Platform for Prescribing Education.

Chapter 5 Investigates the specific content preferences of European Open Platform for Prescribing Education platform users.

Aim 3: To provide innovative and evidence-based open educational resources for clinical pharmacology and therapeutics education.

Chapter 6 Examines the feasibility and value of a novel approach whereby students create their own educational escape room for prescribing education.

Chapter 7 Offers a guide for clinical pharmacology and therapeutics teachers on teaching race-based medical guidelines and improving the inclusivity and diversity of case vignettes.

Chapter 8 Advocates the inclusion of the planetary health impact of medicines in teaching and calls for collaborative efforts to create open educational resources on this topic for availability on the European Open Platform for Prescribing Education.

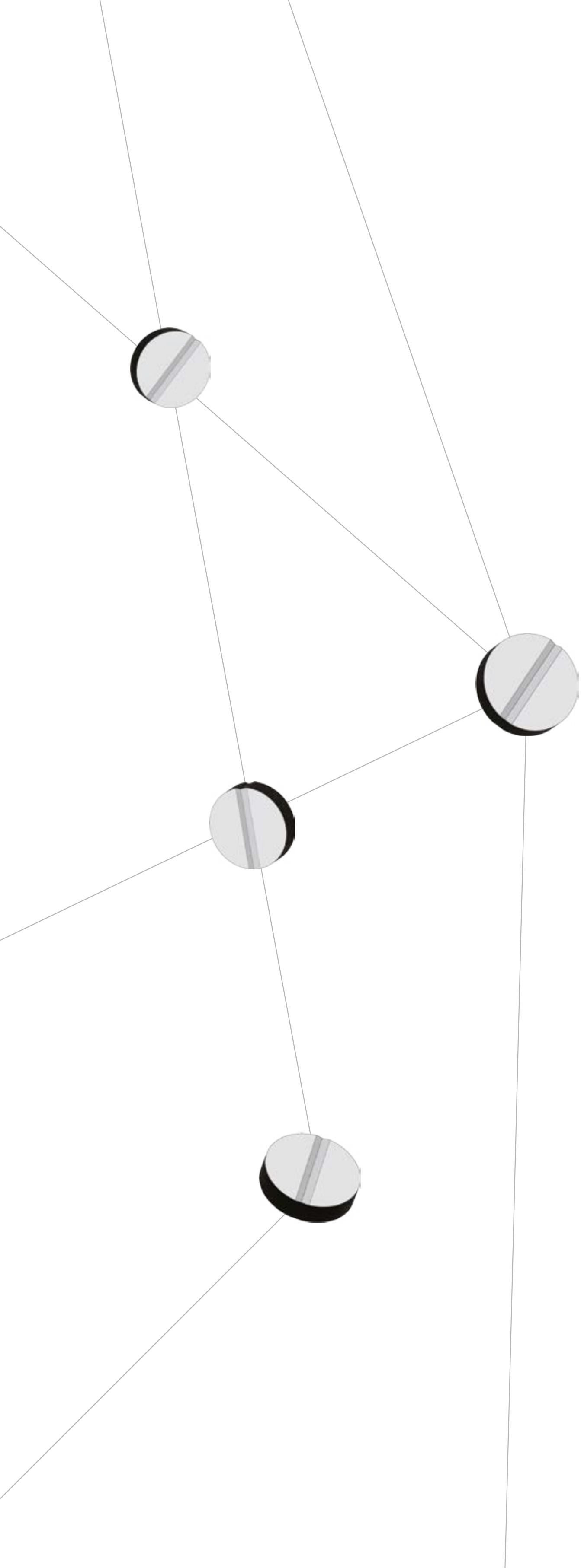
Chapter 9 Demonstrates the feasibility of international students learning from differences in prescribing practices in different countries through online teleconferencing.

Chapter 10 Shows how artificial intelligence chatbots can be used to create diverse and inclusive clinical case vignettes.

REFERENCES

1. World Health Organization. Patient Safety. Accessed January 2, 2023, 2023. https://www.who.int/news-room/facts-in-pictures/detail/patient-safety
2. Division of Pharmacoepidemiology & Pharmacotherapy Utrecht Institute for Pharmaceutical Sciences. *Hospital Admissions Related To Medication (HARM) Een prospectief , multicenter onderzoek naar geneesmiddel gerelateerde ziekenhuisopname*. 2006. https://www.udpmed.com/wp-content/uploads/2018/02/Hospital-admissions.pdf
3. Leendertse AJ, Egberts ACG, Stoker LJ, van den Bemt PMLA, Group HS. Frequency of and Risk Factors for Preventable Medication-Related Hospital Admissions in the Netherlands. *Archives of Internal Medicine*. 2008;168(17):1890-1896. doi:10.1001/archinternmed.2008.3
4. Ministerie van Volksgezondheid, Welzijn en Sport,. HARM-WRESTLING Een voorstel van de Expertgroep Medicatieveiligheid m.b.t. concrete interventies die de extramurale medicatieveiligheid op korte termijn kunnen verbeteren. 2009;
5. van den Bemt P, de Smet P, Hek K, Sturkenboom M. Eindrapport: Vervolgonderzoek Medicatieveiligheid. *Erasmus MC, NIVEL, Radboud UMC and PHARMO*. 2017;
6. Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. *Pharm World Sci*. Apr 2002;24(2):46-54. doi:10.1023/a:1015570104121
7. Leendertse AJ, Van Den Bemt PM, Poolman JB, Stoker LJ, Egberts AC, Postma MJ. Preventable hospital admissions related to medication (HARM): cost analysis of the HARM study. *Value Health*. Jan 2011;14(1):34-40. doi:10.1016/j.jval.2010.10.024
8. Dean B, Schachter M, Vincent C, Barber N. Causes of prescribing errors in hospital inpatients: a prospective study. *Lancet*. Apr 20 2002;359(9315):1373-8. doi:10.1016/s0140-6736(02)08350-2
9. Lewis PJ, Dornan T, Taylor D, Tully MP, Wass V, Ashcroft DM. Prevalence, incidence and nature of prescribing errors in hospital inpatients: a systematic review. *Drug Saf*. 2009;32(5):379-89. doi:10.2165/00002018-200932050-00002
10. Ashcroft DM, Lewis PJ, Tully MP, et al. Prevalence, Nature, Severity and Risk Factors for Prescribing Errors in Hospital Inpatients: Prospective Study in 20 UK Hospitals. *Drug Saf*. Sep 2015;38(9):833-43. doi:10.1007/s40264-015-0320-x
11. Lewis PJ, Ashcroft DM, Dornan T, Taylor D, Wass V, Tully MP. Exploring the causes of junior doctors' prescribing mistakes: a qualitative study. *Br J Clin Pharmacol*. Aug 2014;78(2):310-9. doi:10.1111/bcp.12332
12. Tully MP, Ashcroft DM, Dornan T, Lewis PJ, Taylor D, Wass V. The Causes of and Factors Associated with Prescribing Errors in Hospital Inpatients. *Drug Safety*. 2009/10/01 2009;32(10):819-836. doi:10.2165/11316560-000000000-00000
13. Brinkman DJ, Tichelaar J, Schutte T, et al. Essential Competencies in Prescribing: A First European Cross-Sectional Study Among 895 Final-Year Medical Students. *Clinical Pharmacology & Therapeutics*. Feb 2017;101(2):281-289. doi:10.1002/cpt.521
14. Brinkman DJ, Tichelaar J, Graaf S, Otten RHJ, Richir MC, van Agtmael MA. Do final-year medical students have sufficient prescribing competencies? A systematic literature review. *British Journal of Clinical Pharmacology*. Apr 2018;84(4):615-635. doi:10.1111/bcp.13491
15. Brinkman DJ, Tichelaar J, Okorie M, et al. Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries. *Clinical Pharmacology & Therapeutics*. Nov 2017;102(5):815-822. doi:10.1002/cpt.682
16. De Vries T, Henning RH, Hogerzeil HV, Fresle D, Policy M, World Health Organization. *Guide to good prescribing: a practical manual*. 1994.

17. Yardley S, Teunissen PW, Dornan T. Experiential learning: AMEE Guide No. 63. *Med Teach*. 2012;34(2):e102-15. doi:10.3109/0142159x.2012.650741
18. Celebi N, Kirchhoff K, Lammerding-Köppel M, Riessen R, Weyrich P. Medical clerkships do not reduce common prescription errors among medical students. *Naunyn Schmiedebergs Arch Pharmacol*. Aug 2010;382(2):171-6. doi:10.1007/s00210-010-0530-9
19. Tichelaar J, Richir MC, Avis HJ, Scholten HJ, Antonini NF, De Vries TP. Do medical students copy the drug treatment choices of their teachers or do they think for themselves? *Eur J Clin Pharmacol*. Apr 2010;66(4):407-12. doi:10.1007/s00228-009-0743-3
20. Davis MH. AMEE Medical Education Guide No. 15: Problem-based learning: a practical guide. *Med Teach*. 1999;21(2):130-40. doi:10.1080/01421599979743
21. World Health Organization. *Teacher's guide to good prescribing Hans V. Hogerzeil (editor)... [et al.]*. 2001.
22. Richir MC, Tichelaar J, Stanm F, Thijs A, Danner SA, Schneider AJ, de Vries TP. A context-learning pharmacotherapy program for preclinical medical students leads to more rational drug prescribing during their clinical clerkship in internal medicine. *Clin Pharmacol Ther*. Oct 2008;84(4):513-6. doi:10.1038/clpt.2008.82
23. Schutte T, Tichelaar J, Dekker RS, et al. Motivation and competence of participants in a learner-centered student-run clinic: an exploratory pilot study. *BMC Med Educ*. Jan 25 2017;17(1):23. doi:10.1186/s12909-017-0856-9
24. Schutte T, Tichelaar J, Dekker RS, van Agtmael MA, de Vries TP, Richir MC. Learning in student-run clinics: a systematic review. *Med Educ*. Mar 2015;49(3):249-63. doi:10.1111/medu.12625
25. Schutte T, Tichelaar J, Donker E, Richir MC, Westerman M, van Agtmael MA. Clarifying learning experiences in student-run clinics: a qualitative study. *BMC Med Educ*. Oct 26 2018;18(1):244. doi:10.1186/s12909-018-1352-6
26. Hammick M, Olckers L, Campion-Smith C. Learning in interprofessional teams: AMEE Guide no 38. *Med Teach*. Jan 2009;31(1):1-12. doi:10.1080/01421590802585561
27. Reumerman MO, Richir MC, Domela Nieuwenhuis PM, et al. The clinical and educational outcomes of an inter-professional student-led medication review team, a pilot study. *Eur J Clin Pharmacol*. Jan 2021;77(1):117-123. doi:10.1007/s00228-020-02972-3
28. Reumerman MO, Richir MC, Sultan R, et al. An inter-professional student-run medication review programme. Reducing adverse drug reactions in a memory outpatient clinic: a controlled clinical trial. *Expert Opin Drug Saf*. Dec 2022;21(12):1511-1520. doi:10.1080/14740338.2022.2069748
29. Sultan R, van den Beukel TO, Reumerman MO, et al. An Interprofessional Student-Run Medication Review Program: The Clinical STOPP/START-Based Outcomes of a Controlled Clinical Trial in a Geriatric Outpatient Clinic. *Clin Pharmacol Ther*. Apr 2022;111(4):931-938. doi:10.1002/cpt.2475
30. ten Cate OTJ, Kusurkar RA, Williams GC. How self-determination theory can assist our understanding of the teaching and learning processes in medical education. AMEE Guide No. 59. *Medical Teacher*. 2011/12/01 2011;33(12):961-973. doi:10.3109/0142159X.2011.595435
31. Deci EL, Ryan RM. Self-determination theory. *Handbook of theories of social psychology*. 2012;1(20):416-436.
32. Zawacki-Richter O, Conrad D, Bozkurt A, et al. Elements of Open Education: An Invitation to Future Research. *The International Review of Research in Open and Distributed Learning*. 03/04 2020;21(3):319-334. doi:10.19173/irrodl.v21i3.4659
33. UNESCO. Recommendation on Open Educational Resources (OER). 2020.
34. Creative commons. Creative commons webpage. https://creativecommons.org/



DIGITAL LEARNING TO IMPROVE SAFE AND EFFECTIVE PRESCRIBING: A SYSTEMATIC REVIEW

2

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Clinical Pharmacology & Therapeutics
2019 Dec; 106: 1236-1245.
doi: 10.1002/cpt.1549

ABSTRACT

With the aim to modernize and harmonize prescribing education, the European Association for Clinical Pharmacology and Therapeutics (EACPT) Working Group on education recommended the extensive use and distribution of digital learning resources (DLRs). However, it is unclear whether the complex task of prescribing medicine can be taught digitally. Therefore, the aim of this review was to investigate the effect of diverse DLRs in clinical pharmacology and therapeutics education. Databases PubMed, EMBASE, CINAHL, ERIC, and CENTRAL were systematically searched.

Sixty-five articles were included in the analyses. Direct effects on patients were studied, but not detected, in six articles. Skills and behavior were studied in 11 articles, 8 of which reported positive effects. Knowledge acquisition was investigated in 19 articles, all with positive effects. Qualitative analyses yielded 10 recommendations for the future development of DLRs. Digital learning is effective in teaching knowledge, attitudes, and skills associated with safe and effective prescribing.

INTRODUCTION

There is ample evidence that medical students are insufficiently trained in safe and effective prescribing.[1] A recent European multicenter study showed that only one in four final-year medical students chose the most appropriate therapy in a case-based examination and that roughly half of their prescriptions contained one or more errors.[2] Moreover, recently graduated doctors make more potentially hazardous prescribing errors than consultants[3]. Fortunately, the need for urgent changes in international clinical pharmacology and therapeutics (CPT) education is becoming increasingly apparent, and the first steps toward improvement have been taken. Key learning outcomes were identified in an international multicenter Delphi study, and the European Association for Clinical Pharmacology and Therapeutics (EACPT) Working Group on education has published a list of recommendations to harmonize and modernize CPT education.[4-6] One of these recommendations is for CPT teachers to use more (online) digital learning resources (DLRs) and preferably share these at a national or international level.[7] These resources are not limited to (online or offline) e-learning programs, but may also include more innovative ways of teaching, such as podcasts, simulations, serious games, and virtual or augmented reality. Indeed, the possibility to distribute high-quality content and to reuse this extensively, after only a single investment of time and money, is one of the advantages of DLRs over traditional teaching methods. Other potential advantages for teachers include the possibility to rapidly update, revise, and standardize the content and the use of learning management systems to track individual learner progress. DLRs also have potential advantages for learners, such as the possibility to alter study pace and revise content extensively, to use multimedia and interactive elements, and to study anytime and anywhere. On the other hand, first generation DLRs may also have significant drawbacks because of the lack of interaction with teachers and peers.[8] Studies of healthcare education have shown that DLRs increase knowledge compared with no education and are at least equal to traditional learning methods in terms of knowledge acquisition and learner satisfaction.[9,10] However, safe and effective prescribing is a more complex process, requiring the integration of cognitive skills (e.g., knowledge, problem-solving, and decision making) and attitudes in a busy and potentially stressful workplace[11]. Whether DLRs are suitable to teach these components in an effective manner has been questioned[8]. Unfortunately, the effect of the diverse DLRs on safe prescribing remains largely unclear, and none of the existing review articles on digital health education have focused on prescribing. DLRs are often evaluated in terms of subjective satisfaction and knowledge acquisition only, and studies evaluating more clinically relevant outcomes are scarce because they are costly, time-consuming, and limited by numerous confounding factors.[4,8] In order to help implement the EACPT working group recommendation on internationally distributed DLRs, more information about their effects on prescribing is required. Therefore, the aims of this review are to identify published forms of DLR used to teach rational prescribing and to assess their effect on learner-related and clinically relevant outcomes, with a view to determining which elements are effective in teaching prescribing.

RESULTS

Literature review

The database search yielded 2,110 records, 125 of which were eligible on the basis of title and abstract. Fifty-nine full-text articles were eligible for inclusion.[12-70] Six additional articles were identified from the previously used database,[71-76] making a total of 65 articles. An overview of all included articles (with effect-estimates when available) is presented in ***Table S1*** (online supplements)**.** The complete selection process, as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, is shown in ***Figure 1.***

Digital learning resource characteristics

Table 1 shows the characteristics of the digital teaching interventions. Most (N = 55; 85%) articles described the use of (online) e-learning,[12-17,19-34,36-38,40,41,43,44,48,49,51-63,65-74,76] 11(20%) of which described e-learning combined with traditional classroom teaching, making the intervention blended learning.[15,19,21,26,33,38,41,62,65,66,72,73] Eight articles (15%) combined e-learning with some sort of digital communication channel, such as web forums or chatrooms for interaction with peers and teachers.[17,21,28,36,40,51,63,66] Of the six articles (9%) describing a digital assessment, only one was not combined with e-learning.[45] Nine articles (14%) described more unique learning interventions: gamified e-learning,[18] a text-based virtual patient,[35,64] an augmented reality virtual patient,[50] e-learning with email case discussions,[75] a wiki-like student drug formulary,[46] a drug-dosage simulator,[39] a digital drug repository,[42] and informative podcasts.[47] Fifty-one percent of interventions were aimed at postgraduate physicians,[12,13,15,18-20,23,24,27-31,33,34,36,40,42,50,54,55,58-60,62,64,65,67,68,71-75] 25% were aimed at nonmedical prescribers (all of whom were nurses),[15,17,18,21,22,29,35,44,47,58,61-64,66] 20% at medical students,[14,25,32,37,39,43,45,46,49,53,56,57,76] and 11% at pharmacy students.[14,38,48,51,52,69,70] Nine postgraduate courses (14%) were aimed at prescribers from more than one background;[15,18,29,58,61-64,71] one was an undergraduate course (the Australian National Prescribing Curriculum).[14] Elements such as anywhere, anytime availability and interaction were mostly present, but many interventions were not described in detail.

Research designs and study quality

Ten articles (15%) had a descriptive design,[14,25,32,39,41,49,50,58,63,76] 11 (17%) a qualitative design,[13,15,19-21,30,35,46,47,57,66] and 44 (68%) a quantitative design.[12,16-18,22-24,26-29,31,33,34,36-38,40,42-45,48,51-56,59-62,65,67-75] Twenty-six of the quantitative articles (59%) used a randomized[23,24,28,29,31,34,37,40,52,56,59,64,65,67,72-75] or non-randomized[22,27,38,54,60,62,69,70] trial design; the remaining 18 articles (41%) either used no control or compared one group before and after the intervention.[12,16-18,26,33,36,42-45,48,51,53,55,61,68,71] The nature of the control group

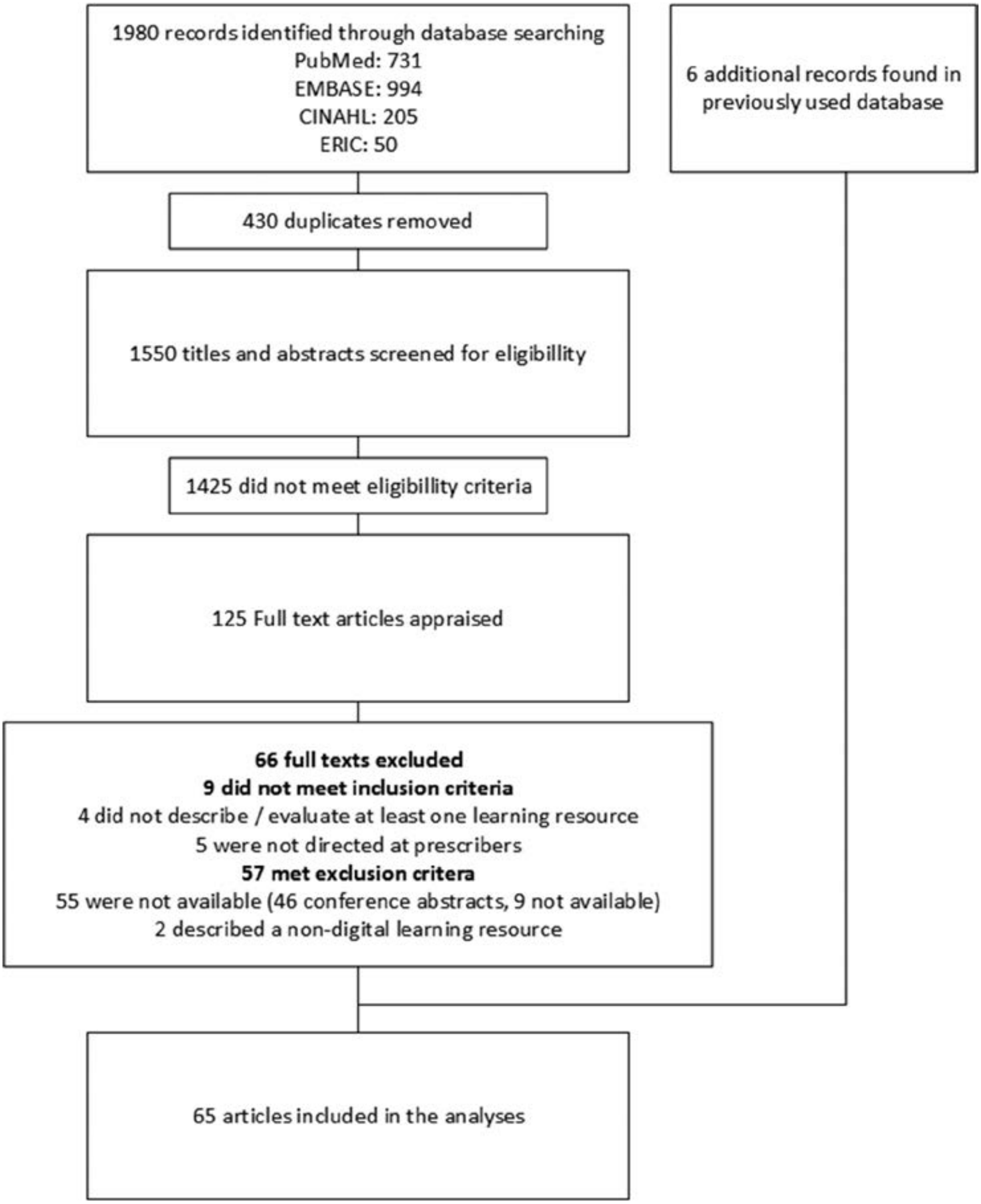


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for study selection. Search strategies used for both databases are described in **Table S2** (online supplements). CINAHL, Cumulative Index to Nursing and Allied Health Literature; ERIC, Education Resources Information Centre

was diverse: five articles (11% of quantitative) compared the use of clinical practice guidelines to DLR[27,28,37,59,64] and six (14%) compared traditional face-to- face teaching with e-learning[22,34,38,54,60,65]. Blended learning was compared with e-learning in only two articles

Table 1. characteristics of the digital learning resources

Intervention characteristics	N (%)
Type of learning intervention*	
E-learning	55 (84.6)
Blended learning	12 (18.5)
Digital assessment	6 (9.2)
Social learning	9 (13.8)
Other	9 (13.8)
Target population*	
Physicians	49 (75.4)
Nurse prescribers	16 (24.6)
Pharmacists	12 (18.5)
Dentists	4 (6.2)
Education level	
Postgraduate	44 (67.7)
Final year	4 (6.2)
Undergraduate	17 (26.2)
Characteristics	
Compulsory	
Yes	16 (24.6)
No	26 (40.0)
Not reported	23 (35.4)
Anytime, anywhere availability	
Yes	42 (64.6)
No	4 (6.2)
Not reported	19 (29.2)
Type of assessment	
Formative	20 (30.8)
Summative	12 (18.5)
Not reported	33 (50.8)
Interactivity	
Yes	41 (63.1)
No	3 (4.6)
Not reported	21 (32.3)
Case oriented	
Yes	34 (52.3)
No	2 (3.1)
Not reported	29 (44.6)

*Multiple interventions and populations possible, percentages add up to >100%. Others may not add up to 100% due to rounding of percentages.

(5%).[38,62] There were also numerous less relevant control groups: eight articles (18%) compared the DLR to no education at all,[23,24,29,31,40,69,72,73] and four articles (9%) compared standard education to standard education with extra e-learning.[52,56,70,75] The scores for the separate Medical Education Research Study Quality Instrument (MERSQI) domains are

Table 2. Study designs and quality

Study characteristics	**N (%)**
Research design	
Descriptive	10 (15.4)
Qualitative	11 (16.9)
Quantitative	44 (67.7)
Medical Education Research Study Quality Instrument (N=44 quantitative)	
Overall (Mean ± SD)	11.6 ± 3.0
Low (5.0 – 8.5)	8 (18.2)
Medium (9.0 – 13.0)	22 (50.0)
High (13.5 – 18.0)	14 (31.8)
Study design (MERSQI score)	
Single group, cross-sectional (1)	11 (25.0)
Single group, before and after intervention (1.5)	7 (15.9)
Prospective cohort (2)	8 (18.2)
Randomized controlled trial (3)	18 (40.9)
Study outcomes – highest Kirkpatrick level (MERSQI score)	
Learner attitude - Kirkpatrick level I (1)	11 (25.0)
Knowledge acquisition - Kirkpatrick level II (1.5)	17 (38.6)
Learner behaviour - Kirkpatrick level III (2)	10 (22.7)
Patient outcomes - Kirkpatrick level IV (3)	6 (13.6)
Sampling: Institutions (MERSQI score)	
Single institution (0.5)	22 (50.0)
Two institutions (1)	5 (11.4)
Three or more institutions (1.5)	17 (38.6)
Sampling: Response rate (MERSQI score)	
< 50% or not reported (0.5)	13 (29.5)
50 – 74% (1)	6 (13.6)
≥ 75% (1.5)	25 (56.8)
Type of data (MERSQI score)	
Assessment by study participant (1)	9 (20.5)
Objective (3)	35 (79.5)
Instrument validity (MERSQI score)	
Not applicable	1 (2.3)
Content validity reported (1)	12 (27.3)
Internal structure reported (1)	6 (13.6)
Relationship with other variables reported (1)	7 (15.9)
Data analysis: Sophistication (MERSQI score)	
Descriptive statistics only (1)	8 (18.2)
Beyond descriptive statistics (2)	36 (81.8)
Data analysis: Appropriate	
Yes (1)	34 (77.3)
No (0)	10 (22.7)

SD = standard deviation; MERSQI = Medical Education Research Study Quality Instrument. Instrument validity consists of three independently scored items (reported or not reported) and therefore does not add up to 100%. Others may not add up to 100% due to rounding of percentages.

shown in ***Table 2.*** The mean MERSQI was 11.6 ± 3.0; there were 8, 22, and 14, articles of low, medium, and high quality, respectively.

Head-to-head comparisons

Four of five studies comparing DLRs to the use of clinical practice guidelines found no between-group difference. The other article reported a significant increase in knowledge (8.4 ± 0.8 vs. 6.1 ± 1.3 on a 9-question scale) and self-reported competence (3.8 ± 0.6 vs.3.5 ± 0.7 on a 10-point Likert scale from incompetent to competent) in opioid prescribing after interactive web-based training as compared with guideline only.[59] Articles directly comparing traditional teaching methods to DLRs reported equal effects in two,[38,54] higher knowledge test scores after interventions with e-learning in two,[60,65] and a better performance on knowledge tests after a traditional lecture in one.[22] One article reported a 5% increase of prescribing errors made by physicians after e-learning, but a decrease from 58% to 37% after pharmacist-led feedback and targeted education.[34] The two articles comparing blended learning with non-blended DLRs found the intervention to be beneficial, but no relevant between-group differences were found.

Patient outcomes (Kirkpatrick level IV)

Six articles reported outcomes at a patient level.[12,28,42,55,73,74] One found a relative risk of antibiotics being preferred by the patient of 0.48 (95% confidence interval 0.34–0.68) after an online training on shared decision making.[73] Another evaluated the effect of online training in the use of a point-of-care CRP test and online enhanced communications training, when these interventions were combined a relative risk of 0.38 (95% CI 0.25–0.55) was observed.[74] Both articles report no harm to patients. Three articles found no effects on prescribing errors of online trainings on the management of diabetes, elderly, and chronic opioid use.[12,28,55] One found no effect of a series of interventions, one of which was the introduction of a digital drug repository and e-learning.[42]

Behavioral outcomes (Kirkpatrick level III)

Eleven studies investigated behavioral change in learners.[24,29,34,56,60,62,65,68,72,74,75] Three found no clear benefit on prescribing errors as measured with medication chart reviews,[34,60,65] whereas the other eight reported positive effects, such as a reduction in antibiotic prescriptions,[24,72,74] the correct use of a Broselow pediatric dosing tape,[29] and improved legibility and completeness of written prescriptions.[62]

Knowledge outcomes (Kirkpatrick level II)

All 19 articles that used knowledge acquisition as outcome reported the intervention to increase test scores as compared with pre-intervention testing or no education.[16,18,23,31,37,38,45,48,51,52,54,56,59,60,64,65,69-71] Three studies reported sustained effects on knowledge lasting up to 6 months.[23,31,59]

Learner satisfaction (Kirkpatrick level I) and self-reported outcomes

Twenty-one articles reported the reaction of participants, mostly assessed using 5-point Likert scales or open questions.[17-22,27,30,31,33,35,38,40,43,51,53,54,61,65-67] All results were positive, but no structural differences between DLRs and traditional teaching methods were identified. Thirteen studies found an increase in self-reported confidence and knowledge on different domains of safe prescribing.[12,15,23,26,31,40,48,53,55,57,59,60,67]

Recommendations for future DLRs

Recommendations for elements to include in future DLRs for safe prescribing were compiled on the basis of recurrent themes mentioned in qualitative reports and are shown in ***Table 3***.

DISCUSSION

To the best of our knowledge, this article is the first to systematically assess the effects of different types of digital teaching in the context of prescribing education. E-learning, blended learning, and digital assessment are commonly used in prescribing education, and the effects on knowledge acquisition are comparable with those of traditional teaching methods. Additionally, DLRs seem to be effective in teaching skills associated with safe and effective prescribing, but whether this directly benefits the patient remains questionable. The most advantageous and disadvantageous elements, as identified from qualitative reports, are compiled into recommendations for best practice.

Types of DLR

Novel techniques, such as augmented reality and serious games, are increasingly used for training healthcare providers. Perhaps unsurprisingly, these techniques focus primarily on teaching the visuo- spatial aspects of subjects, such as anatomy and surgery.[77,78] While Nifakos and Zary[50] describe the potential to combine virtual patients with augmented reality for teaching safe and effective pre- scribing, only two studies actually used a text-based (not augmented) virtual patient for this purpose.[35,64] Bond et al.[18] reported the use of serious game design principles in their e-learning program, but no serious games were identified. The use of an antibiotic dose-response simulator for teaching dose regimens was described but was not assessed for effectiveness.[39] Most DLRs were produced and used locally. Only Australia (National Prescribing Curriculum[79]), England (SCRIPT and Prescribe[80,81]), and the Netherlands (Pscribe[82]) have nationally available prescribing e-learning modules. An example of a more international DLR is the Teaching Resource Center (TRC), produced by the Centre of Human Drug Resource (CHDR) and Leiden University Medical Centre in the Netherlands.[83,84] Although this longitudinal program is used for teaching the six-stepmodels of rational prescribing from the World Health Organization's Guide to good prescribing, it was not included in the current analyses because published articles on the TRC focused on basic pharmacology rather than on prescribing training. It is, however,

Table 3. Recommendations for future digital learning resources on safe and effective prescribing

#	Element to include in DLR	Mentioned in
1	**Anytime, anywhere availability** By far the most appreciated feature of DLRs is the possibility to study anytime and anywhere. It promotes just-in-time learning, puts the student in charge of his/her learning process, and enhances time efficiency. This is especially beneficial for postgraduates, because they often have little study time available because of their clinical duties and have external (e.g. continuous education points) or internal (e.g. interest in the topic) motivation to start learning.	13 articles [15,17,20,21,26,33,35,40,43,46,47,51,70]
2	**Time demand** The anytime, anywhere availability impinges on time scheduled for other activities, including social life. This may lead to motivational problems, and DLRs are often perceived as too long and time consuming. Openness about the required time investment and offering sufficient 'protected' study time may help overcome these problems. Additionally, the use of bite-size chunks of information is advocated, in accordance with the cognitive load theory.	8 articles [17,20-22,44,53,66,70]
3	**Learning pace and revision** Associated with the anywhere, anytime availability is the possibility for students to alter pace, skip sections and revise parts of the DLR extensively. This can be facilitated by structuring the DLR and offering clear navigational menus.	6 articles [22,26,33,44,47,51]
4	**The use of quizzes and game design principles** Interactive elements, such as quizzes and other game design principles (e.g. competition with peers), are stimulating. Moreover, they help students to gauge their learning needs and may direct them to parts of the DLR that require revision	4 articles [21,44,47,69]
5	**Feedback** The possibility to offer direct feedback on (multiple-choice) questions is found to be helpful, but is limited to generic pre-generated content that may sometimes be insufficient.	6 articles [22,35,43,53,57,69]
6	**Contact with peers and teachers** The lack of social interaction with peers and teachers is not easily overcome by using digital communication channels such as web forums and e-mail, as these features remained largely unused.	5 articles [15,22,36,51,66]
7	**Content** Generic, irrelevant, or unauthentic content should be avoided. Instead, there should be a clear connection with predefined and clearly communicated learning goals. The DLR is appreciated if acquired skills and knowledge are directly applicable.	12 articles [13,15,17-22,44,53,57,69]
8	**Accessibility and design** Limited accessibility due to low internet connectivity, other IT problems, or insufficient computer knowledge of the users is highly demotivating, as is an outdated or visually unattractive design. Some accessibility issues may be limited by offering on-demand computer support.	10 articles [13,15,17,18,22,44,51,57,69]
9	**Multimedia and learning styles** The use of multimedia such as audio podcasts, videos, or animations can be very helpful in explaining challenging content. However, different users prefer different learning styles and it advisable to present content in various ways.	4 articles [18,20,22,44]
10	**Web links** Links to other resources (e.g. scientific articles, online drug formularies) may aid learning and are easily incorporated in the DLR. They can be distracting if too numerous or not entirely relevant.	5 articles [17,21,35,45,66]

DLR = Digital learning resource

a good example of how the free distribution of resources could lead to widespread and international adoption. Higher numbers of users will increase cost-effectiveness, and it is known that sharing DLRs as open educational resources (free to use, modify, and distribute derivatives) enhances their timely improvement and overall quality.[85] Unfortunately, only one of the included articles mentioned sharing the DLR in a truly open manner.[43]

Effects of DLRs on safe and effective prescribing

A recent overview of review articles on medical education found that DLRs are at least as efficacious as traditional teaching methods when it comes to knowledge acquisition and student satisfaction.[9] However, these results were found for healthcare education in general and might not be applicable to prescribing education, because prescribing is a complex skill that is affected by the prescriber's attitude and by the workplace environment.[11] Moreover, the effects of DLRs on skills and patient outcomes are less evident and often reported for specific skills (e.g., intubation) only.[86,87] This review identified several effects of DLRs on diverse skills and attitudes associated with safe and effective prescribing, such as moderation of antibiotic use. Therefore, it seems that DLRs are efficacious in teaching safe and effective prescribing skills and attitudes. However, we did not find DLR use to be accompanied by a reduction in prescribing errors or by a benefit to patients. This is probably because the process of prescribing medication is multifactorial and aspects, such as work- place environment and workload, may influence the results.[88] Most studies assessing effects on knowledge acquisition only compared outcomes before and after the intervention or did not use a control. Unsurprisingly, these studies found positive effects of DLRs. Of the five studies directly comparing pharmacotherapeutic DLRs with traditional teaching methods, two favored DLRs, two had equivocal findings, and one favored traditional teaching methods. However, the effect of DLRs relative to guideline use and for other healthcare disciplines is well established, and, overall, DLRs are found to be no better or worse than traditional teaching methods.[9,10] Sikkens et al.[56] reported a mixture of knowledge and behavioral outcomes by examining students by means of a simulated pharmacotherapeutic consultation with a patient actor. This type of objective structured clinical examination (OSCE) may be the best surrogate we have to real-life prescribing for undergraduate students. Interestingly, they found that students performed significantly better on the OSCE 6 months after the e-learning intervention than did students who did not follow the e-learning intervention. Several other articles reported sustained effects for up to 3 months, suggesting that DLRs have a long-term effect on knowledge. Overall, learners are well satisfied with DLRs for safe and effective prescribing. However, a positive feeling about DLRs is no guarantee for their quality, and it is more interesting to find which elements of DLRs improve quality.[8]

Recommendations for the production of DLRs for safe prescribing

The Association for Medical Education in Europe (AMEE) guide #32 on e-learning in medical education highlights the potential advantages of DLRs, but provides relatively little information about which elements to include or avoid when producing a DLR.[89] In addition to providing a practical framework to create postgraduate medical DLRs, de Leeuw et al.[90-92] identified relevant elements on the basis of focus interviews and an international Delphi study. Although their research focused on postgraduate continuous medical education in general, the recommendations are likely to be relevant for (undergraduate and postgraduate) prescribing education as well. Unfortunately, owing to heterogeneous study designs, outcomes, and insufficient reporting of DLR characteristics (e.g., presence of cases and interactive quizzes), quantitative analyses were not feasible. However, on the basis of qualitative reports, we were able to compile a list of 10 recommendations for the future development of DLRs for safe and effective prescribing (***Table 3***). These recommendations are in accordance with those previously identified for (postgraduate) medical education in general.[9,90] The most appreciated element is anytime–anywhere availability. Not only may this save the learner precious (travel) time, but the autonomy associated with this is a pillar of adult learning theory and stimulates just-in-time learning, improving the relevance and applicability of the content. On the other hand, the anytime–anywhere availability affects the learner's time scheduled for other (e.g., social) activities. This is one of the reasons why DLRs are often perceived as requiring too much time. Practical solutions exist (e.g., offering protected study time), but this does not address the underlying problem: a lack of motivation. Unsurprisingly, many of the other recommended elements (game design principles, multimedia, and directly applicable content) aim to increase the learner's motivation.[90] Many articles report the lack of peer and teacher interaction to be disadvantageous or mention the presence of such contact (with blended learning) as beneficial. Several DLRs tried to accommodate this by making digital communication possible. Unfortunately, many of these techniques were insufficiently used by the students. Therefore, it seems that while DLRs are complementary to traditional prescribing education, it remains questionable whether they will ever be able to replace face-to-face prescribing education.

Limitations

Undoubtedly, useful digital teaching tools are being used but not scientifically studied or published. This is evidenced by the numerous relevant conference abstracts that have never appeared as full-text articles. Therefore, it seems that underreporting (and perhaps publication bias) may have limited the integrity of this review article. In order to thoroughly assess the types of DLR used for prescribing education, other research designs, such as (international) surveys among prescribing educators, may be valuable. The mean quality of the articles included in this review was low-to-moderate, but surprisingly slightly higher (difference 1.1, $P = 0.03$ compared with Brinkman et al.) than that found in previous review studies.[1,93] This is most likely due to the nature of DLRs, making it relatively easy to perform multicenter trials with adequate response rates. Moreover, a high proportion of studies used a randomized controlled trial design, leading to high MERSQI scores.[94] However, the relevance of the control groups is not scored in the MERSQI, and an alarming number of studies compared the DLR with no education at all. The obvious findings of these articles are of limited value and outcomes may be easily biased due to the Hawthorne effect.[95] Although the search was compiled and performed with the assistance of an experienced medical information specialist, it is possible that we missed relevant literature because our search criteria were too strict. This is supported by the finding that a previously used database, not focused on prescribing education, contained six previously unidentified relevant articles. During the selection process, it seemed that our predefined eligibility criteria left some gray area as to what is considered "teaching safe and effective prescribing." However, consensus was reached by including up to three experts in the decision process. For example, although relevant to optimal medication use, we chose to exclude DLRs that teach drug dosage calculations to (unspecialized) nurses, because in many countries nurses are not licensed to prescribe medicine. These decisions limit the repeatability of our findings.

CONCLUSION

E-learning is the most-used type of digital learning for safe and effective prescribing education and is efficacious in teaching undergraduate and postgraduate prescribers the required knowledge, skills, and attitudes. Although this may ultimately benefit patient care, direct effects on patient outcomes have not yet been established. Ten recommendations for the future development of pharmacotherapeutic DLRs are provided ***(Table 3).***

Implications for future research

Now that we know DLRs can be used to teach safe and effective prescribing, future research should focus on their broad implemen- tation in European (and perhaps worldwide) medical curricula. Because the included articles rarely reported DLRs to be openly shared between universities, future research should focus on improving the sharing of educational resources and on understanding why educators are hesitant to do so. Obviously, patient care is influenced by many factors other than educational interventions for prescribers. Therefore, it remains difficult to show the effects of such interventions on "hard" outcomes. However, our data show that it is feasible to achieve effects directly influencing the patient, and that this results in the most relevant articles. Therefore, we recommend future DLRs to be evaluated as high as possible on the Kirkpatrick pyramid of educational outcomes, preferably on the level of patient outcomes. In addition, future articles evaluating the effects of DLRs should compare these interventions with relevant control interventions rather than no education.

METHODS

Search strategy an data analysis

Databases PubMed, EMBASE, Education Resources Information Centre (ERIC), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Cochrane database (CENTRAL) were searched for articles on digital methods (e-learning, online course, virtual reality, etc.) for teaching CPT or prescribing (prescribing, drug therapy, pharmacovigilance, etc.) to graduate or undergraduate prescribers (physicians, advance nurse practitioners, medical students, etc.). A complete list of the search terms used, as well as the complete searches, can be found in ***Table S2***. The search in the first four databases was performed on July 30, 2018; the search in CENTRAL was added on March 6, 2019. No other date restrictions were used. Additionally, colleagues from the Centre for Population Health Sciences (CePHaS), Singapore, provided a previously compiled database (unpublished data) of the effects of e-learning on healthcare education. This database was manually searched for articles relevant to prescribing education. The search details are presented in ***Table S2.***

Study selection

Articles were included if they described or evaluated at least one DLR for teaching safe and effective prescribing to graduate and undergraduate medical and nonmedical prescribers (doctors, nurse specialists, dentists, and pharmacists). Exclusion criteria were: (i) articles not written in English or Dutch, (ii) not an original research article (e.g., conference abstracts) or unavailability of the full text, (iii) learning resources not using digital technologies, and (iv) DLRs aimed at prescribing other therapies than medications (e.g., dietary and transfusion). Articles were selected independently by two reviewers (M.B. and A.W.); discrepancies were discussed, and when no agreement was reached a third reviewer (J.T.) was consulted.

Definitions, data extraction, and study quality assessment

Table 4 lists the definitions used to classify the DLRs. These classifications and other data were extracted into a spreadsheet independently by two reviewers (M.B. and A.W.) and cross-checked between them. Differences were resolved by discussion. Research designs were categorized as descriptive (articles describing the production of a DLR without evaluation), qualitative (open-ended survey questions or interviews, but no quantitative outcomes), or quantitative (studies using any kind of quantitative measurement, including Likert-type surveys). The qualitative and quantitative results of mixed-methods articles are presented separately, but the research design was scored on the quantitative part. The quality of the quantitative studies was assessed using the MERSQI.[94] The MERSQI consists of six domains. Per domain, a maximum of three points may be scored; the minimum varies, leading to a possible score of 5–18 points. Some domains may be scored nonapplicable, leading to a lower maximum score; this was corrected using the formula: MERSQI = (total score/maximum possible)*18. Although no official cutoff

Table 4. Definitions of digital learning resources

Type of digital learning resource	Definition used for this review
E-learning	Web-based (online) or offline course offering a mixture of text, multimedia and interactive elements.
Digital assessment	Formative or summative examination, exceeding the use of simple interactive questions in E-Learning.
Social component	(Mostly online) learning environment including any type of digital interaction with peers or teachers, such as webforums, chatrooms, or e-mail support.
Podcasts	Informative digital audio files
Blended learning	Any type of digital learning resource combined with face-to-face teaching.
Virtual patient	Patient simulator (may vary from simple text-based to virtual / augmented reality)
Virtual reality / patient	Interactive computer-generated experience in a virtual environment
Augmented reality	virtual elements projected on real world environment
Serious / educational game	A videogame with the purpose of training an individual.

The definitions used for this review are adapted from van den Berg et al. and Piovesan et. al.[98,99]

values exist, scores of <8.5, 8.5–13.5, and >13.5 were used as cutoff for low, intermediate, and high quality, respectively, in line with previous articles.[93,96] The outcomes were grouped according to Kirkpatrick's pyramid model of educational outcomes.[97]

Data analysis

Data were analyzed using SPSS (IBM SPSS Statistics for Windows, version 22.0; IBM, Armonk, NY) and Microsoft Excel 2016 (Redmond, WA). Owing to heterogeneity in study design and outcomes, only descriptive statistics were used.

SUPPORTING INFORMATION

Supplementary information accompanies this paper on the Clinical Pharmacology & Therapeutics website (www.cpt-journal.com).

Table S1. Included articles.

Table S2. Search strategies.

ACKNOWLEDGMENTS

The authors would like to thank René H.J. Otten, information specialist of the medical library, VU University Amsterdam for his assistance with the database searches. The authors thank Louise S. van Galen, Lorainne Tudor Car, and Josip Car from the Centre for Population Health Sciences (CePHaS), Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, for the provision of a previously used database on e-learning for

health sciences. This research was conducted on behalf of the education working group of the European Association of Clinical Pharmacology and Therapeutics (EACPT).

FUNDING

No funding was received for this work.

CONFLICT OF INTEREST

The authors declared no competing interests for this work.

REFERENCES

1. Brinkman DJ, Tichelaar J, Graaf S, Otten RHJ, Richir MC, van Agtmael MA. Do final-year medical students have sufficient prescribing competencies? A systematic literature review. *British Journal of Clinical Pharmacology*. Apr 2018;84(4):615-635. doi:10.1111/bcp.13491
2. Brinkman DJ, Tichelaar J, Schutte T, et al. Essential Competencies in Prescribing: A First European Cross-Sectional Study Among 895 Final-Year Medical Students. *Clinical Pharmacology & Therapeutics*. Feb 2017;101(2):281-289. doi:10.1002/cpt.521
3. Ashcroft DM, Lewis PJ, Tully MP, et al. Prevalence, Nature, Severity and Risk Factors for Prescribing Errors in Hospital Inpatients: Prospective Study in 20 UK Hospitals. *Drug Saf*. Sep 2015;38(9):833-43. doi:10.1007/s40264-015-0320-x
4. Brinkman DJ, Keijsers C, Tichelaar J, Richir MC, van Agtmael MA. Evaluating pharmacotherapy education: urgent need for hard outcomes. *British Journal of Clinical Pharmacology*. May 2016;81(5):1000-1001. doi:10.1111/bcp.12862
5. Jansen BHE, Disselhorst GW, Schutte T, et al. Essential diseases in prescribing: A national Delphi study towards a core curriculum in pharmacotherapy education. *British Journal of Clinical Pharmacology*. Nov 2018;84(11):2645-2650. doi:10.1111/bcp.13730
6. Brinkman DJ, Tichelaar J, Mokkink LB, et al. Key Learning Outcomes for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study. *Clinical Pharmacology & Therapeutics*. Aug 2018;104(2):317-325. doi:10.1002/cpt.962
7. Brinkman DJ, Tichelaar J, Okorie M, et al. Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries. *Clinical Pharmacology & Therapeutics*. Nov 2017;102(5):815-822. doi:10.1002/cpt.682
8. Maxwell S, Mucklow J. e-Learning initiatives to support prescribing. *British Journal of Clinical Pharmacology*. Oct 2012;74(4):621-631. doi:10.1111/j.1365-2125.2012.04300.x
9. McCall M, Spencer E, Owen H, Roberts N, Heneghan C. Characteristics and efficacy of digital health education: An overview of systematic reviews. *Health Education Journal*. Aug 2018;77(5):497-514. doi:10.1177/0017896918762013
10. Cook DA, Levinson AJ, Garside S, Dupras DM, Erwin PJ, Montori VM. Internet-based learning in the health professions - A meta-analysis. *Jama-Journal of the American Medical Association*. Sep 2008;300(10):1181-1196. doi:10.1001/jama.300.10.1181
11. McLellan L, Tully MP, Dornan T. How could undergraduate education prepare new graduates to be safer prescribers? *British Journal of Clinical Pharmacology*. Oct 2012;74(4):605-613. doi:10.1111/j.1365-2125.2012.04271.x
12. Al-Yassin A, Al-Khaja A, Jichi F, Clarke C, Lisk C, Katz JR. Introducing a diabetes e-learning module: a means of improving junior doctors' confidence and ability in managing inpatients with diabetes. *Practical Diabetes*. Apr 2013;30(3):122-127. doi:10.1002/pdi.1756
13. Anthierens S, Tonkin-Crine S, Douglas E, et al. General practitioners' views on the acceptability and applicability of a web-based intervention to reduce antibiotic prescribing for acute cough in multiple European countries: a qualitative study prior to a randomised trial. *Bmc Family Practice*. Oct 2012;13101. doi:10.1186/1471-2296-13-101
14. Baskett K. Using E-Learning to Improve Prescribing Practice in Emerging Prescribers. *Teaching English with Technology*. 2011;11(1):98-109.
15. Bekkers MJ, Simpson SA, Dunstan F, et al. Enhancing the quality of antibiotic prescribing in Primary Care: Qualitative evaluation of a blended learning intervention. *Bmc Family Practice*. May 2010;1134. doi:10.1186/1471-2296-11-34

16. Berr L, Donaldson N, Hatzipanagos S, Paganelli C, Reynolds PA. The impact on dental students' knowledge in three European countries through an online module on antibiotic prescribing: a preliminary study. *Bulletin du Groupement international pour la recherche scientifique en stomatologie & odontologie*. May 2013;51(3):e25-6.
17. Betts H, Burgess J. A preliminary evaluation of the first e-learning nurse prescribing course in England. *Studies in health technology and informatics*. 2006;122:153-7.
18. Bond SE, Crowther SP, Adhikari S, et al. Design and Implementation of a Novel Web-Based E-Learning Tool for Education of Health Professionals on the Antibiotic Vancomycin. *Journal of Medical Internet Research*. Mar 2017;19(3)e93. doi:10.2196/jmir.6971
19. Bordman R, Bajcar J, Kennie N, Fernandes L, Iglar K. Curriculum to enhance pharmacotherapeutic knowledge in family medicine Interprofessional coteaching and Web-based learning. *Canadian Family Physician*. Nov 2013;59(11):E493-E498.
20. Brooks HL, Pontefract SK, Vallance HK, et al. Perceptions and Impact of Mandatory eLearning for Foundation Trainee Doctors: A Qualitative Evaluation. *Plos One*. Dec 2016;11(12)e0168558. doi:10.1371/journal.pone.0168558
21. Burgess J. A Nurse Prescribing Programme Incorporating e-Learning. *Electronic Journal of E-Learning*. Dec 2007;5(4):251-259.
22. Coleman IP, Watts AS. Use of PharmaCALogy Software in a PBL programme to teach nurse prescribing. *Bioscience Education*. 2007;10(1):1-11.
23. Cullinan S, O'Mahony D, Byrne S. Use of an e-Learning Educational Module to Better Equip Doctors to Prescribe for Older Patients: A Randomised Controlled Trial. *Drugs & Aging*. May 2017;34(5):367-374. doi:10.1007/s40266-017-0451-0
24. Dekker ARJ, Verheij TJM, Broekhuizen BDL, et al. Effectiveness of general practitioner online training and an information booklet for parents on antibiotic prescribing for children with respiratory tract infection in primary care: a cluster randomized controlled trial. *Journal of Antimicrobial Chemotherapy*. May 2018;73(5):1416-1422. doi:10.1093/jac/dkx542
25. Dowden A. Prescribe: an e-learning initiative to improve prescribing. *Prescriber*. 2017;28(9):18-22.
26. Eachempati P, Kumar KK, Sumanth K. Blended learning for reinforcing dental pharmacology in the clinical years: A qualitative analysis. *Indian journal of pharmacology*. 2016;48(Suppl 1):S25.
27. Franchi C, Mari D, Tettamanti M, et al. E-learning to improve the drug prescribing in the hospitalized elderly patients: the ELICADHE feasibility pilot study. *Aging Clinical and Experimental Research*. Aug 2014;26(4):435-443. doi:10.1007/s40520-013-0187-6
28. Franchi C, Tettamanti M, Djade CD, et al. E-learning in order to improve drug prescription for hospitalized older patients: a cluster-randomized controlled study. *British Journal of Clinical Pharmacology*. Jul 2016;82(1):53-63. doi:10.1111/bcp.12922
29. Frush K, Hohenhaus S, Luo XM, Gerardi M, Wiebe RA. Evaluation of a web-based education program on reducing medication dosing error - A multicenter, randomized controlled trial. *Pediatric Emergency Care*. Jan 2006;22(1):62-70. doi:10.1097/01.pec.0000195760.97199.7e
30. Gaetani L, Yeo WW. How can we improve junior doctor prescribing? *Internal Medicine Journal*. Sep 2012;42(9):1050-1052. doi:10.1111/j.1445-5994.2012.02882.x
31. Gordon M, Chandratilake M, Baker P. Improved junior paediatric prescribing skills after a short e-learning intervention: a randomised controlled trial. *Archives of Disease in Childhood*. Dec 2011;96(12):1191-1194. doi:10.1136/archdischild-2011-300577
32. Gordon M, Chandratilake M, Baker P. Low fidelity, high quality: a model for e-learning. *Clinical Teacher*. Aug 2013;10(4):258-263. doi:10.1111/tct.12008
33. Gunderson EW, Fiellin DA, Levin FR, Sullivan LE, Kleber HD. Evaluation of a combined online and in person training in the use of buprenorphine. *Substance abuse*. Sep 2006;27(3):39-45. doi:10.1300/J465v27n03_06

34. Gursanscky J, Young J, Griffett K, Liew D, Smallwood D. Benefit of targeted, pharmacist-led education for junior doctors in reducing prescription writing errors–a controlled trial. *Journal of Pharmacy Practice and Research*. 2018;48(1):26-35.
35. Hurst HM, Marks-Maran D. Using a virtual patient activity to teach nurse prescribing. *Nurse education in practice*. May 2011;11(3):192-8. doi:10.1016/j.nepr.2010.08.008
36. Janssen A, Robinson T, Shaw T. The Evolution of a Professional Practice Forum: Balancing Peer-to-Peer Learning With Course Objectives. *Jmir Research Protocols*. Oct-Dec 2014;3(4)e58. doi:10.2196/resprot.3287
37. Keijsers C, van Doorn ABD, van Kalles A, et al. Structured Pharmaceutical Analysis of the Systematic Tool to Reduce Inappropriate Prescribing Is an Effective Method for Final-Year Medical Students to Improve Polypharmacy Skills: A Randomized Controlled Trial. *Journal of the American Geriatrics Society*. Jul 2014;62(7):1353-1359. doi:10.1111/jgs.12884
38. Kouti L, Aghsam Z, Bargard MS, Javadi MR, Aghakouchakzadeh M, Eslami K. Comparison of the effectiveness of three educational methods (e-learning, lectures and blended) on pharmacy students' knowledge of non-prescription drugs. *Pharmacy Education*. 2018;18(1):197-201.
39. Le Normand Y, Drugeon HB, Potel G, et al. Teaching individualized antibiotic dosage regimens by means of two computer-assisted learning programs. *International journal of bio-medical computing*. Jun 1994;36(1-2):117-9. doi:10.1016/0020-7101(94)90101-5
40. Le TT, Rait MA, Jarlsberg LG, Eid NS, Cabana MD. A Randomized Controlled Trial to Evaluate the Effectiveness of a Distance Asthma Learning Program for Pediatricians. *Journal of Asthma*. Apr 2010;47(3):245-250. doi:10.3109/02770900903560209
41. Leikola SNS, Tuomainen L, Ovaskainen H, et al. Continuing Education Course to Attain Collaborative Comprehensive Medication Review Competencies. *American Journal of Pharmaceutical Education*. 2009;73(6)108. doi:10.5688/aj7306108
42. Leonard MS, Cimino M, Shaha S, McDougal S, Pilliod J, Brodsky L. Risk reduction for adverse drug events through sequential implementation of patient safety initiatives in a children's hospital. *Pediatrics*. Oct 2006;118(4):E1124-E1129. doi:10.1542/peds.2005-3183
43. Likic R, White C, Cinti S, et al. Online learning applied to a course on rational therapeutics: an international comparison between final year students of two medical schools. *British Journal of Clinical Pharmacology*. Feb 2013;75(2):373-380. doi:10.1111/j.1365-2125.2012.04370.x
44. Lymn JS, Bath-Hextall F, Wharrad HJ. Pharmacology education for nurse prescribing students - a lesson in reusable learning objects. *Bmc Nursing*. 2008;72. doi:10.1186/1472-6955-7-2
45. Maxwell SRJ, Cameron IT, Webb DJ. Prescribing safety: ensuring that new graduates are prepared. *Lancet*. Feb 2015;385(9968):579-581. doi:10.1016/s0140-6736(14)62339-4
46. Maxwell SRJ, McQueen DS, Ellaway R. eDrug: a dynamic interactive electronic drug formulary for medical students. *British Journal of Clinical Pharmacology*. Dec 2006;62(6):673-681. doi:10.1111/j.1365-2125.2006.02777.x
47. Meade O, Bowskill D, Lymn JS. Pharmacology podcasts: a qualitative study of non-medical prescribing students' use, perceptions and impact on learning. *Bmc Medical Education*. Jan 2011;112. doi:10.1186/1472-6920-11-2
48. Morris JL, Knoderer CA. Assessment of web-based training modules on learning facilitation for advanced pharmacy practice experiences in pediatrics. *The journal of pediatric pharmacology and therapeutics : JPPT : the official journal of PPAG*. Jul 2011;16(3):210-5. doi:10.5863/1551-6776-16.3.210
49. Nierenberg D, Cannon E. A New Initiative With Multiple Sponsors to Help Prepare Medical Students to Be Safe and Effective Prescribers. *Clinical Pharmacology & Therapeutics*. Mar 2015;97(3):208-210. doi:10.1002/cpt.46

50. Nifakos S, Zary N. Virtual patients in a real clinical context using augmented reality: impact on antibiotics prescription behaviors. *Studies in health technology and informatics*. 2014;205:707-11.

51. Patel PB, Patel T, Saurabh MK, Thakkar S. Perceptions and Effectiveness of Use of E-Learning in Pharmacology Education. *Journal of Clinical and Diagnostic Research*. Jul 2018;12(7):FC12-FC16. doi:10.7860/jcdr/2018/35791.11829

52. Peeters MJ, Kamm GL, Beltyukova SA. A Computer-based Module for Prescribing Error Instruction. *American Journal of Pharmaceutical Education*. 2009;73(6)101. doi:10.5688/aj7306101

53. Rajoo SG, Ng FL, Lobo M. e-Learning to facilitate preparation for prescribing skills assessment. *Medical Education*. May 2013;47(5):520-520. doi:10.1111/medu.12169

54. Ryan G, Lyon P, Kumar K, Bell J, Barnet S, Shaw T. Online CME: an effective alternative to face-to-face delivery. *Medical Teacher*. 2007;29(8):E251-E257. doi:10.1080/01421590701551698

55. Saunders KW, Shortreed S, Thielke S, et al. Evaluation of Health Plan Interventions to Influence Chronic Opioid Therapy Prescribing. *Clinical Journal of Pain*. Sep 2015;31(9):820-829. doi:10.1097/ajp.0000000000000159

56. Sikkens JJ, Caris MG, Schutte T, Kramer MHH, Tichelaar J, van Agtmael MA. Improving antibiotic prescribing skills in medical students: the effect of e-learning after 6 months. *Journal of Antimicrobial Chemotherapy*. Aug 2018;73(8):2243-2246. doi:10.1093/jac/dky163

57. Smith A, Tasioulas T, Cockayne N, Misan G, Walker G, Quick G. Construction and evaluation of a web-based interactive prescribing curriculum for senior medical students. *British Journal of Clinical Pharmacology*. Dec 2006;62(6):653-659. doi:10.1111/j.1365-2125.2006.02651.x

58. Stearn VL. Anticoagulant therapy: Staff training using e-learning. The West Suffolk Hospital NHS Trust experience. *British Journal of Haematology*. May 2010;149:26-26.

59. Sullivan MD, Gaster B, Russo J, et al. Randomized Trial of Web-based Training About Opioid Therapy for Chronic Pain. *Clinical Journal of Pain*. Jul 2010;26(6):512-517. doi:10.1097/AJP.0b013e3181dc7adc

60. Tamler R, Green DE, Skamagas M, Breen TL, Looker HC, LeRoith D. Effect of Case-Based Training for Medical Residents on Confidence, Knowledge, and Management of Inpatient Glycemia. *Postgraduate Medicine*. Jul 2011;123(4):99-106. doi:10.3810/pgm.2011.07.2309

61. Teoh SW, Lebedevs T. Using e-learning and lightning presentations to communicate medication-related problems. *Journal of Pharmacy Practice and Research*. 2018;48(2):173-175.

62. Thomas JS, Gillard D, Khor M, Hakendorf P, Thompson CH. A comparison of educational interventions to improve prescribing by junior doctors. *Qjm-an International Journal of Medicine*. May 2015;108(5):369-377. doi:10.1093/qjmed/hcu213

63. TRIKIC A. Supplementary prescribing training: the CPPE e-learning programme. *Pharmaceutical journal*. 2004;272(7300):645-646.

64. Trudeau KJ, Hildebrand C, Garg P, Chiauzzi E, Zacharoff KL. A Randomized Controlled Trial of the Effects of Online Pain Management Education on Primary Care Providers. *Pain Medicine*. Apr 2017;18(4):680-692. doi:10.1093/pm/pnw271

65. van Stiphout F, Zwart-van Rijkom JEF, Versmissen J, et al. Effects of training physicians in electronic prescribing in the outpatient setting on clinical, learning and behavioural outcomes: a cluster randomized trial. *British Journal of Clinical Pharmacology*. Jun 2018;84(6):1187-1197. doi:10.1111/bcp.13540

66. Wilkinson A, Forbes A, Bloomfield J, Gee CF. An exploration of four web-based open and flexible learning modules in post-registration nurse education. *International Journal of Nursing Studies*. May 2004;41(4):411-424. doi:10.1016/j.ijnurstu.2003.11.001

67. Yardley L, Douglas E, Anthierens S, et al. Evaluation of a web-based intervention to reduce antibiotic prescribing for LRTI in six European countries: quantitative process analysis of

the GRACE/INTRO randomised controlled trial. *Implementation Science*. Nov 2013;8134. doi:10.1186/1748-5908-8-134

68. Yeoh BSK, Taylor DM, Taylor SE. Education initiative improves the evidence-based use of metoclopramide following morphine administration in the emergency department. *Emergency Medicine Australasia*. Jun 2009;21(3):178-183. doi:10.1111/j.1742-6723.2009.01179.x
69. Zlotos L, Kayne L, Thompson I, Kane KA, Boyter A. A Web-based Tool for Teaching Pharmacy Practice Competency. *American Journal of Pharmaceutical Education*. 2010;74(2)27. doi:10.5688/aj740227
70. Zlotos L, Thompson ID, Boyter AC. Integration of an Online Simulated Prescription Analysis into Undergraduate Pharmacy Teaching Using Supplemental and Replacement Models. *American Journal of Pharmaceutical Education*. 2015;79(3)37. doi:10.5688/ajpe79337
71. Al Mohajer M, Matthias KR, Nix DE. Improving the knowledge of students and physicians regarding appropriate use of antibiotics for respiratory infections through an online educational module. *American Journal of Infection Control*. Jan 2017;45(1):E15-E17. doi:10.1016/j.ajic.2016.09.027
72. Butler CC, Simpson SA, Dunstan F, et al. Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. *Bmj*. 2012;344
73. Legare F, Labrecque M, Cauchon M, Castel J, Turcotte S, Grimshaw J. Training family physicians in shared decision-making to reduce the overuse of antibiotics in acute respiratory infections: a cluster randomized trial. *Canadian Medical Association Journal*. Sep 2012;184(13):E726-E734. doi:10.1503/cmaj.120568
74. Little P, Stuart B, Francis N, et al. Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. *Lancet*. Oct 2013;382(9899):1175-1182. doi:10.1016/s0140-6736(13)60994-0
75. Midmer D, Kahan M, Marlow B. Effects of a distance learning program on physicians' opioid- and benzodiazepine-prescribing skills. *Journal of Continuing Education in the Health Professions*. Fal 2006;26(4):294-301. doi:10.1002/chp.82
76. Paknikar S. Treatment of urinary tract infections: A simple module to instruct medical students. *Indian journal of pharmacology*. 2005;37(4):264.
77. Moro C, Stromberga Z, Raikos A, Stirling A. The Effectiveness of Virtual and Augmented Reality in Health Sciences and Medical Anatomy. *Anatomical Sciences Education*. Nov-Dec 2017;10(6):549-559. doi:10.1002/ase.1696
78. Overtoom EM, Jansen FW, van Santbrink EJP, Koops SES, Veersema S, Schreuder HWR. Training in Basic Laparoscopic Surgical Skills: Residents Opinion of the New Nintendo Wii-U Laparoscopic Simulator. *Journal of Surgical Education*. Mar-Apr 2017;74(2):352-359. doi:10.1016/j.jsurg.2016.10.004
79. National Prescribing Curriculum (Australia). Accessed August 8, 2018. https://learn.nps.org.au/
80. SCRIPT. Accessed August 16, 2018. https://www.safeprescriber.org/
81. Prescribe. Accessed August 16, 2018. https://www.e-lfh.org.uk/programmes/safe-prescribing/
82. Pscribe. Accessed August 16, 2018. https://www.pscribe.nl/en-GB/Entrance/Home/Index
83. Teaching Resource Center Pharmacology. Accessed March 13, 2023. https://trc-p.nl/
84. Franson KL, Dubois EA, de Kam ML, Cohen AF. Measuring learning from the TRC pharmacology E-Learning program. *British Journal of Clinical Pharmacology*. Jul 2008;66(1):135-141. doi:10.1111/j.1365-2125.2008.03167.x
85. McKiernan EC. Imagining the "open" university: Sharing scholarship to improve research and education. *Plos Biology*. Oct 2017;15(10)e1002614. doi:10.1371/journal.pbio.1002614

86. George PP, Papachristou N, Belisario JM, et al. Online eLearning for undergraduates in health professions: A systematic review of the impact on knowledge, skills, attitudes and satisfaction. *Journal of Global Health*. Jun 2014;4(1)010406. doi:10.7189/jogh.04.010406

87. Rasmussen K, Belisario JM, Wark PA, et al. Offline eLearning for undergraduates in health professions: A systematic review of the impact on knowledge, skills, attitudes and satisfaction. *Journal of Global Health*. Jun 2014;4(1)010405. doi:10.7189/jogh.04.010405

88. Dean B, Schachter M, Vincent C, Barber N. Causes of prescribing errors in hospital inpatients: a prospective study. *Lancet*. Apr 2002;359(9315):1373-1378. doi:10.1016/s0140-6736(02)08350-2

89. Ellaway R, Masters K. AMEE Guide 32: e-Learning in medical education - Part 1: Learning, teaching and assessment. *Medical Teacher*. 2008;30(5):455-473. doi:10.1080/01421590802108331

90. de Leeuw RA, Walsh K, Westerman M, Scheele F. Consensus on Quality Indicators of Postgraduate Medical E-Learning: Delphi Study. *JMIR medical education*. 04 2018;4(1):e13. doi:10.2196/mededu.9365

91. De Leeuw RA, Westerman M, Nelson E, Ket JCF, Scheele F. Quality specifications in postgraduate medical e-learning: an integrative literature review leading to a postgraduate medical e-learning model. *Bmc Medical Education*. Jul 2016;16168. doi:10.1186/s12909-016-0700-7

92. de Leeuw RA, Westerman M, Scheele F. Quality indicators for learner-centered postgraduate medical e-learning. *International Journal of Medical Education*. Apr 2017;8:153-162. doi:10.5116/ijme.58ce.60aa

93. Reumerman M, Tichelaar J, Piersma B, Richir MC, van Agtmael MA. Urgent need to modernize pharmacovigilance education in healthcare curricula: review of the literature. *European Journal of Clinical Pharmacology*. Oct 2018;74(10):1235-1248. doi:10.1007/s00228-018-2500-y

94. Reed DA, Cook DA, Beckman TJ, Levine RB, Kern DE, Wright SM. Association between funding and quality of published medical education research. *Jama-Journal of the American Medical Association*. Sep 2007;298(9):1002-1009. doi:10.1001/jama.298.9.1002

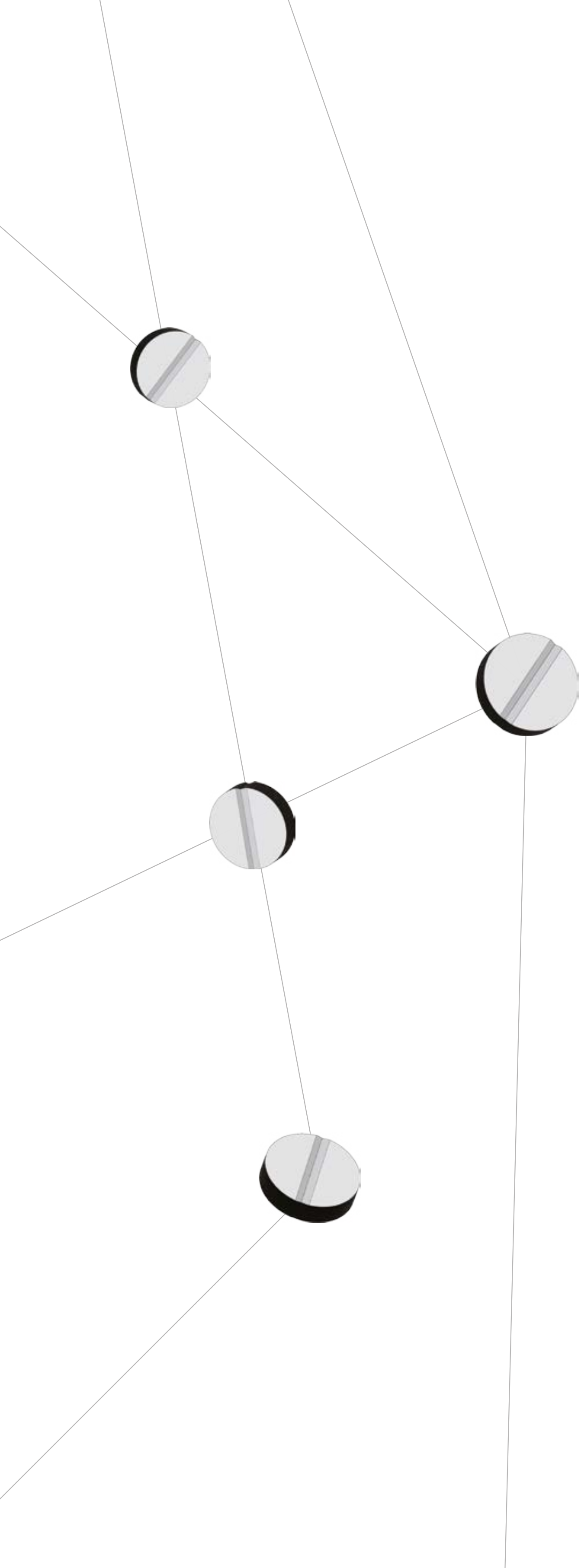
95. Cook DL. THE HAWTHORNE EFFECT IN EDUCATIONAL-RESEARCH. *Phi Delta Kappan*. 1962;44(3):116-122.

96. Bogetz JF, Rassbach CE, Bereknyei S, Mendoza FS, Sanders LM, Braddock CH. Training Health Care Professionals for 21st-Century Practice: A Systematic Review of Educational Interventions on Chronic Care. *Academic Medicine*. Nov 2015;90(11):1561-1572. doi:10.1097/acm.0000000000000773

97. Kirkpatrick D. Revisiting Kirkpatrick's four-level model. *Training & Development*. Jan 1996;50(1):54-57.

98. Piovesan SD, Passerino LM, Pereira AS. Virtual Reality as a Tool in the Education. *International Association for Development of the Information Society*. 2012;

99. van den Akker JJ, Kuiper W, Hameyer U. *Curriculum landscapes and trends*. Springer; 2003.



HARMONIZING AND IMPROVING EUROPEAN EDUCATION IN PRESCRIBING: AN OVERVIEW OF DIGITAL EDUCATIONAL RESOURCES USED IN CLINICAL PHARMACOLOGY AND THERAPEUTICS

3

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British Journal of Clinical Pharmacology
2021 Mar; 87:1001–1011.
doi: 10.1111/bcp.14453

ABSTRACT

Aim

Improvement and harmonization of European clinical pharmacology and therapeutics (CPT) education is urgently required. Because digital educational resources can be easily shared, adapted to local situations and re-used widely across a variety of educational systems, they may be ideally suited for this purpose.

Methods

With a cross-sectional survey among principal CPT teachers in 279 out of 304 European medical schools, an overview and classification of digital resources was compiled.

Results

Teachers from 95 (34%) medical schools in 26 of 28 EU countries responded, 66 (70%) of whom used digital educational resources in their CPT curriculum. A total of 89 of such resources were described in detail, including e-learning (24%), simulators to teach pharmacokinetics and/or pharmacodynamics (10%), virtual patients (8%), and serious games (5%). Together, these resources covered 235 knowledge-based learning objectives, 88 skills, and 13 attitudes. Only one third (27) of the resources were in-part or totally free and only two were licensed open educational resources (free to use, distribute and adapt). A narrative overview of the largest, free and most novel resources is given.

Conclusion

Digital educational resources, ranging from e-learning to virtual patients and games, are widely used for CPT education in EU medical schools. Learning objectives are based largely on knowledge rather than skills or attitudes. This may be improved by including more real-life clinical case scenarios. Moreover, the majority of resources are neither free nor open. Therefore, with a view to harmonizing international CPT education, more needs to be learned about why CPT teachers are not currently sharing their educational materials.

INTRODUCTION

An academic degree in medicine (medical qualification) granted by the governing medical body in one country of the European Economic Area or Switzerland is valid for all countries of the European Union (EU).[1] Common requirements for a medical qualification in these countries are at least 5,500 training hours and sufficient knowledge and skills on broadly defined topics (e.g. diagnosis, therapy and human reproduction).[2] However, when it comes to the safe and effective prescribing of medicines, there are large differences in the number of hours of education and teaching methods within the EU.[3] On the basis of the interquartile range of active instruction hours, a recently graduated doctor with less than 36 hours of traditional clinical pharmacology and therapeutics (CPT) lectures and another doctor with more than 100 hours of experience solving authentic case-based prescribing scenarios may both be at the same bedside in any given EU hospital. A European study has shown that while more education and training in prescribing led to better results in a case-based examination of prescribing skills, 46% of prescriptions still contained one or more errors.[4] On the basis of these results, the European Association for Clinical Pharmacology and Therapeutics (EACPT) has recognized the need to improve and harmonize European CPT education.[3] Digital educational resources are ideal for this, because they can be easily shared over the Internet, translated and adapted to local standards— they can be reused widely across a variety of educational systems. Moreover, digital educational resources are effective in teaching the complex cognitive skills and attitudes required for safe prescribing.[5] For this reason, the EACPT and its affiliated Network of Teachers in Pharmacotherapy (NOTIP) seek to promote international collaboration via an online platform for sharing and creating digital educational CPT resources. The aims of this study were to provide an overview of the digital educational resources currently used in European CPT education, to assess the learning objectives they address, and to evaluate their suitability for international use.

METHODS

Population

Principal CPT teachers at medical schools in the 28 countries of the EU were sent an invitation to a cross-sectional online survey. The single medical school in Luxembourg was excluded, because it only offers a bachelor's degree. All invitations included a personal link and were automatically sent via the certified electronic case report program CastorEDC (www.castoredc.com). During the study period (from 27 March 2019 to 13 May 2019), invitees who had not completed the survey received up to two reminders (sent 16 March and 1 May). The process of retrieving contact information is described in detail elsewhere.3 In brief, one representative in each country was asked to provide the email addresses of his/her colleagues; missing information was retrieved via national pharmacological societies.

Survey

Participants were asked to describe their four most valued ("best practice") digital resources in detail. Questions about the target population (e.g. medical students, junior doctors or nurse-prescribers, etc.) and the features listed in ***Table 2*** were mandatory and answered by checking boxes. The estimated time it took to use the resource was scored on a skewed scale (0–20; 20–40; 40–60; 60–90; 90–120 and >120 minutes). Optional open-text-questions were available to provide additional information about the resource (e.g. on learning objectives, a web link and possible literature references). Participants could suggest how the resource should be classified according to the definitions in ***Table 1***, but the final classification was made by the researchers. Multiple descriptions about (parts of) the same resource were combined into one and incomplete descriptions were excluded.

Resource inspection

A researcher (M.B.) logged in to resources available on the Internet to verify and complete the information supplied by the teacher and to appraise the copyright license. If the resource was in English or Dutch and access was limited with login restrictions, the author was contacted with a request for demo login credentials. If the resource could not be accessed and the information supplied was insufficient, the author was contacted with follow-up questions via e-mail. The Key Learning Objectives for Clinical Pharmacology and Therapeutics Education in Europe, as published by Brinkman et al., were used to identify learning objectives.[6] The copyright licenses are described using the Creative Commons (CC) terminology: "BY" means that attribution of the original source is required; "NC" means that non-commercial use is allowed, but commercial use is prohibited; "ND" indicates that adaptation and re-distribution is not allowed; and "SA" means that adaptation and re-distribution is only allowed when the license is left unchanged.[7]

Ethical considerations

The medical ethics board of Amsterdam UMC location VUmc declared that this study did not fall within the scope of the Medical Research Involving Human Subjects Act (WMO). The Dutch Ethics Review Board of Medical Education approved the study (NVMO-ERB 2018.8.12). All participants provided digital informed consent prior to receiving access to the survey. Consent to re-analyse the data gathered in previous EACPT education working group surveys was asked separately and was not required to access the survey.[3]

Data analyses

Data were downloaded to Excel and analysed using SPSS (IBM version 24.0). The International Monetary Fund 2018 data for gross domestic product (GDP) per capita were used.[8] Correlations between GDP and number of resources were tested using Pearson coefficients. All other data are shown using descriptive statistics only, mean ± standard deviation or median (25th-75th percentile).

Table 1. Definitions used for the classification of resources

Resource type	Definition used for this study
E-learning*	Computer-based course that offers a variety of texts, multimedia, and interactive elements. Often, though not necessarily, online.
PK/PD simulator	Interactive visualization of pharmacokinetics and/or pharmacodynamics modelling.
Video	Educational video (other than recorded lecture).
Digital assessment	Formative or summative examination using computer technology.
Virtual patient	Interactive patient scenario (may be text-based or high-fidelity software simulations, no mannequins or real-life actors).
Knowledge databases and computerized clinical decision support systems	Database with drug information or clinical practice guidelines, drug-drug interaction checker or other computerized clinical decision support.
Student formulary	A digital drug formulary created by students (as personal or collaborative effort), used for educational purposes.
Digital book	Digitized books, primarily text based but may contain interactive elements and multimedia.
(In-class) social media	Software applications that enable students to interact with peers and/or teachers
Serious game	Game designed to educate its users (may be text-based or high-fidelity simulation, no non-digital games).
Slide repository	A digital archive of slides or images used for educational purposes
Audio	Educational audio files (other than recorded lecture).
Recorded lectures	Recordings of lectures to be replayed at a later time. May be audio files, screen-captures or a combination of both.
EPS sandbox	A copy of the electronic health records and/or prescribing system, created for educational purposes. May contain fictional or anonymized patients.
Augmented reality	Computer-generated images projected on a real-world view.

*E-learning is also commonly used as synonym for all types of digital educational resources. Please note that for this study the more-strict definition was used in order distinguish computer-based courses from other types of digital education.

RESULTS

Participating medical schools

Three hundred and ninety-three CPT teachers from 279 (of 304, 92%) medical schools in the EU were invited to participate. A total of 99 teachers answered a sufficient number of questions (more than just demographics) to allow data analysis (91 teachers answered all the questions). In four universities two teachers answered the survey. Therefore, the total number of distinct medical schools was 95 (34% of all). Medical schools in 26 of 27 eligible EU countries were represented in the analyses (none of the five invitees from Austria answered the survey). The participating teachers were on average 54 ± 0.8 years old and had a mean 20 ± 0.9 years of teaching experience. The median time allocated to teaching was 25% (15-40%) of their full-time job.

Current use of digital resources

Figure 1 shows the proportion of medical schools per country that used at least one digital resource in their CPT curriculum. Overall, 66 (69.5%) medical schools used digital resources in their CPT curricula. Re-analysing data from the previous EACPT education working group survey showed a 10.5% increase in the use of digital resources since 2016.3

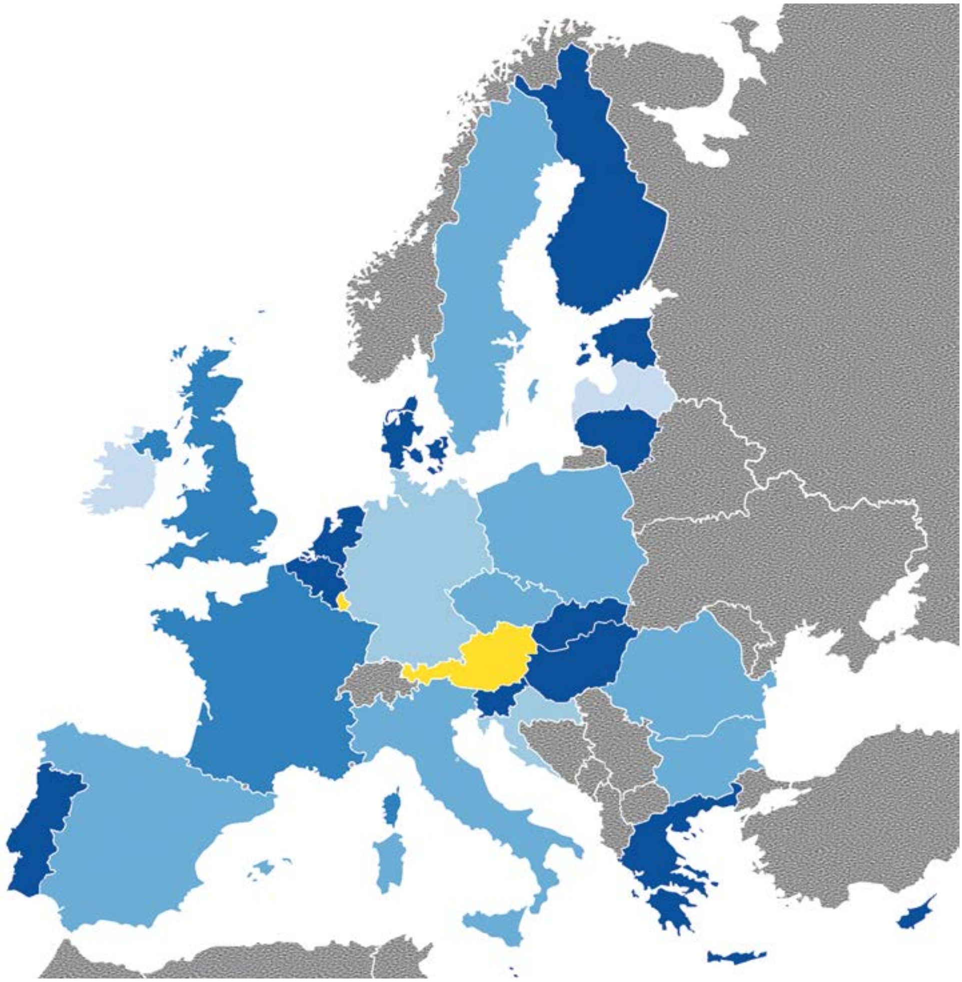

Figure 1. Use of digital educational resources in the European Union

Twenty-one medical schools had started using digital resources since then, whereas seven schools had stopped. The median number of digital resources used per school was 2 (range 1–4). Neither the proportion of schools using digital resources per country, nor the median number of digital resources used per medical school was correlated with GDP per capita ($r = 0.25$; $P = 0.23$ and $r = -0.17$; $P = 0.44$, respectively).

Best practices and resource characteristics

The teachers from the 66 medical schools that used digital resources provided 111 detailed descriptions of 88 distinct resources. Eighteen descriptions were combined into 5 resources used by multiple universities, 13 descriptions about modules of the same resource were combined into 5 resources, and 2 descriptions were excluded because they were not digital resources. A complete overview of all included resources is shown in Supporting Information ***Table S1***. The majority of resources were categorized as e-learning (23.9%), followed by pharmacokinetics (PK) and pharmacodynamics (PD) simulators (10.2%), videos (9.1%), and digital assessments (8.0%). Most resources (23.9%) took more than 120 minutes to complete, but resources taking 20–40 and 40–60 minutes to complete were common (18.2% each). While we asked about the total time needed to complete the resource, many resources consisted of shorter modules. Slightly more than half of resources (55.7%) were available to students anytime and anywhere, but not all resources were suitable for on-demand availability (digital assessments, in-class socials and PK/PD simulators). Fifty-seven per cent of the digital resources were considered "blended" and could be used before ("flipped classroom"), during or after in-class teaching on the same subject. ***Table 2*** shows an overview of the different types of digital resources and their characteristics. All resources were primarily used in medical education (88% to teach medical students, 28% junior doctors and 17% consultants). Overall, 33% of the resources were used in more than one type of education (pharmacy, dental and nurse-prescribing students).

Learning objectives

For 66 resources (75%) there was enough information to score learning objectives. The median number of learning objectives addressed per resource was 3 (range 2–6). The highest number was 24 in the SCRIPT e-learning resource from the UK.[9] The resources addressed a total of 235 knowledge-based learning objectives, 88 skills and 13 attitudes. ***Table 3*** shows the number of resources that addressed a learning objective; the learning objectives per resource are shown in Supporting Information ***Table S1***.

Narrative overview of digital educational resources

E-learning

E-learning was the most frequently used type of digital resource. These resources were highly heterogeneous in their learning objectives, duration and characteristics. The resource described most often was the Dutch/Flemish Pscribe,[10] a modular e-learning

Table 2. Overview of resource characteristics

Type of resource	Frequency	Median time to complete	Available on-demand	Blended	Case-based	Compulsory
E-learning	21 (23.9%)	90 – 120 min.	14 (66.7%)	13 (61.9%)	7 (33.3%)	7 (33.3%)
PK/PD simulator	9 (10.2%)	40 – 60 min.	2 (22.2%)	8 (88.9%)	2 (22.2%)	4 (44.4%)
Video	8 (9.1%)	20 – 60 min.	5 (62.5%)	6 (75.0%)	2 (25.0%)	0 (0%)
Digital assessment	7 (8.0%)	60 – 90 min.	1 (14.3%)	1 (14.3%)	3 (42.9%)	4 (57.1%)
Virtual patient	7 (8.0%)	60 – 90 min.	3 (42.9%)	5 (71.4%)	7 (100%)	2 (28.6%)
CDSS	7 (8.0%)	20 – 40 min.	4 (57.1%)	3 (42.9%)	0 (0%)	2 (28.6%)
Student formulary	4 (4.5%)	> 120 min.	4 (100%)	3 (75%)	2 (50%)	2 (50%)
Digital book	5 (5.7%)	90 – 120 min.	3 (60%)	3 (60%)	2 (40%)	0 (0%)
(In-class) social media	5 (5.7%)	0 – 20 min.	3 (60%)	3 (60%)	3 (60%)	1 (20%)
Serious game	4 (4.5%)	20 – 40 min.	2 (50%)	2 (50%)	0 (0%)	0 (0%)
Slide repository	3 (3.4%)	20 – 40 min.	2 (66.7%)	0 (0%)	1 (33.3%)	1 (33%)
Audio	2 (2.3%)	20 – 40 min.	1 (50%)	0 (0%)	1 (50%)	0 (0%)
Recorded lectures	2 (2.3%)	> 120 min.	2 (100%)	1 (50%)	1 (50%)	1 (50%)
EPS sandbox	2 (2.3%)	90 – 120 min.	1 (50%)	0 (0%)	1 (50%)	0 (0%)
Augmented reality	1 (1.1%)	90 – 120 min.	1 (100%)	1 (100%)	1 (100%)	0 (0%)
Faculty website	1 (1.1%)	40 – 60 min.	1 (100%)	1 (100%)	0 (0%)	0 (0%)
Total	**88 (100%)**	**40 – 60 min.**	**49 (55.7%)**	**50 (56.8%)**	**33 (37.5%)**	**24 (27.3%)**

Blended means combined with in-class teaching on the same subject. PK = Pharmacokinetics; PD = Pharmacodynamics; CDSS is clinical decision support system; EPS = Electronic prescribing system

program with its own content management system built around the six-step method of the WHO Guide to Good Prescribing (WHO GGP).[11] The focus is on rational prescribing, but modules on adverse drug reactions and pharmacokinetics also exist. Access is restricted to the universities that helped co-develop the program. SCRIPT[9] e-learning for effective and appropriate prescribing practice is the most widely used resource in the UK (used by 13 of 33 medical schools). The resource is commercial and accessible via a paid personal or institutional login. It is used to teach almost all (student) prescribers and is a mandatory part of foundation-year residency training in selected regions. The UK government also funds the E-learning for healthcare platform, which contains two CPT resources (Safe prescribing[12] and Prescribing simulator[13]). These appear to be widely used, but are only accessible to UK-based academic institutes. An example of a European collaboration is the commercial EU2P[14] program on pharmacoepidemiology and pharmacovigilance. The Teaching Resource Centre (TRC)[15] is the only open-access e-learning (equivalent to CC-BY, Internet and mobile application). It focuses on basic pharmacology but offers case-based WHO-GGP six-step modules as well. The IUPHAR education project[16] is a hybrid between e-learning and an online book. It is freely available (CC By-NC-ND) and offers text, videos and hyperlinks to other resources on a range of subjects varying from basic pharmacology to clinical pharmacology and therapeutics. The other 15 included e-learning programs were local initiatives (see Supporting Information ***Table S1***).

Table 3. Learning objectives

Learning objectives	# of resources	Learning objectives	# of resources
Knowledge		**Knowledge (continued)**	
1. Introduction to clinical pharmacology and therapeutics	5	13. Legal and ethical aspects of prescribing	3
1.1 Basis principles	*5*	*13.1 Legal aspects*	*3*
1.2 Drugs in healthcare and society	*4*	*13.2 Ethical aspects*	*2*
2. Pharmacodynamics	17	14. Prescribing for patients with special requirements	16
2.1 Mechanism of action	*15*	*14.1 Elderly patients*	*11*
2.2 Dose-response relationships	*13*	*14.2 Impaired liver function*	*10*
3. Pharmacokinetics	23	*14.3 impaired renal function*	*13*
3.1 Drug absorption, distribution, metabolism, and excretion	*23*	*14.4 Pregnant women and women of childbearing potential*	*13*
3.2 Concentration-time relationships	*20*	*14.5 Lactation*	*10*
3.3 Repeated drug dosing	*19*	*14.6 Children*	*11*
4. Individual variability in the response to drugs	13	15 Rational prescribing	18
4.1 Basic principles	*10*	*15.1 Rational approach to prescribing*	*16*
4.2 Pharmacokinetic variability	*12*	*15.2 Dose selection*	*17*
4.3 Pharmacogenetic variability	*6*	16. Clinical toxicology	2
5. Adherence, compliance, and concordance	4	17. Misuse of drugs	3
5.1 Adherence and compliance	*4*	18. Complementary and alternative medicine	2
5.2 Concordance	*3*	19. Use of antibiotics and antibiotic resistance	15
6. Therapeutic drug monitoring	2	20. Commonly used and high-risk medicines	34
6.1 Basic principles	*2*		
6.2 Using drug effect and concentration	*2*	**Skills**	
7. Adverse drug reactions	21	21. Medication history taking	4
7.1 Basic principles	*18*	22. Rational prescribing	20
7.2 Drug allergy	*18*	23. Drug dose calculation	11
7.3 Diagnosis, management, and prevention	*17*	24. Prescription writing	12
7.4 pharmacovigilance	*15*	25. Non-drug therapy	2

Table 3. (continued)

Learning objectives	# of resources	Learning objectives	# of resources
8. Drug interactions and contraindications	18	26. Communication	6
8.1 Interactions	*17*	27. Reviewing prescriptions	4
8.2 Contraindications	*15*	28. Adverse drug reactions	7
9. Medication errors	10	29. Clinical toxicology	0
10. Drug discovery, development, and regulation	6	30 Obtaining information from guidelines and protocols to support prescribing	14
10.1 Drug discovery and development	*4*	31. Monitoring medication	8
10.2 Drug regulation	*4*		
11. Medicines management	5	**Attitudes**	
11.1 National and local processes	*4*	32. Risk-benefit analysis	8
11.2 Formularies and guidelines	*4*	33. Recognizing personal limitations and knowledge	1
12. Evidence-based prescribing	18	34. Balanced approach to the introduction of new drugs	4
12.1 Basic principles	*13*		
12.2 Critical appraisal of clinical studies	*12*		
12.3 Find reliable information about drugs	*16*		

Sub-objectives are shown in italic. When a resource addressed more than one sub-objective, the main objective was only counted once. Learning objectives were previously defined in: Brinkman et al - Key Learning Objectives for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study.

PK/PD simulators

PK/PD simulators were the next most-used resource. They are used to teach basic pharmacokinetic principles, such as the freely online accessible Interactive pharmacology,[17] which came from New Zealand but was described by two Spanish and one Romanian CPT teacher. These simulators can also be used to model the pharmacodynamic effects of drugs, such as Biosoft Cardiolab,[18] which models the effects of sympathetic agonists and antagonists on blood pressure and heart rate.

Videos

Eight video resources were described, addressing a variety of learning objectives such as how to use the British National Formulary[19] and dose reductions in renal insufficiency. Most of these resources are accessible only via institutional login. Open-access alternatives include the Medscape[20] continuing medical education (CME) videos on diverse classes of drugs and the Dutch Medicine of the week videos[21] on YouTube (CC By-NC-ND). An Italian teacher showed how YouTube[22] videos on physiology and pharmacology can be used as preparation for a flipped classroom experience.

Digital assessments

Seven digital assessments were described, varying from practice questions offered in local Moodle systems to large national or international prescribing safety examinations. The best known is the Prescribing safety assessment,[23] which is used in all UK medical schools and in Ireland and Malta. Students are allowed access to the British National Formulary during the examination, which focuses on essential skills, such as writing a prescription, reviewing it and drug-dosage calculations. Successful completion is mandatory for all foundation year 1 doctors. The Dutch-Flemish equivalent is the Assessment for safe prescribing. An increasing number of universities uses it as a summative final pharmacotherapy assessment.[24]

Virtual patients

Virtual patients allow students to diagnose and/or treat a patient without doing harm. The most interesting virtual patients, made by Queen Mary University London, cover anticoagulation and oxygen therapy and include several game-design principles, such as freedom of choice and achievements, which make these patients highly entertaining and motivating for students to use. The other six included_virtual patients are text-based scenarios, such as the Croatian Advanced Medical Therapeutics course, which offers 90 short clinical cases as well as e-learning-like background information. This course was first created by the University of Michigan Medical School and then openly translated and adapted for use in Croatia.[25] Another example of a well-described virtual patient is the Cypriot resource on Thyroid pathology and pharmacotherapy. In this longitudinal case, one patient is followed through pregnancy and lactation, a thyroid storm, and even an adverse drug reaction. Its complete storyboard was recently published.[26]

Computerized clinical decision support systems and knowledge databases

Three drug formularies (e.g. the Swedish Janusinfo[27]), two drug– drug interaction checkers (e.g. UpToDate[28]), a national clinical practice guideline platform (i.e. the Finnish Terveysportti.fi[29]), and a tool for prescribing gastric ulcer prophylaxis (i.e. the Dutch DrugChoice[30]) are used in medical education. Learning objectives focus on the skill of finding reliable information in a timely manner.

Student formularies

Rather than using existing drug databases, five teachers described the use of a formulary created by students. These so-called personal drugs or "p-drugs" are routinely used medications that students should be familiar with and able to prescribe rationally. They were first introduced by the WHO-GGP as offline documents, but now several digital variants are available.[11] Examples include collaborative lists such as the Southampton Student Formulary, which has restricted access but is based on eDrug[31] made in Edinburgh (not described, CC-BY). In the Spanish/English Pdrugs[32] (website and mobile app-based), students can easily create and access their own personal formularies according to the six steps of the WHO-GGP. SmartDrug[33] was created by Brighton and Sussex medical school and lets students create a formulary that mirrors their clinical rotations.

Digital books

The Top 100 Drugs[34] is a formulary of essential drugs made by teachers rather than students. Four other digital books were also described. The two volumes of the iBooks Prescribing Skills Handbook[35] are interactive books with videos and quiz questions, available for free on Apple iPhones and iPads, and were created by the University of Manchester to prepare students for the Prescribing Safety Assessment. A Portuguese university uses Access Medicine,[36] which is a digital library containing books, but also a drug database and interactive cases files.

(In-class) social media

Kahoot!,[37] Socrative,[38] and WooClap[39] are three examples of digital tools that can encourage in-class interactivity with students. Teachers in France, Slovenia and Spain use these tools to teach a variety of learning objectives. All three resources offer free (limited) as well as paid (full) subscriptions; functionalities for asynchronous use, open questions and gamification vary slightly. Alternatively, Twitter is used for CME with a weekly bilingual (French and English) formative PharmacoQuiz,[40] with questions being posted on Friday and answered on Monday.

Serious games

Four resources could be described as serious games. All are in essence quizzes, with varying game elements such as high scores and competition. The Dutch Battle of the Meds[41] mobile application challenges doctors and students to compete in 1-versus-1 quizzes and provides monthly high scores. Learning objectives include commonly used medications, adverse drug events, and PK/PD. The Swedish Läkemedelsquiz ("Medicine quiz")[42] offers a range of short factual knowledge questions on medication names, indications and dosages of diverse groups of medications. However, due to a lack of competition or scores, it appears to be more of a formative assessment than a serious game. Flippity.net[43] can be used to create a "Jeopardy!"-like gameshow which can be hosted in-class, making teams of students compete for most points. Cram.com[44] is a similar resource used to create a "Candy Crush"-like game called Jewels of wisdom that can be played independently by students.

Slide repositories, recorded lectures and audio

Many universities make their slides available to students, as PowerPoint files, audio recordings, or a combination of both. Seven such resources were described, one of which stands out because it is an image and slide repository on Neuropharmacology[45] made openly available (equivalent to CC-BY) by the pharmaceutical company Lundbeck.

Electronic prescribing system sandboxes

The Erasmus Medical Center in Rotterdam and the universities of Birmingham and Manchester have created a copy of their electronic patient records and prescribing system (EPS)[46] for use in medical education. Students can experience the complexity of an EPS without doing harm to real patients. Learning objectives for the Rotterdam resource include selecting the right drug dosages and administration routes, dealing with automatic medication safety signals and drug– drug interactions.

Augmented reality

One British teacher mentioned the use of the mobile augmented reality application Blippar[47] to teach prescribing. A camera is used to project an interactive image over the real-world environment when a specific object is scanned (e.g. the summary of product characteristics when a specific pillbox is scanned). Teachers can use the free Blippbuilder to link information to the objects.

DISCUSSION

Back in 2012, Maxwell and Mucklow predicted that digital resources would be used extensively in the future.[48] Now, 7 years later, almost 70% of European CPT curricula use digital educational resources. The nature of these resources is diverse, ranging from e-learning programs to serious games and electronic prescribing system sandboxes. The goal of this study was to provide an overview of these resources, to characterize them, and to assess their potential for international use as a way to harmonize CPT education. This article provides a crucial next step in the plans of the EACPT education working group to stimulate European collaboration via an online platform. The underlying aim is to help international CPT teachers to collaboratively create new educational materials and to share existing materials among colleagues.

We have previously published a list of recommendations for the creation of digital educational resources for CPT.[5] From a student perspective, an ideal resource is one that can be accessed on demand (anywhere and anytime), that provides the student with autonomy to choose the order and depth of review, and that is split up in "bite-size" chunks of information that do not exceed the capacity of the student's working memory. The use of game-design principles (e.g. competition, collaboration or a time limit) and/or providing authentic patient problems may increase motivation to use these resources. For teachers, the potential to easily share, adapt and distribute educational materials after only a single investment of time and money is undoubtedly the most important aspect of digital educational resources.

Unfortunately, many of the resources mentioned do not exhibit more than a few of the above-mentioned features, mainly because of copyright and access issues. Currently, only 31% of resources are available for free without the requirement for an institutional login. For successful international sharing, free access is an absolute requirement. However, free access alone may not be sufficient because resources may need to be adapted to address international differences (in guidelines, prescribing etiquette, etc.) and translated. Only two resources (Teaching resource center and Lundbeck's neuropharmacology slides) explicitly state that this kind of adaptation is allowed in their copyright license. These resources can be classified as open educational resources according to the UNESCO definition: teaching, learning and research materials in any medium—digital or otherwise—that reside in the public domain or have been released under an open license that permits no-cost access, use, adaptation and redistribution by others with no or limited restrictions.[49,50] Such open licenses are uncommon for commercial products, but it is not clear why universities, and especially those that are publicly funded, have imposed copyright restrictions on the resources they have developed. Previous research suggests that teachers are hesitant to use and create open educational resources because of a lack of awareness, motivation and training in their use.[51] Other possible reasons why resources are rarely shared include language issues and local differences (in educational systems, guidelines, rates of antimicrobial resistance, etc.). This needs to be investigated among European CPT teachers. Besides the overall increase in use of digital resources over the last years, our data also show that seven universities that used digital educational resources in 2016 have since stopped. In line with our own experience, this may be because it is difficult to find the time and money to maintain and update digital resources in the years after they were first developed. International collaboration could help improve the sustainability of digital resources.

Another important finding was the learning objectives of these resources. The WHO Guide to Good Prescribing is well-established as the best way to teach CPT,[11,52] because it advocates a problem-based teaching approach whereby students train the actual prescribing process rather than receive factual knowledge only. However, in the current overview, only 37.5% of resources used case-based problems. Moreover, while all the resources aimed to teach one or more knowledge objectives, only 31 addressed at least one skill and 12 an attitude. The lack of skills teaching is not an issue for digital resources, as it has been previously shown that these resources can be used to teach skills and attitudes as well as knowledge,[5] and there are many examples of resources that focus on skills acquisition, such as the Prescribing safety assessment and Prescribing system sandboxes. Unfortunately, conventional curricula with more traditional teaching than problem-based teaching methods are still dominant in many European medical schools.[3] Therefore, we recommend that future educational methods (digital and otherwise) should be based on authentic clinical scenarios as much as possible.

Limitations

Because of login restrictions, we were unable to inspect all the resources mentioned. In these cases, we asked the teachers who recommended the resource for additional information and requested a demonstration login for inaccessible Dutch and English resources. As with any voluntary survey, there is a risk of participation bias. In this case, digitally active teachers may have been more likely to participate than their less-active colleagues, thus overestimating the number of digital resources used. The proportion of participants per country showed an equal geographic distribution across Europe. The overview of resources is less likely to be biased, because teachers were asked to describe maximally four of their most valued or "best-practice" resources per medical school. Thus, this overview should be seen as providing a list of potentially useful resources rather than a comprehensive overview. It should also be noted that the definitions used for the classification of resources, as provided in ***Table 1***, are ill-defined in the literature and were restricted to digital resources only, whereas serious games, virtual patients and student formularies are not necessarily digital.

CONCLUSION

Digital educational resources are used to teach CPT in European medical schools and vary from well-established tools, such as e-learning and digital assessments, to novel and innovative resources, such as prescribing system sandboxes and virtual patients. Prescribing is a complex cognitive skill, but current resources tend to have knowledge-based learning objectives rather than skill-based learning objectives. Therefore, we recommend that a more problem-based teaching approach be used, which would allow students to practise prescribing on authentic case scenarios. Collaboratively creating new resources and sharing existing ones are important means to harmonize and improve European CPT education. However, copyright restrictions and login requirements currently severely limit the potential to share resources.

Future research should focus on the reasons why these restrictions are in place and what other challenges, such as differences in language, teaching methods or prescribing regulations, teachers perceive about sharing their resources with international colleagues.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

ACKNOWLEDGMENTS

This study was initiated and financially supported by the Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT) and its affiliated Network of Teachers in Pharmacotherapy (NOTIP).

COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

All authors were responsible for writing the manuscript and designing the research. M.B., J.T., M.R. and M.A. analysed the data. M.B. also performed the research.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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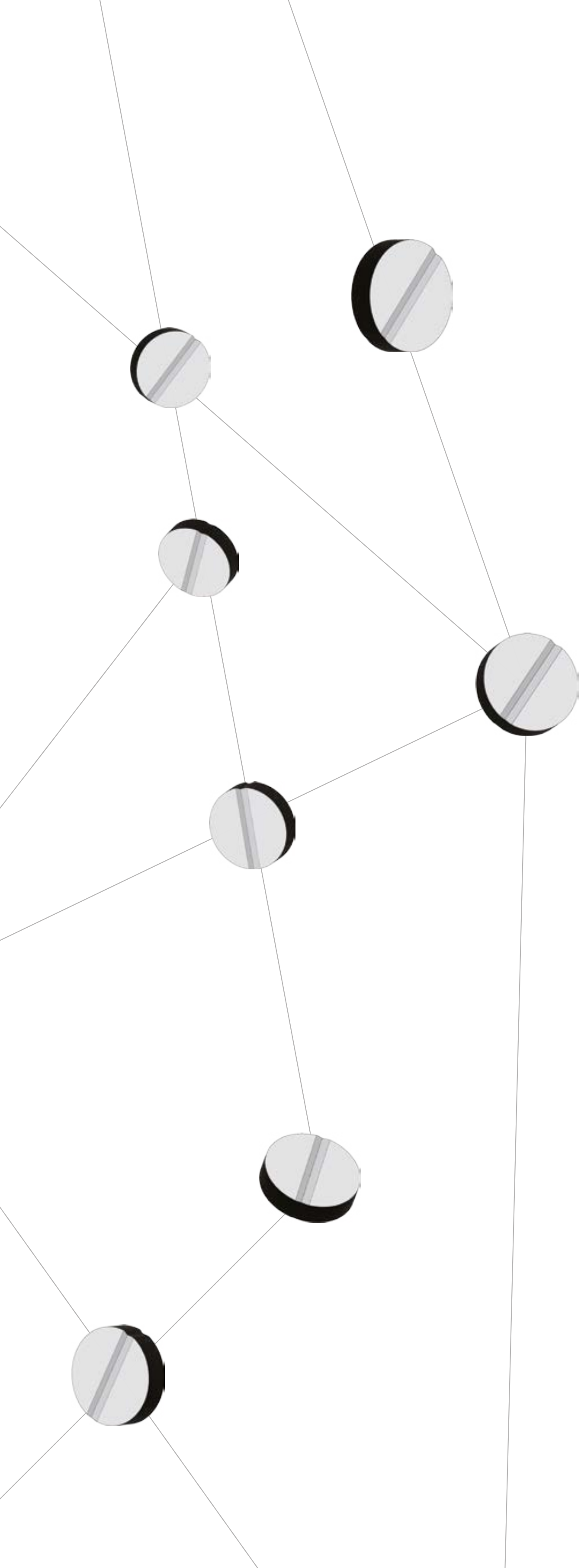
REFERENCES

1. Kovacs E, Schmidt AE, Szocska G, Busse R, McKee M, Legido-Quigley H. Licensing procedures and registration of medical doctors in the European Union. *Clinical Medicine*. Jun 2014;14(3):229-238. doi:10.7861/clinmedicine.14-3-229
2. Council EPat. *Directive 2013/55/EU of 7 sepember 2005 on the recognition of professional qualifications*. Official Journal of the European Union, volume 48, 30 September 2005; 2005.
3. Brinkman DJ, Tichelaar J, Okorie M, et al. Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries. *Clinical Pharmacology & Therapeutics*. Nov 2017;102(5):815-822. doi:10.1002/cpt.682
4. Brinkman DJ, Tichelaar J, Schutte T, et al. Essential Competencies in Prescribing: A First European Cross-Sectional Study Among 895 Final-Year Medical Students. *Clinical Pharmacology & Therapeutics*. Feb 2017;101(2):281-289. doi:10.1002/cpt.521
5. Bakkum MJ, Tichelaar J, Wellink A, Richir MC, van Agtmael MA. Digital Learning to Improve Safe and Effective Prescribing: A Systematic Review. *Clinical Pharmacology & Therapeutics*. Dec 2019;106(6):1236-1245. doi:10.1002/cpt.1549
6. Brinkman DJ, Tichelaar J, Mokkink LB, et al. Key Learning Outcomes for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study. *Clinical Pharmacology & Therapeutics*. Aug 2018;104(2):317-325. doi:10.1002/cpt.962
7. Carroll MW. Creative Commons and the Openness of Open Access. *New England Journal of Medicine*. Feb 2013;368(9):789-791. doi:10.1056/NEJMp1300040
8. Fund IM. Gross domestic product per capita. https://www.imf.org/en/data
9. Script. www.safeprescriber.org
10. Pscribe. www.pscribe.eu
11. De Vries T, Henning RH, Hogerzeil HV, Fresle D, Policy M, Organization WH. *Guide to good prescribing: a practical manual*. 1994.
12. e-LFH: Safe prescribing. https://www.e-lfh.org.uk/programmes/safe-prescribing/
13. e-LFH: Prescribing simulator. https://www.e-lfh.org.uk/programmes/prescribing-simulator/
14. EU2P. https://www.eu2p.org/
15. Teaching Resource Center. https://coo.lumc.nl/TRC/
16. IUPHAR Education Project. https://www.pharmacologyeducation.org/clinical-pharmacology
17. Interactive Pharmacology. http://www.icp.org.nz/index.html
18. Biosoft: Cardiolab.
19. British National Formulary. https://www.bnf.org/
20. Medscape. www.medscape.com
21. Medicine of the week videos. https://www.youtube.com/playlist?list=PL-J9RGSpAwsTUz3q-4-Iv-v4i4FBO8Avf
22. Youtube. www.Youtube.com
23. Prescribing Safety Assessment. https://prescribingsafetyassessment.ac.uk/
24. Assessment for safe prescribing. https://nvkfb.nl/onderwijs/farmacotherapie-eindtoets/
25. Likic R, White C, Cinti S, et al. Online learning applied to a course on rational therapeutics: an international comparison between final year students of two medical schools. *British Journal of Clinical Pharmacology*. Feb 2013;75(2):373-380. doi:10.1111/j.1365-2125.2012.04370.x

26. Nicolaou P, McCrorie P, Nicolaou SA. Using virtual patients to integrate physiology, pathophysiology, and pharmacology in preclinical teaching. *Advances in Physiology Education*. Sep 2019;43(3):277-281. doi:10.1152/advan.00010.2019
27. Janusinfo. www.janusinfo.se
28. UpToDate. www.uptodate.com
29. Terveysportti. www.terveysportti.fi
30. DrugChoice: Protonpump inhibition. http://apps.medicatiereview.nl
31. Maxwell SRJ, McQueen DS, Ellaway R. eDrug: a dynamic interactive electronic drug formulary for medical students. *British Journal of Clinical Pharmacology*. Dec 2006;62(6):673-681. doi:10.1111/j.1365-2125.2006.02777.x
32. Pdrugs. www.pdrugs.org
33. Bissell L, Vincent T, Taylor CJ, Okorie M. SmartDrug: an interactive student e-formulary. presented at: The Future of Safe Prescribing; 2019; Royal College of Physicians of Ireland, Dublin. http://sro.sussex.ac.uk/id/eprint/82897/
34. Hitchings A, Lonsdale D, Burrage D, Baker E. *The top 100 drugs: clinical pharmacology and practical prescribing*. Elsevier; 2018.
35. Prescribing skills handbook volume 1. https://books.apple.com/gb/book/prescribing-skills-handbook-1/id643681802
36. Access Medicine. www.accessmedicine.com
37. Kahoot! www.Kahoot.com
38. Socrative. www.socrative.com
39. Wooclap. www.wooclap.com
40. Twitter Pharmacoquiz. https://twitter.com/reseau_crpv?lang=en
41. Battle of the Meds. http://www.battleofthemeds.com/
42. Läkemedelsquiz. www.lakemedelsquiz.se
43. Flippity.net. www.flippity.net
44. Cram.com. www.cram.com
45. Lundbeck Institute Neuropharmacology. https://institute.progress.im/en/content/slide-library
46. Patient record replicator tool. https://institute.progress.im/en/content/slide-library
47. Blippar. www.blippar.com
48. Maxwell S, Mucklow J. e-Learning initiatives to support prescribing. *British Journal of Clinical Pharmacology*. Oct 2012;74(4):621-631. doi:10.1111/j.1365-2125.2012.04300.x
49. Pawlowski J, Hoel T. Towards a global policy for open educational resources: The Paris OER declaration and its Implications. *White Paper, Version 02, Jyväskylä, Finland*. 2012;
50. UNESCO. 2012 Paris OER Declaration. http://www.unesco.org/new/fileadmin/MULTIMEDIA/HQ/CI/WPFD2009/English_Declaration.html
51. Hassall C, Lewis DI. Institutional and technological barriers to the use of open educational resources (OERs) in physiology and medical education. *Advances in Physiology Education*. Mar 2017;41(1):77-81. doi:10.1152/advan.00171.2016
52. Kamarudin G, Penm J, Chaar B, Moles R. Educational interventions to improve prescribing competency: a systematic review. *Bmj Open*. 2013;3(8)e003291. doi:10.1136/bmjopen-2013-003291



EUROP²E – THE EUROPEAN OPEN PLATFORM FOR PRESCRIBING EDUCATION, A CONSENSUS STUDY AMONG CLINICAL PHARMACOLOGY AND THERAPEUTICS TEACHERS

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European Journal of Clinical Pharmacology
2019 Dec; 77:1209–1218
doi: 10.1007/s00228-021-03101-4

ABSTRACT

Purpose

Sharing and developing digital educational resources and open educational resources has been proposed as a way to harmonize and improve clinical pharmacology and therapeutics (CPT) education in European medical schools. Previous research, however, has shown that there are barriers to the adoption and implementation of open educational resources. The aim of this study was to determine perceived opportunities and barriers to the use and creation of open educational resources among European CPT teachers and possible solutions for these barriers.

Methods

CPT teachers of British and EU medical schools completed an online survey. Opportunities and challenges were identified by thematic analyses and subsequently discussed in an international consensus meeting.

Results

Data from 99 CPT teachers from 95 medical schools were analysed. Thirty teachers (30.3%) shared or collaboratively produced digital educational resources. All teachers foresaw opportunities in the more active use of open educational resources, including improving the quality of their teaching. The challenges reported were language barriers, local differences, lack of time, technological issues, difficulties with quality management, and copyright restrictions. Practical solutions for these challenges were discussed and include a peer review system, clear indexing, and use of copyright licenses that permit adaptation of resources.

Conclusion

Key challenges to making greater use of CPT open educational resources are a limited applicability of such resources due to language and local differences and quality concerns. These challenges may be resolved by relatively simple measures, such as allowing adaptation and translation of resources and a peer review system.

INTRODUCTION

Clinical pharmacology and therapeutics (CPT) education throughout Europe insufficiently prepares medical students and young doctors to prescribe safely[1]. There are large differences in the quantity and quality of CPT education in different European medical schools. Furthermore, the majority of European CPT curricula use a traditional rather than problem-based teaching style[2]; even though the latter is more appropriate because prescribing is a complex skill that requires knowledge, skills, attitudes, and active training[3]. Previous research has shown that students who had a problem-based education significantly outperformed their traditionally educated peers in a case-based examination [1,4]. The Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT) proposes to improve education and training in prescribing knowledge and skills, by harmonizing medical curricula and making them more problem-based[2]. For this purpose, several initiatives, such as the establishment of universal learning outcomes for undergraduate CPT[5] and the introduction of a pan-European prescribing skills examination[6], have been introduced. Another promising strategy to achieve harmonization is to create educational resources collaboratively and to actively share existing resources. To this end, the EACPT education working group aims to launch an online platform for open educational resources and collaboration amongst teachers.

Open educational resources are typically digital learning and teaching materials that are freely accessible that can be revised and redistributed by anyone other than the original author[7]. In addition to their potential to augment and harmonize international education, without forgoing the need for local adaptation, these resources may reduce educational costs, increase accessibility, and promote continual improvement. However, the implementation of open educational resources in existing curricula is challenging [8-13]. The "not invented here syndrome", questionable quality, and a lack of time to find appropriate open educational resources and/or adapting them are previously reported examples of barriers to the use of these resources mentioned by teachers. These and other potential barriers (such as national differences in CPT curricula, prescribing guidelines, and drug availability) challenge to the uptake of our proposed collective online platform. Therefore, the aims of this study were to determine opportunities and challenges perceived by European CPT teachers to creating and implementing open educational resources and identifying solutions to potential challenges.

METHODS

First an online survey was done about teachers' current use of, and opinion about, digital and open educational resources. Secondly an international consensus meeting was held at the 2019 EACPT conference in Stockholm, Sweden.

Part 1: The online survey

An invitation to participate in the survey was sent by email to all known CPT teachers of the medical schools in all 28 EU states (including the UK, prior to Brexit). The single medical school in Luxembourg was later excluded because it did not offer a complete medical degree. The survey was created, and data were collected using the electronic case-report system CastorEDC (www.castoredc.com). The survey was open from 27 March 2019 to 13 May 2019. The questions were divided into four themes: expectations regarding digital education compared to face-to-face teaching, current sharing and collaborating practices, conditions for sharing, and foreseeable advantages and challenges of the online platform. A combination of yes/no, multiple-answer, Likert-type, and open questions was used. The first set of Likert-type questions was adapted from Kirkpatrick's pyramid of educational outcomes [14]; the original second tier of the pyramid ("learning") was subdivided into learning of knowledge, skills, and attitudes. A 5-point scale from much worse than face-face teaching [1] to much better than face-to-face education [5] was used. For the second set of Likert-type questions, a 5-point scale with level of agreement ([1] completely disagree to [5] completely agree) was used. The teachers were also asked to describe their current best practice digital educational resources. An overview and characterization of these resources has been published elsewhere[15].

Part 2: The consensus meeting

The results of the survey, in particular the challenges for the platform, were discussed in a dedicated meeting during the EACPT conference 2019 in Stockholm. Affiliates to the EACPT education working group and its Network Of Teachers In Pharmacotherapy Education (NOTIP) received an invitation beforehand, but the meeting was open to all conference attendees. All challenges and potential solutions were discussed, with participants being asked to suggest additional solutions. Then a plenary discussion was held to reach consensus on which solutions to adopt for the platform. The meeting was audio-recorded, subsequently transcribed verbatim, and is summarized here.

Copyright license terminology

The Creative Commons (www.creativecommons.org) terminology for copyright licenses was used. There are seven licenses (Table 1), which are modular and contain up to four rights: "By" for Attribution, "SA" for Share-Alike, "NC" for Non-Commercial, and "ND" for No Derivatives, as explained in more detail by Bissel[16]. The first five statements about conditions under which teachers would be willing to share their resources were laymen descriptions of these four rights. The copyright licenses that the teachers felt most comfortable with were determined by combining their answers to these five statements. Neutral answers were considered to agree with the most open variant of copyright (e.g. if someone felt neutral about the need for attribution, this was scored as attribution not required; if someone felt neutral about commercial use, this was scored as commercial use allowed). Educational resources are only considered open if they can be re-used, revised, and redistributed without cost. Therefore, resources with a ND-license are not considered open[16,17].

Ethical considerations

All participants were required to give their informed consent before the survey. The local ethics committee at Amsterdam UMC, VUmc, declared that the study did not fall within the scope of the Medical Research Involving Human Subjects Act (WMO). The Ethical Review Board of the Dutch Society for Medical Education (NVMO) approved the study protocol (NVMO-ERB 2018.8.12). The intention to record the meeting and use it for research purposes was stated at the beginning of the consensus meeting, and attendees

Table 1. Appropriateness of copyright licenses

License	Symbols	Most appropriate
Public domain / CC zero *No rights reserved*		0 %
CC attribution (CC BY) *Re-use, revision and redistribution is allowed if the original author is acknowledged appropriately*		1.1%
CC attribution + share-alike (CC BY-SA) *Re-use, revision and redistribution is allowed if the original author is acknowledged appropriately. Derivate works must be shared under the same license.*		1.1%
CC attribution + non-commercial (CC BY-NC) *Re-use, revision and redistribution is allowed for non-commercial purposes only, if the original author is acknowledged appropriately.*		37.6%
CC attribution + non-commercial + share-alike (CC BY-NC-SA) *Re-use, revision and redistribution is allowed for non-commercial purposes only, if the original author is acknowledged appropriately Derivate works must be shared under the same license.*		46.2%
CC attribution + no-derivatives (CC BY-ND) *Re-use is allowed if the original author is appropriately acknowledged. Adaptations may not be distributed.*		0%
CC attribution + non-commercial + no-derivatives (CC BY-NC-ND) *Re-use is allowed for non-commercial purposes only, if the original author is appropriately acknowledged. Adaptations may not be distributed.*		6.5%
All rights reserved Re-use, revision and redistribution are not allowed.	©	7.5%

The results are based on the combination of individual answers on each of the laymen descriptions of Creative Commons rights (figure 2). CC = Creative Commons; BY = attribution; SA = Share-Alike; NC = Non-commercial; ND No-derivatives.

were given the opportunity to leave if they objected. All comments made by non-authors during the meeting were anonymized in the transcript.

Data analyses

Data were gathered in CastorEDC, downloaded to Microsoft Excel, and analysed using SPSS (IBM version 26.0). The answers to yes/no, multiple-answer, and Likert-type questions are expressed as a percentage (number of participants that chose that answer option relative to the total number of participants). The open-answer questions were analysed using thematic analyses. The choice for a thematic approach was made because it best describes the answer to the "what"-type questions that were asked and because we expected the answers to be insufficiently detailed for a phenomenological approach. Author M.B. categorized the answers in proposed themes and subthemes. All of these themes were subsequently discussed with author J.T. until both authors reached consensus on the final definition and wording. A member check of the final themes was performed by presenting them during the consensus meeting and allowing the participants to question, add to, or propose alterations to these themes.

RESULTS

Three-hundred ninety-three teachers were invited to participate in this study, 99 of whom answered at least one survey question. They represent 95 (34%) distinct medical schools in the UK and EU countries except Austria and Luxembourg. Teacher demographics and the use of digital resources in medical schools have been reported elsewhere[15].

Current sharing and collaborating practices

Teachers from 66 of the 95 medical schools (69%) used digital educational resources in their CPT curriculum. Almost half of them (30) indicated that (for at least one of the resources) they shared or collaborated with another institution and half of them (33) did not share or collaborate. In an open-ended question, teachers were asked why they did or did not share/collaborate. The results are presented in Supplementary Table 1.

Opinion and expectations of digital teaching

Ninety-four teachers completed these Likert-type questions. Almost two-thirds (64.9%) believed that students like digital education better (or much better) than face-to-face education. For knowledge acquisition, 92.6% felt that digital education is as effective or more effective than face-to-face teaching, but 46.8% believed digital education to be worse (or much worse) for teaching attitudes. In general, teachers believed that the lower levels ("reaction" and "learning of knowledge, skills, and attitudes") of the adapted Kirkpatrick pyramid can be effectively taught digitally, but that higher tiers ("behaviour" and "clinical results") require face-to-face teaching (Fig. 1). With regard to the advantages of digital teaching, the most common answers were the re-usability of digital resources (73 times), the belief that students prefer it (58 times), and possibilities to share the resources with others (54 times). Disadvantages were the time (79 times), costs (65 times), and skills (30 times) required to develop digital educational resources. Supplementary Table 2 shows all advantages and disadvantages.

Conditions for sharing resources

Ninety-four teachers rated the conditions under which they would be willing to share their resources (Fig. 2). Only 8.7% thought their institution had a policy that prevented the sharing of resources, and only 13% knew what open resources their students used. The copyright licenses that teachers felt most comfortable with were based on the first five statements and shown in Table 1. Only two teachers chose licenses that would allow

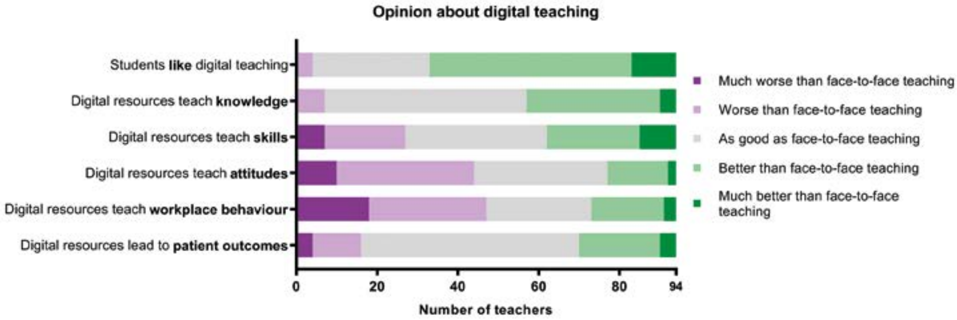


Figure 1. Opinions about digital education compared to face-to-face education Statements are based on Kirkpatrick's pyramid model of educational outcomes. Tier 2 ("learning") was split into knowledge, skills, and attitudes.

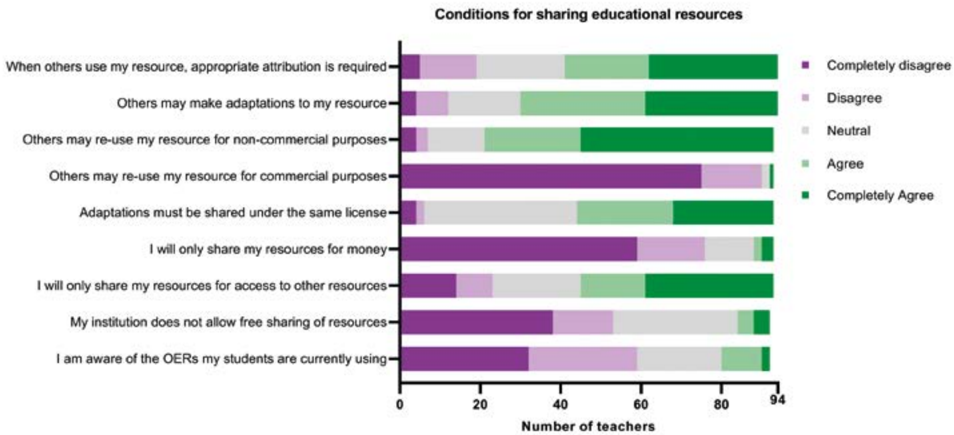


Figure 2. Conditions under which teachers are willing to share their resources. Statements 1 through 5 are lay descriptions of Creative Commons Rights, on which table 1 is based. OERs = open educational resources.

commercial use (1 CC BY and 1 CC BY-SA); 86% of the teachers chose an "open" license (i.e. one that allows adaptations).

Opportunities and challenges for the open educational resource platform

The teachers could indicate opportunities and challenges to the use of the online open educational resources platform. Thematic analyses revealed a total of 7 opportunities in 20 subthemes and 7 challenges in 15 subthemes (Table 2). Some quotes to exemplify the advantages include the following:

"To benefit my students by enabling them to access material from other institutions without having to replicate it ourselves". (theme: To access resources)

"Finding new ideas to explain CPT". (theme: To get inspired, subtheme: on new teaching approaches)

"I think that using this platform could improve the level of education, as I would be able to compare my way of teaching students with that of other CPT educators". (theme: To improve quality of teaching and resources, subtheme: by comparing to others)

"To standardize the requirements among native and foreign students, to find what is common to European pharmacology education". (theme: to harmonize teaching, subtheme: in Europe)

The following quotations illustrate some of the challenges:

"One barrier could be language. Teaching in most countries will probably not be in English but rather in the national language. Therefore, many resources either must be translated or can be used only by a few native (English) speakers". (theme: language barriers)

"Education in clinical pharmacology varies from country to country in Europe. Some topics are not present in the curricula of all countries and thus resources on such topics cannot be used efficiently by all educators". (theme: local differences, subtheme: in curricula)

"Time to go through it, it would have to be very user friendly to allow easy searching for fit-for-purpose learning resources". (theme: investment of time and resources, subtheme: time required to find and adapt resources)

"Risk of garbage in, garbage out". (theme: quality issues, subtheme: risk of low-quality conten

Consensus on the framework of the open educational resource platform

Forty-seven conference attendees participated in the live consensus meeting in Stockholm, Sweden. Based on the aforementioned opportunities and challenges, the researchers presented the following mission statement: We should facilitate an active network of CPT teachers to improve and harmonize teaching via shared resources, collaboration, and inspiration via means of an online platform. After a brief discussion, it was emphasized that CPT teachers include graduate and undergraduate pharmacology and clinical

Table 2. Opportunities and challenges of the online open educational resource and collaboration platform

Opportunities		Challenges	
Theme - subtheme	**n**	**Theme - subtheme**	**n**
To get access to resources	**25**	**Language barriers**	**29**
… of high quality	3	**Local differences**	**21**
… more up to date	3	… in prescribing ethics, guidelines and drug availability	10
… in a greater variety	3	… in curricula / teaching methods	11
… for free	2	**Investment of time and money**	**21**
To get inspired	**18**	… for maintenance of the platform	8
… on new teaching approaches	5	… difficulties obtaining funding	4
… and adjust own content accordingly	2	… to find and adapt the resources	4
To improve quality	**26**	... costs for users	**5**
… via specialized resources	2	**Technological barriers**	
… by comparing to others	5	… the need for a very clear overview and indexation	7
… via peer-reviewed resources	2	… compatibility issues with currently used software	2
To harmonize curricula, learning goals and teaching	**18**	…. limited availability of on-campus computers	1
… in Europe	6	… digital resources do not fit in the current curriculum	1
To contribute	**14**	**Quality control**	**10**
To improve collaboration	**14**	… risk of low-quality content	**7**
… by learning from local differences	5	… the requirement for quality control	3
… by promoting harmonization	4	**Problems with ownership**	**5**
… by scientifically evaluating educational resources	3	… copyright issues	3
… by communicating about meetings and conferences	2	… a lack of responsibility for what is placed on the platform	1
To save valuable resources	**9**	… poor return value for sharing	1
Time	6	**Dissemination problems**	**2**
Time and costs	3	**No barriers**	**10**
Unthematized codes		… if cost-free	3
Because it is easy	5	**Undefined codes***	**4**
To assure sustainability	1		
To fulfil the internationalization policies of my university	1		
Due to the possibility to link w/ national drug databases	1		

Table 2. (continued)

Opportunities		Challenges	
Theme - subtheme	**n**	**Theme - subtheme**	**n**
Codes with reservations rather than advantages			
Only if it is aligned with my teaching / regional situation	3		
Only if it is better than currently available	2		
Only teachers should have access	1		
What's the point, similar project exists	1		

Themes in bold; corresponding subthemes underneath. Subtheme numbers do not add up to theme total, because not every code was given a subtheme. *The following codes were not thematised because they were insufficiently understood: "Need for blended learning", "Need to define learning goals", "depends on topics and subjects", "no practical information enough".

pharmacology teachers of any background. No other alterations were proposed, and the mission statement was accepted.

Next, the possible solutions for local differences were discussed. The main local differences were prescribing ethics, local availability of medicines, differences in guidelines, and differences in curricula and educational systems. One suggestion was to provide information about these differences on the platform. Another was that the resources on the platform should mainly concern universal teaching objectives such as pharmacokinetics and medication safety. All attendees agreed that both of these solutions were fitting and easily implementable.

The easiest solution to potential language barriers would be to make the platform and its content in English. However, it was pointed out that teachers are unlikely to go through the trouble of translating their educational resources prior to uploading them onto the platform. Therefore, it was decided that the main language would be English, but that resources in other languages would be allowed. There was agreement that the platform should be free. Some suggestions for funding the platform were discussed, although none in detail.

With regard to quality management, two suggestions were made. First, users could review and rate resources. Secondly, each resource could be reviewed and validated by international colleagues. Both these suggestions were approved. Additionally, it was suggested that people who upload resources should be asked to check that the content is still up to date. However, there was no agreement about how this should be achieved, and so this aspect would be discussed in the future. In order to increase the resources available, one attendee suggested that teachers could only download resources if they had also contributed a resource, but this was perceived as being contrary to the goal of the platform. The meeting closed with a discussion of the most appropriate copyright license, based on survey findings. It was agreed that the most appropriate license would be CC BY-NC, with or without a share-alike (SA) feature. More open licenses would be welcomed, but less-open licenses (i.e. that do not allow adaptation) would greatly reduce the usability and usefulness of resources.

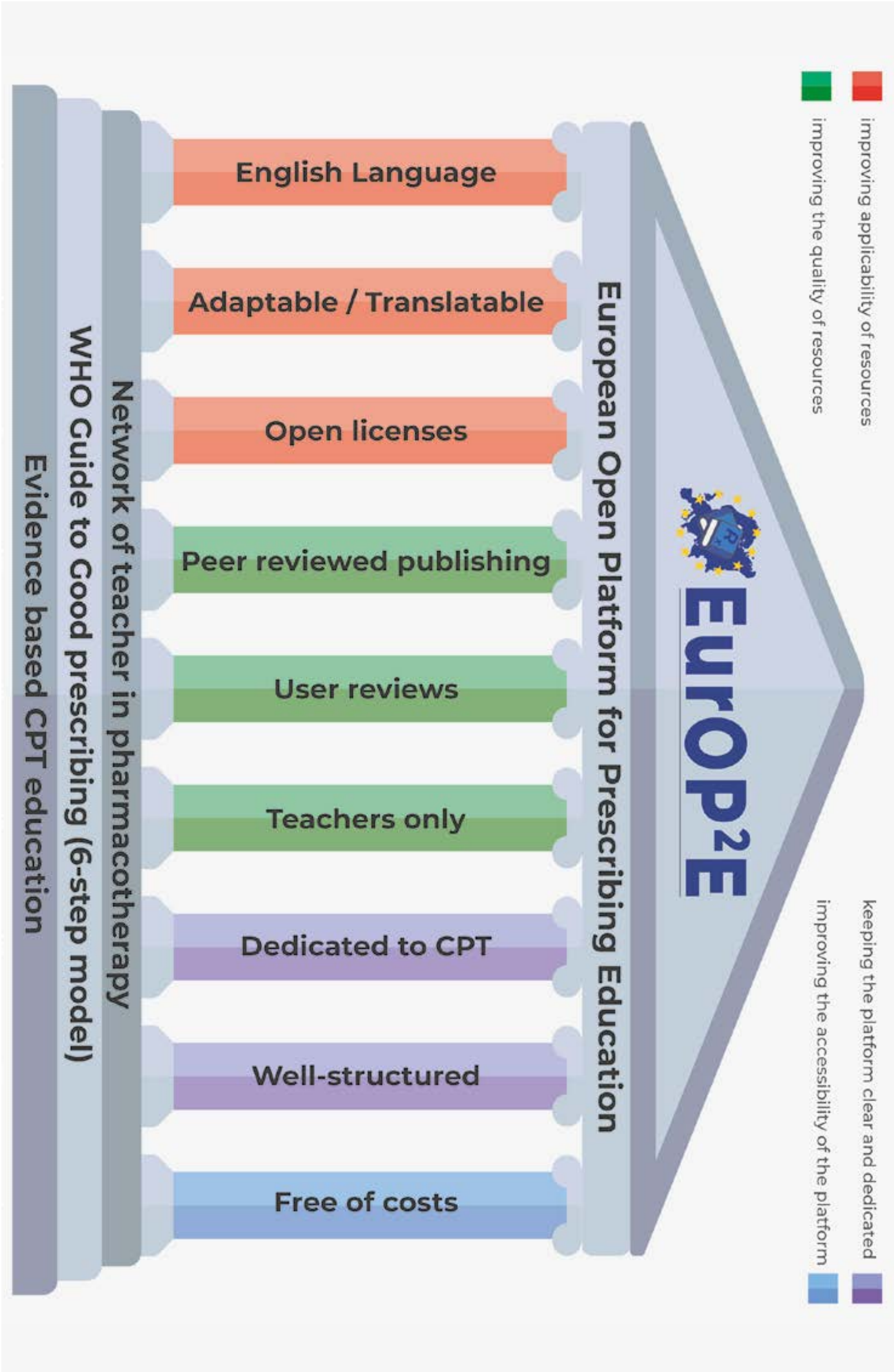
DISCUSSION

This article provides valuable insights into the attitude of teachers towards digital and open educational resources, as well as the challenges they foresee about sharing their resources on an international online platform. More importantly, this study also provides practical solutions to these challenges that can be easily implemented within the framework of such open educational resource platforms.

Several studies have identified the challenges or barriers associated with wider adoption of open educational resources[8,10,13]. Findings are very similar, regardless of whether they come from a large international survey amongst higher and adult education professionals[8], an action research amongst users of the Open Discovery Space for primary and secondary education[13], or a survey among teachers of physiology[10]. The OPAL report[8] categorized these challenges into five dimensions: lack of institutional support for the creation and use of open educational resources; lack of technological tools, such as insufficient computer availability; lack of skills and time to find or create open educational resources; lack of quality or fitness of open educational resources; and personal issues. With a few exceptions, our results reflect these findings. Although the lack of institutional support was not specifically mentioned, this may underlie the time (and financial)-related challenges reported. Even though the OPAL report stems from 2011 and there have been technological advances since then, technological issues still remain an important challenge, but the problems appear to have shifted from a lack of computers and internet connectivity to problems with software compatibility. One way to increase compatibility and adaptability is to specifically allow resource sharing in the intellectual property license and to provide an editable source file[17] (e.g. MS Office rather than a PDF). The lack of time and skills to find and adapt open educational resources was reported in earlier studies and remains a problem. Both in the present study and a survey of physiology teachers[10], finding suitable open educational resources on existing platforms was described as a very tedious task, much like finding a needle (suitable resource) in a haystack (of unfitting and poor-quality resources). This is directly related to another dimension of the OPAL study: a lack of quality or fitness. Language barriers, local differences, and poor quality all limit the applicability of a resource and were the issues that most concerned the teachers in our study. Several promising solutions were suggested in the consensus meeting. In addition, we believe that the dedicated nature (CPT education) of the proposed platform will prevent it from becoming overwhelming or confusing. Moreover, limiting access to the platform to teachers only will improve the quality of its content, because this allows curation, adaptation to the local standards, and (if required) translation before content is used for teaching. The last dimension (called "personal issues" in the OPAL report) basically describes the "not invented here syndrome", which is a distrust of products created elsewhere[18]. This was not specifically mentioned in the present survey, but probably underlies some teachers' concerns about the quality of resources. We believe that the past accomplishments of the EACPT's education working group, close collaborations in the Network Of Teachers In Pharmacotherapy, and well established partner universities will help to reduce this distrust. Not mentioned in the OPAL report, but reported as a challenge by our teachers and in other studies, is the question of who is responsible for the correctness and currency of the resource after distribution?[13] The main consensus is that it is always the user and never the original author who is responsible. However, to avoid inaccuracies in later adaptions which might reflect badly on the original author (and his/her institution), it is important to work with alternate versions that coexist alongside (and not replace) the original resource.

Based on the survey, consensus meeting, and previous literature, we created the following framework for the platform (Fig. 3). It should be built on a strong foundation of evidence based CPT education, problem-based learning according to the WHO Guide to Good Prescribing, and the active NOTIP community. The pillars represent the essential aspects that will be incorporated in the platform. To maximize the user friendliness of the platform, it will be kept small, dedicated to CPT, and clearly organized according to previously established key learning outcomes. In order to improve resource applicability, the content will be primarily in English, easily adaptable and translatable, and licensed in a way that allows re-use, adaptation, and redistribution at no cost. To ensure resource quality, resources will be peer-reviewed both prior to publication and after publication (by means of a star rating and user comment-system). Moreover, limiting platform access to teachers will help ensure resource quality because teachers can curate and adapt resources before using them in teaching. While these measures may provide practical solutions for other open educational resource platforms as well, it must be stressed that ours is not a conventional open educational resource repository. One may even wonder how "open" our platform really is, if we choose to restrict access to teachers only. Our goal is not to facilitate self-learning, but rather to improve existing institutional CPT education. Therefore, we aim to help CPT teachers (in Europe and elsewhere) to make their education more problem-based and provide them with tools to do so. The exact nature of these tools is to be decided in the peer review process and may vary from complete courses to showcases of best practices and teach-the-teacher trainings. In analogy to the simultaneous

Figure 3. Framework for the European Open Platform for Prescribing Education. CPT = clinical pharmacology and therapeutics.


EurOP²E
European Open Platform for Prescribing Education
English Language
Adaptable / Translatable
Open licenses
Peer reviewed publishing
User reviews
Teachers only
Dedicated to CPT
Well-structured
Free of costs
Network of teacher in pharmacotherapy
WHO Guide to Good prescribing (6-step model)
Evidence based CPT education
improving applicability of resources
improving the quality of resources
keeping the platform clear and dedicated
improving the accessibility of the platform

European Prescribing Exam project (EuroPE+), this project was named EurOP2E: European Open Platform for Prescribing Education (www.prescribingeducation.eu).

Recently, due to the COVID19 pandemic, teachers worldwide got faced with the challenge to transfer their onsite education to online education. In addition to the aforementioned goals, EurOP2E will help to assure that we can continue to train medical and non-medical prescribing students to safely prescribe medicines during these challenging times.

Several limitations to our study must be acknowledged. First, as with any uncontrolled study with voluntary participation, the results of both the survey and consensus meeting may have been biased. Teachers who are inherently interested in open and digital education may have been more likely to participate than others, thus giving a slightly one-sided view. Secondly, the survey was large and took approximately 20– 30 min to complete, which may have discouraged teachers from participating and may explain why some answers were not detailed. Not all NOTIP associates had the possibility to travel to Stockholm, Sweden, to attend the conference and consensus meeting. As signing in for the consensus meeting was not obligatory, the number of attendees (n=47) may have been As signing in for the consensus meeting was not obligatory, the number of attendees (n=47) may have been underestimated. Lastly, the consensus meeting lasted only 60 min, which means that some topics were not discussed or discussed inadequately.

CONCLUSION

Teachers recognize many potential advantages of using digital and open educational resources but also the challenges to more widespread use and creation of such resources. The expected challenges mostly revolve around the applicability of resources, such as language barriers, local differences, or quality concerns, but also a lack of time and technological barriers. We aim to remove these barriers by providing a framework for a free, easy-to-use platform dedicated to CPT education for CPT teachers, with English language, peer-reviewed, universal open educational resources that are easily adaptable and translatable to accommodate local differences.

Implications for further research

In order to make the platform successful, more needs to be learned about the educational content that international CPT teachers are currently missing and which could be collaboratively produced and made available on the platform. Moreover, future research should aim to find the criteria on which to base peer review of proposed resources.

SUPPLEMENTARY INFORMATION

The online version contains supplementary material available at https://doi.org/10.1007/s00228-021-03101-4.

ACKNOWLEDGEMENTS

The authors would like to thank Chris Happé for his help in designing the EurOP²E logo and the visual representation of the framework in Fig. 3.

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AUTHOR CONTRIBUTION

All authors were responsible for writing the manuscript and designing the research. M.B., J.T., M.R., and M.A. analysed the data. M.B. also performed the research.

FUNDING

This study was initiated and financially supported by the Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT) and its affiliated Network of Teachers in Pharmacotherapy (NOTIP).

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

DECLARATIONS

Ethical considerations (consent to participate/publish)

All participants were required to give their informed consent before the survey. The local ethics committee at Amsterdam UMC, VUmc, declared that the study did not fall within the scope of the Medical Research Involving Human Subjects Act (WMO). The Ethical Review Board of the Dutch Society for Medical Education (NVMO) approved the study protocol (NVMO-ERB 2018.8.12).

Conflict of interest

All authors declared no competing interests for this work. Please note that author Emilio J. Sanz and Michiel A. van Agtmael have a position as managing and advisory editor for this journal, respectively. They should not be involved in any editorial decisions regarding this manuscript.

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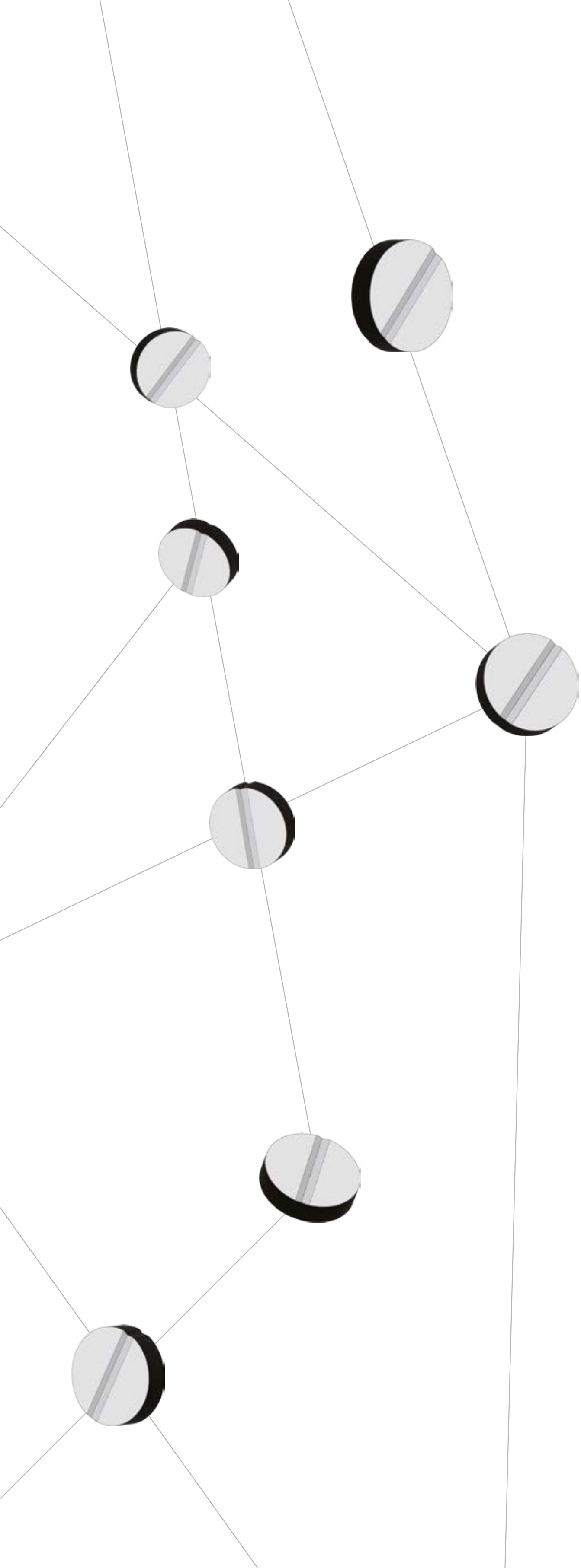
REFERENCES

1. Brinkman DJ, Tichelaar J, Schutte T, et al. Essential competencies in prescribing: A first european cross-sectional study among 895 final-year medical students. *Clin Pharmacol Ther*. Feb 2017;101(2):281-289. doi:10.1002/cpt.521
2. Brinkman DJ, Tichelaar J, Okorie M, et al. Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries. *Clin Pharmacol Ther*. Nov 2017;102(5):815-822. doi:10.1002/cpt.682
3. De Vries T, Henning RH, Hogerzeil HV, Fresle D, Policy M, Organization WH. *Guide to good prescribing: a practical manual*. 1994. *{UNESCO, #54}*.
4. van der Voort T, Brinkman DJ, Benemei S, et al. Appropriate antibiotic prescribing among final-year medical students in Europe. *International journal of antimicrobial agents*. Sep 2019;54(3):375-379. doi:10.1016/j.ijantimicag.2019.05.008
5. Brinkman DJ, Tichelaar J, Mokkink LB, et al. Key Learning Outcomes for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study. *Clin Pharmacol Ther*. Aug 2018;104(2):317-325. doi:10.1002/cpt.962
6. Tichelaar J, Richir M, Garner S, Hogerzeil H, de Vries TP. WHO guide to good prescribing is 25 years old: quo vadis? *European Journal of Clinical Pharmacology*. 2020:1-7.
7. UNESCO. 2012 Paris OER Declaration. http://www.unesco.org/new/fileadmin/MULTIMEDIA/HQ/CI/WPFD2009/English_Declaration.html
8. Andrade A, Ehlers U-D, Caine A, et al. Beyond OER–Shifting Focus to Open Educational Practices: OPAL Report 2011. 2011;
9. Barrett BFD, Grover VI, Janowski T, van Lavieren H, Ojo A, Schmidt P. Challenges in the adoption and use of OpenCourseWare: experience of the United Nations University. *Open Learning: The Journal of Open, Distance and e-Learning*. 2009/02/01 2009;24(1):31-38. doi:10.1080/02680510802627803
10. Hassall C, Lewis DI. Institutional and technological barriers to the use of open educational resources (OERs) in physiology and medical education. *Adv Physiol Educ*. Mar 1 2017;41(1):77-81. doi:10.1152/advan.00171.2016
11. Murphy A. Open educational practices in higher education: institutional adoption and challenges. *Distance Educ*. Aug 1 2013;34(2):201-217. doi:10.1080/01587919.2013.793641
12. Richter T, Ehlers UD. Barriers and motivators for using open educational resources in schools. 2010;
13. Richter T, Kretschmer T, Stracke CM, et al. Open educational resources in the context of school education: Barriers and possible solutions. *European Scientific Journal*. 2014;10(19)
14. Kirkpatrick D. Great Ideas Revisited. Techniques for Evaluating Training Programs. Revisiting Kirkpatrick's Four-Level Model. *Training and development*. 1996;50(1):54-9.
15. Bakkum MJ, Tichelaar J, Wellink A, Richir MC, van Agtmael MA. Digital Learning to Improve Safe and Effective Prescribing: A Systematic Review. *Clin Pharmacol Ther*. Dec 2019;106(6):1236-1245. doi:10.1002/cpt.1549
16. Bissell AN. Permission granted: open licensing for educational resources. *Open Learning: The Journal of Open, Distance and e-Learning*. 2009/02/01 2009;24(1):97-106. doi:10.1080/02680510802627886
17. Hilton Iii J, Wiley D, Stein J, Johnson A. The four 'R's of openness and ALMS analysis: frameworks for open educational resources. *Open Learning: The Journal of Open, Distance and e-Learning*. 2010/02/01 2010;25(1):37-44. doi:10.1080/02680510903482132
18. Antons D, Piller FT. Opening the black box of "Not Invented Here": Attitudes, decision biases, and behavioral consequences. *Academy of Management Perspectives*. 2015;29(2):193-217.



5

TEACHING RESOURCES FOR THE EUROPEAN OPEN PLATFORM FOR PRESCRIBING EDUCATION (EUROP^{2}E) – A NOMINAL GROUP TECHNIQUE STUDY

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NPJ Science of Learning
2022, Sep; 7:23
doi: 10.1038/s41539-022-00141-y

ABSTRACT

The European Open Platform for Prescribing Education (EurOP^{2}E) seeks to improve and harmonize European clinical pharmacology and therapeutics (CPT) education by facilitating international collaboration and sharing problem-based, online, open educational resources. The COVID-19 pandemic forced teachers to switch to virtual modalities, highlighting the need for high-quality online teaching materials. The goal of this study was to establish the online problem-based teaching resources needed to sustain prescribing education during the pandemic and thereafter. A nominal group technique study was conducted with prescribing teachers from 15 European countries. Results were analysed through thematic analysis. In four meetings, 20 teachers from 15 countries proposed and ranked 35 teaching materials. According to the participants, the most necessary problem-based-online teaching materials related to three overarching themes. Related to learning outcomes for CPT, participants proposed creating prescription scenarios, including materials focusing on background knowledge and resources on personalized medicine and topical/ethical issues such as the prescription impact on planetary health. Second, related to teaching, they proposed online case discussions, gamification and decision support systems. Finally, in relation to faculty development, they recommend teacher courses, a repository of reusable exam questions and harmonized formularies. Future work will aim to collaboratively produce such materials.

INTRODUCTION

Previous studies show that final-year medical students and junior doctors throughout Europe feel insufficiently prepared to prescribe medicines safely, effectively, and responsibly[1,2]. Their lack of preparedness is reflected in the poor scores on case-based prescribing examinations and the high number of (potentially harmful) prescribing errors made in the first years after graduation[3,4]. Prescribing is a skill that is underpinned by both knowledge and attitudes. Students who have actively trained to prescribe medicines in a problem-based curriculum (i.e. with cases and simulations) are much better equipped than students who received a traditional (lecture and textbook) based training[3]. However, a recent European survey of clinical pharmacology and therapeutics (CPT) curricula found that the majority of universities still use a predominantly traditional teaching style and that transitioning to problem-based teaching is difficult[1]. In recognition of this, the international community of CPT teachers represented by the Education Working Group of the European Association of Clinical Pharmacology and Therapeutics (EACPT) has made 11 recommendations to improve and harmonize CPT education (table 1)[1]. The European Open Platform for Prescribing Education (EurOP²E) was set up to specifically address recommendation 6: to utilize more online learning resources and share them nationally and internationally. From a teacher's perspective, one of main advantages of online learning resources is that they can be easily reused in diverse settings and locations. Previous research shows that these resources can be effective in teaching the knowledge, skills and attitudes required for safe, effective and responsible prescribing[5]. A large variety of online problem-based resources is already being used for CPT training in universities throughout Europe, but while teachers reported that they are willing to share these materials, they currently rarely do so[6,7]. Actively sharing these materials will aid local teachers to improve their CPT curricula by making them more problem-based. Moreover, the platform will allow teachers to be inspired, share teaching experiences and collaborate on new international teaching resources[6]. In light of the recent COVID-19 pandemic – which forced educators to abruptly adopt online teaching methods - the need for high-quality online teaching resources is high. Therefore, the aim of this study was to find what type of resources international CPT teachers would like to find on the platform, so that these can subsequently be developed in an international collaborative manner.

RESULTS

Sufficient data were collected by the fourth scheduled meeting (no new suggestions were made in this meeting). In total, 20 CPT teachers from 20 institutions in 15 countries participated. Two additional teachers provided informed consent, but did not participate (one was a "no show" for the first meeting and one could not attend any of the four meetings). The meetings lasted 85–110 minutes.

Table 1. Recommendations of the European Association for Clinical Pharmacology and Therapeutics Education Working Group to improve and harmonize clinical pharmacology and therapeutics (CPT) education

1	CPT should be a clear and visible programme throughout the entire medical curriculum, starting as early as possible, and should be emphasized in all clinical modules and attachments.
2	Prescribing should be trained in simulated and clinical environments, with emphasis on completing drug prescriptions, reviewing medication charts, and real responsibility for patient care.
3	Schools should formulate clear and specific learning objectives, preferably using a detailed list of core drugs ('student formulary') and diseases that students should be familiar with before graduation.
4	Schools should ensure that learning objectives are compatible with the learning environment and assessment activities.
5	The WHO 'Guide to Good Prescribing' should be used more intensively in order to teach and train rational prescribing.
6	Schools should utilize more online learning resources and preferably share these at national or international level.
7	Medical/pharmacy students and junior doctors should be engaged in 'near peer' education, supervised and trained by clinical pharmacologists and senior clinicians.
8	Clinical pharmacists and nurse prescribers should be given a greater role in the development and delivery of CPT education.
9	Schools should implement a robust and separate CPT assessment structure throughout the curriculum, with no compensatory mechanism (i.e. the possibility to get a sufficient score based on other subjects).
10	Schools should implement a valid and reliable final prescribing assessment at or near the end of the medical curriculum to assess whether graduates are able to prescribe safely and effectively.
11	Prescribing should be assessed in a simulated or clinical context, with emphasis on writing prescriptions, verifying the suitability of the treatment choice, giving information to patients, and drug monitoring.

These recommendations were previously published by Brinkman et al.(1) (CC BY-NC-ND 4.0)

Ranking results

Table 2 shows the final rankings of the four meetings.

Thematic analysis

The suggestions of the participants fitted into ten themes which were prioritized according to the ranking results (table 3). They related to three overarching themes: learning outcomes for CPT, the format of teaching and resource and faculty development. Figure 1 presents an overview of these themes and the relationships between them.

Themes related to learning outcomes for CPT

Prescribing scenarios - Prescribing scenarios for clinical cases were ranked as being the most important. According to the participants, these cases should focus prescribing

Table 2. Nominal group results

Ranking	The participants suggested to include:	Average score (out of 5)	Number of votes
a, first meeting *(5 participants from Ireland, Malta, Netherlands, Poland, and Romania)*			
1	Training teachers in problem-based learning	3	4
2	Prescribing scenarios enriched with real patient data	2.6	4
3	Virtual interactive patients	2	3
4	Database of exam questions	1.8	4
5	A collection of what is new in pharmacotherapy education	1.6	3
6	Prescribing scenario about pharmacogenomics	1.6	2
7	Teacher community (discussion platform)	1	3
8	Transdisciplinary education between MD/pharm students	0.4	1
9	Role playing clinical cases	0.2	1
b, second meeting (5 participants from Belgium, Croatia, Estonia, Netherlands, and Serbia)			
1	International online debate	3.6	5
2	Prescribing games	3.4	5
3	Clinical case repository with background information	3	5
4	Case-based therapeutic reasoning	2.6	4
5	Polypharmacy tool	1	3
6	Tool about medication safety in pregnancy/lactation	0.8	1
7	Prescribing scenarios on drug allergies	0.4	1
8	Adverse drug reaction tool	0.2	1
c, third meeting *(4 participants, 2 from UK, 1 from Finland and 1 from Spain)*			
1	Realistic interactive cases	3.75	3
2	Practicality of prescribing	2.5	4
3	Topical societal issues ("not in the textbook stuff")	2.25	3
4	Interprofessional problem solving	1.75	2
5	Database of exam questions	1.5	3
6	Interactive digital resource on medicine regulations, drug discovery and ethics	1.25	1
7	Task on clinical situations where there is low/no evidence	1	1
8	"Meta-competences" in prescribing	0.75	2
9	Resource on rapidly evolving areas	0.25	1

Table 2. (continued)

Ranking	The participants suggested to include:	Average score* (out of 5)	Number of votes
d, Fourth meeting *(6 participants, from Denmark, Finland, Germany, Italy, Netherlands, and Spain)*			
1	Repository of clinical cases	4.0	6
2	Knowledge multimedia - Clips, Images, podcast sessions	3.2	6
3	Adaptive e-modules on longitudinal cases.	2.5	4
4	Prescribing scenarios including clinical decision support	2.3	4
5	Personalized formularies	1.2	3
6	Database of exam questions	1.0	4
7	Slides/videos on topical issues	0.7	2

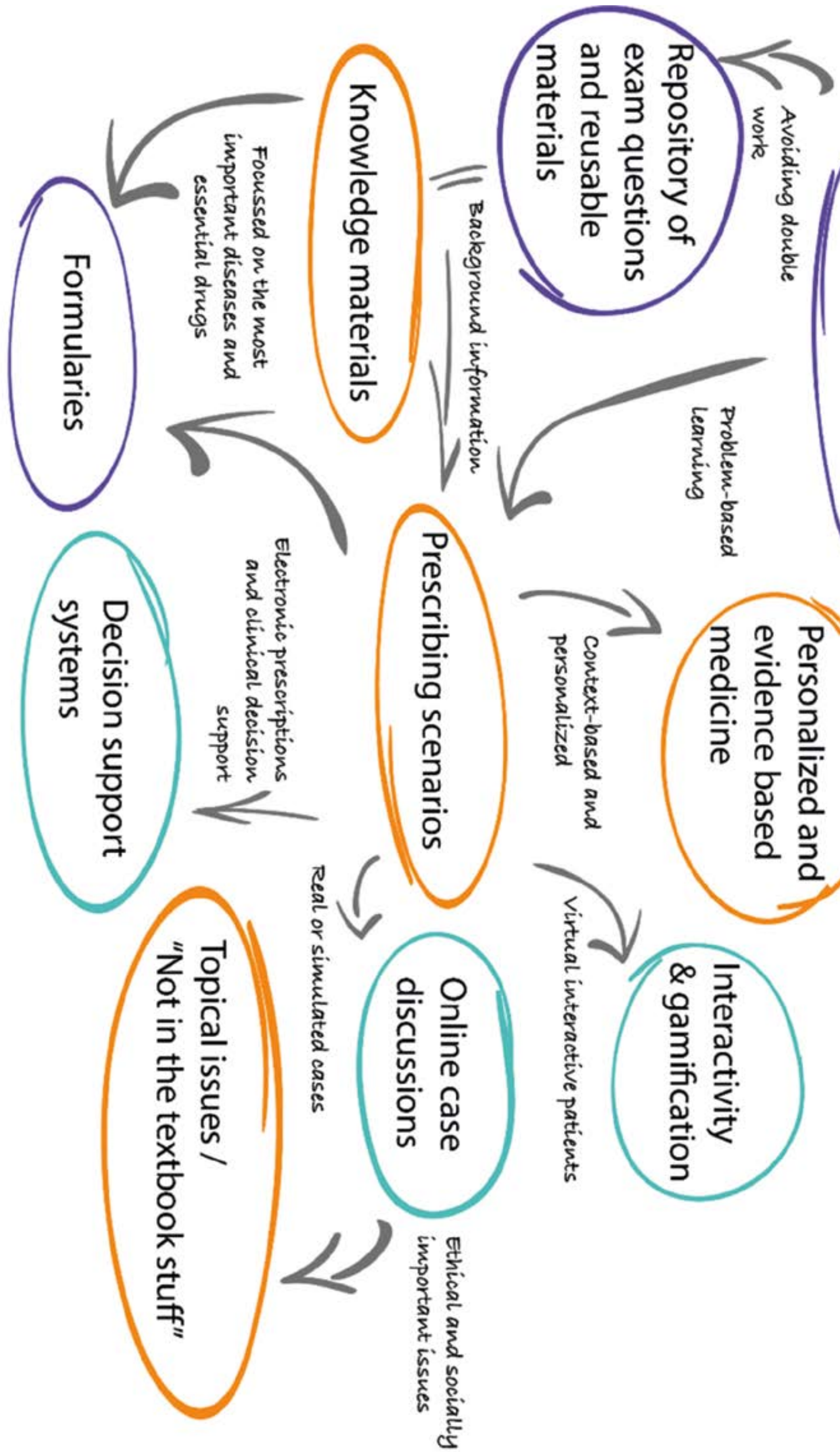
*One participant provided a top four instead of top five.

Table 3. Overview and prioritization of the identified themes

Priority	Theme
1	Prescribing scenarios
2	Interactivity & Gamification
3	Repository of exam questions and reusable materials
4	Online case discussions
5	Decision support systems
6	Teaching the teacher
7	Knowledge materials
8	Topical issues / "not in textbook stuff"
9	Personalized and evidence-based medicine
10	Formularies

Figure 1. Visual representation of the thematic analysis. Orange = related to learning outcomes for Clinical Pharmacology and Therapeutics; Cyan = related to format of teaching; purple = related to resource and faculty development

essential drugs for the most common diseases and be aligned to student level, ranging from patients with single health problems for first-year students to more real-life patients with multiple health problems for advanced students, including training in medication review and deprescribing. Besides deprescribing, three other specific subjects were suggested, namely, pharmacogenomics, drug allergies, and rapidly evolving areas such as biologicals. Since diagnostic and therapeutic reasoning are often not linked in CPT cases, participants proposed they be combined, so that students also learn to interpret clinical data, such as physical examination findings, laboratory results, and radiological


Teaching the teacher
Avoiding double work
Repository of exam questions and reusable materials
Problem-based learning
Background information
Knowledge materials
Focussed on the most important diseases and essential drugs
Formularies
Prescribing scenarios
Context-based and personalized
Personalized and evidence based medicine
Electronic prescriptions and clinical decision support
Decision support systems
Virtual interactive patients
Interactivity & gamification
Real or simulated cases
Online case discussions
Ethical and socially important issues
Topical issues / "Not in the textbook stuff"

findings. Participants suggested that these cases could be presented in the form of pre-recorded videos of clinical consultations, role-playing simulations in which the students alternate between playing the doctor and the patient, *live online case discussions*, and *interactive gamified virtual patients*. To emphasize how prescribing is context based and should be aimed at the *personal needs of the patients*, the participants proposed (in two of the meetings) making adaptive and/or longitudinal cases where the patients' situations change or their health problems progress.

Knowledge materials - Participants suggested creating (video) clips and podcasts about thematic issues that – other than most *prescribing scenarios* – should focus on the common denominators of clinical pharmacology (i.e. that do not differ per country), such as prescribing for special populations, renal function, and deprescribing. It was acknowledged that it would be challenging to condense 2-hour lectures into clips of maximally 10–12 minutes. Videos of the working mechanisms of different classes of drugs, rather than of specific drugs, would also improve the international generalizability. The participants suggested that these materials be used as pre-class activity in flip-the-classroom style lessons.

Topical issues ("Not in textbook stuff") - A suggestion made in two meetings was to cover "important aspects of prescribing that you will not find in textbooks" [participant from UK(1)], such as socially important, topical, and more ethical issues (antimicrobial resistance, the opioid pandemic, environmentally sustainable prescribing or "ecopharmacostewardship", and inequality in medicine). These topics, or "attitudes underpinned by knowledge" [participant from UK(2)], are difficult to teach but vitally important. Generating international standpoints on these matters may help teachers to integrate them in their local curricula. A specific example of a topical issue was the interaction with the pharmaceutical industry. Participants argued that students and doctors are insufficiently exposed to the processes of drug discovery, drug development, and medicines regulation and marketing, and an appreciation of these topics would probably influence how doctors prescribe and appraise potential conflicts of interest.

Personalized and evidence-based medicine - Although it could be classified as *"not in textbook stuff"*, the need to pay more attention to personalized medicine was mentioned separately, sometimes in the context of *prescribing scenarios*. According to one participant [UK(1)], students need to appreciate the nuance between prescribing as science and prescribing as art and should be taught to "challenge the heuristics" and learn when not to trust or apply evidence-based guidelines. This participant explained "It drives me mad when a 95-year-old bedbound patient is put on 80 milligrams of atorvastatin just because she had a mild troponin rise". It was further noted that "medical students have no idea of the reimbursement of medicines" [participant from Italy], and that this is a very practical and important point to consider in personalized prescribing. Lastly, students should be taught how to appraise the literature in situations where there is no or limited evidence available, such as treatment for COVID-19 at the start of the pandemic.

Themes related to the format of teaching

Interactivity & gamification - Gamification was mentioned, both as separate resource and in the context of *prescribing scenarios.* Participants suggested that interactive virtual patients could be created that respond realistically to different treatments or management strategies, thereby giving students (instant) feedback and making it possible for them to assess their treatment choices. This could be especially useful for acute medical situations that students may otherwise not be exposed to. A time-limit could be imposed to create a sense of urgency. One participant was already using gamification, whereby students progressed through a patient case by opening lockers, as in an escape room. This participant found that gamification helped keep students engaged with what was being taught. Other forms of gamification mentioned were short quizzes with in-class competition (like Kahoot!, www.kahoot.it) and a suggestion for a drug-drug interactions rehearsing-game.

<u>*Online transdisciplinary, transnational case discussions*</u> – The participants suggested holding online discussions of (real or simulated) cases, which would enable students from different health professions to collaborate in real-time, much like they will do in their future professions. Additionally, online discussions would allow students to identify and discuss differences in prescribing guidelines and attitudes between countries, so that they could learn that "in many situations there is no such thing as one right answer" [participant from Belgium]. Participants suggested that these meetings be held via live videoconferencing, with students rather than teachers taking the lead. These sessions could be recorded for later reference. The discussions should include ethical aspects such as planetary health and other *problems not found in textbooks.* The platform would function as meeting place and catalyst for teachers who wish to organize such meetings.

<u>*Decision support systems*</u> - Participants suggested using (clinical decision) support and electronic prescribing systems for educational purposes. Medical students appear to be more comfortable with the therapeutic decision-making process than with the practical aspects of prescribing, and participants suggested that students should be trained "in the scribing bit of prescribing" [participant from UK(1)], using electronic prescribing systems. Ideally, these systems should show realistic decision support alerts so that students learn to react to prescribing red flags. Several participants were already training students in the sandbox environment of their electronic patient files and stated that making such a resource available for international use would have to account for local/national differences in these systems. Other suggestions included standalone polypharmacy tools, such as an interaction checker. As pointed out, these systems already exist and are helpful in teaching students about drug-drug interaction and how to interpret alerts. The participants also suggested creating similar tools regarding the safety of medication during pregnancy and lactation, and identifying adverse drug reactions on the basis of patient symptoms.

Themes related to resource and faculty development

Repository of exam questions and other reusable materials - Participants suggested keeping existing teaching materials in online repositories so that they can directly re-use them in their own teaching or use as a source of inspiration. They suggested collecting knowledge-oriented and case-based exam questions (including rubrics), slides of lectures, videos and figures. Additionally, because "most students only like to learn the minimum of minimum" [Participant from Serbia], participants proposed collecting web links to further reading materials for the more interested students.

Teaching the teachers - The top-ranking suggestion in the first meeting was for so-called teach the teacher materials. In the other meetings, this resource was discussed in relation to international differences and the digital readiness of teachers. Teaching teachers how to use problem-based learning was considered most important because there are relatively few teachers, and problem-based learning is more time intensive (and therefore costly) than traditional teaching. Moreover, teachers are often unwilling to change their way of teaching, because "they think they know it all" [participant from Malta] and are too busy to do so. Participants who experienced a shortage of teaching colleagues agreed that an international teach-the-teacher course on problem-based learning may help to attract more teachers or enable pharmacists and other paramedical professionals to qualify to teach CPT. Keeping up-to-date with the newest teaching innovations was considered essential, and the platform should keep an overview of new innovations. Additionally, participants would like a forum or Twitter-like discussion board so that they could ask each other for help.

Formularies - Lastly, participants discussed the need to focus our efforts on the most common diseases and/or the most commonly prescribed drugs. A European reference should be established for the most important drugs that medical students should know about. The participants believed that such a list would easily contain 200–300 drugs, which they deemed too many. Therefore, they suggested to include ways to extract information into personalized formularies with fewer drugs. The Spanish and English P-drugs app (and website) already exist, and this app could be easily translated and made available to other countries.

DISCUSSION

This study marks an important step in improving and harmonizing CPT education. It provides a clear and prioritized overview of the teaching resources European CPT teachers need and helps the community with practical ideas for the creation of these resources. The open (free to reuse, adapt, and redistribute) distribution of these resources on EurOP^{2}E will likely help to make high quality problem-based CPT education accessible for all.

Comparison of our findings with those of an earlier overview of digital educational resources used for prescribing education[7] shows that many of the proposed resources already exist in a similar form. However, with few exemptions (e.g. a repository of pharmacological illustrations, which is available as the *teaching resource centre* via http://trc-p.nl), such resources are restricted to local universities and not known or available to the participants. This shows how little CPT educators currently collaborate and emphasizes that EurOP²E should not only be about creating new resources, but also about making existing ones openly available. The list of suggestions will probably change once CPT educators have become more accustomed to collaborating and sharing materials, and EurOP²E will have to be dynamic towards this.

When we compare the learning outcomes mentioned in this study to the previously established list of key learning outcomes for CPT education published in 2017[8], we see a remarkable new interest for overprescribing and the impact of pharmaceuticals on planetary health (as well as much emphasis on the potentially mitigating effects of non-pharmacological interventions and deprescribing). The Association for Medical Education in Europe (AMEE) has recently published a global, collaborative, representative, and inclusive vision on how to educate an interprofessional workforce that can provide sustainable healthcare and promote planetary health[9]. The Association recommends improving faculty engagement and development[9,10]. Therefore, we suggest that standpoints be established collaboratively and teach-the-teacher materials and (templates for) specific lessons developed and then shared via EurOP²E[11]. A similar approach may be viable for other topical/ethical issues that were mentioned in this study, such as race-based medicine[12], gender inequality in the medical literature, and working with the pharmaceutical industry.

The COVID-19 pandemic forced medical educators to abruptly switch to online teaching. While this has brought challenges, such as student engagement and focus, the pandemic has also been described as the "long-awaited and much-needed catalyst for a new online teaching era in medical education"[13]. This silver lining is particularly apparent for interprofessional education, partly because of positive experiences gained in the interprofessional anti-COVID approach[14], but also because experience with online education has made it much easier to bring students (and healthcare workers) of different professions together. The goal of interprofessional education is to learn with, from, and about each other to improve collaboration and the quality of care[15]. For prescribing education, this usually means pharmacy students and medical (and/or non-medical prescribing) students learning together[16,17]. Although the participants suggested facilitating this type of interprofessional education via EurOP²E, they also thought that contact among international students would lead to an understanding/awareness about international differences in guidelines, medicine regulations, and prescribing attitudes. These very differences have previously been described as major barriers to international collaboration[6]. While these differences may indeed reduce the applicability of existing resources and exam questions, this could be overcome by making the teaching materials adaptable and/or aimed at common elements of prescribing education (e.g. pharmacokinetics and dynamics). Moreover, identifying and discussing international differences may raise awareness of context-based medicine and that there is not necessarily one correct prescribing solution.

Providing learning experiences for teachers was another theme identified in this study. The overall goal of EurOP^{2}E is to help teachers improve their teaching practice. While this may in itself be viewed as a teach the teacher activity, the results of this study have helped us realize that the actual teaching of teachers should be viewed as one of the means to this goal. Unfortunately, it can be a challenge to motivate professionals to adopt new techniques/methods and therefore attention should be paid to good practice in faculty development[18,19]. Unlike institutional faculty development programmes, which often use external motivators (i.e. promotion on the academic ladder), EurOP^{2}E will have to appeal to the intrinsic motivation of teachers. Being mindful of the principles of the self-determination theory may help to do so[20,21]. However, the participants also thought that high-quality teach-the-teacher courses would help to attract new CPT teachers, but this remains to be seen. Depending on the need, teach-the-teacher courses could cover generic skills and learning theories, such as courses on problem-based learning and what is new in CPT education or about more specific topics.

This study had some limitations. First, about half of the sent out invitations to participate remained unanswered and because of that we did not include participants from some of the larger EU member states (i.e. France, Portugal and Hungary). However, we believe this is not a problem because we gathered sufficient data from the other countries and have no reason to assume intercountry differences. Moreover, we view the results as a starting point to a dynamic list of resources to create and new suggestions remain welcome. Secondly, because the participants were all busy professionals, we thought that a time investment of approximately 90 minutes was the most we could ask of them. In retrospect, this was a bit short because in three of the four meetings we had to stop the second phase before all suggestions had been made and slightly rushed the third phase. This was adequately handled by allowing the participants to add all suggestions that they felt were crucial. Because we continued interviewing groups until no new suggestions came to light, we are confident that we captured all relevant ideas. Thirdly, we noted before that not all suggestions were truly new, and we recognize that this may be due to priming. For example, many of the participants had also participated in a Delphi study aimed at developing a European list of essential medicines[22], which may explain how this came to be a theme in this study.

CONCLUSION

In conclusion, the most urgently needed online problem-based educational resources for clinical pharmacology and therapeutics related to the learning outcomes, format of teaching and resource and faculty development. Depending on the theme, the function of EurOP^{2}E will vary from supporting and facilitating international communication and collaboration to providing teach-the-teacher materials and/or (initiating) the collaborative production of ready-to-use teaching materials. We identified the planetary health impact of prescribing as a new learning outcome for clinical pharmacology and therapeutics education.

METHODS

This study used the nominal group technique (NGT) combined with thematic analysis of the discussions. NGT is a consensus-building technique wherein participants have an equal and uninterrupted opportunity to present their expert opinions and ideas to the group[23]. After all participants have presented their ideas, the group then discusses, alters, scraps, or combines ideas. Thereafter, the participants independently and anonymously rank these ideas. We chose this method because it leads to a clearly prioritized list of suggestions and prevents certain more vocal participants from promoting their ideas or dominating the meeting, and, compared with other consensus methods (e.g. Delphi), enables participants to present their ideas in detail[23]. We additionally performed a thematic analysis of the group discussions. This allowed us to gain a more conceptual understanding of the nominal results and thus identify commonalities between the individual group discussions. The original ranking results helped us in prioritizing the identified themes.

Study participants

Members of the Network of Teachers in Pharmacotherapy education (NOTIP), which consists of 400+ teachers in pharmacology and CPT from all EU countries, United Kingdom, Norway, and Serbia, were asked to participate in the study. We used a purposive sampling whereby one or two NOTIP members per country were selected on the premise that they were active in teaching innovation and probably motivated to participate, and/or had participated in previous research studies. In total, 39 participants were asked to participate via e-mail. Invitees were free to forward the e-mail to one or more colleagues if they deemed them to be more qualified to participate. Non-responders received one reminder after 2 weeks.

Data collection

Four meetings were scheduled in October 2021, with the possibility to have additional meetings if insufficient data were collected. The meetings were held online via Microsoft Teams in groups of 4-6 participants. After a brief presentation on the study aims and a round of introductions, the interviews continued in four phases: 1) Participants silently and privately organized their thoughts for 5 minutes; 2) One by one (in a round-Robin fashion), participants presented their ideas; 3) group discussions were held with a view to clarifying and combining the ideas from step 2; 4) The participants anonymously voted for their top-5 of remaining ideas. For the second phase, we continued until all participants ran out of ideas, or until (after a minimum of three full rounds) time demanded that we continued to the next phase, in which case all participants were given a last opportunity to present any crucial ideas. The meeting host recorded all ideas on a virtual flip-over (google Jamboard, http://jamboard.google.com) which was visible to all participants via screen-sharing. For the voting-phase, we used Mentimeter's (http://mentimeter.com) multi-voting question-type. To make the overall ranking, a participant's first choice was awarded 5 points, second choice 4 points etc. We concluded the meetings by sharing this overall ranking with the participants.

Three researchers were present for all meetings: MB was the host; BL provided technical assistance to participants and prepared and launched the voting system; JT observed, kept time, and double checked the host (intervened when necessary). Right after each meeting, the researchers discussed points of improvement for the next meetings and whether sufficient data had been collected. All meetings were audio and video recorded using Microsoft teams.

Data analysis

The voting results for the individual suggestions are presented as the average score per participant (sum of scores/number of participants) and ranked accordingly. When there was a tie, the number of participants that voted for a given suggestion decided the ranking. Additionally, we transcribed the recordings of the meetings verbatim and used a thematic analysis[24], whereby BL and MB together (through repeated reading of the transcripts and discussion) developed a final set of codes and initial themes in MAXQDA (standard 2020). Using these codes, they recoded all transcripts and independently reviewed the themes. In a meeting together with JT, they finalized and named the themes. Lastly, the remaining authors who are CPT teachers, provided feedback on the results. Six of the authors had also participated in the meetings, thus for them this was check of internal validity (member check). For the other five authors it was an external validation of the results. The consolidated criteria for reporting qualitative research (COREQ) checklist[25] guided the reporting of this study.

Reflexivity

MB is a doctor and PhD student in the EurOP^{2}E project, with 4 years of experience in research in CPT education and teaching pharmacotherapy. JT is a PhD-grade associate professor in pharmacotherapy with over 17 years of experience as teacher and coordinator of pharmacotherapy education and research in CPT education. BL is a medical student and student-teacher in pharmacotherapy who joined the research team for his master's thesis. All other authors are (associate) professors in clinical pharmacology and part of the international EurOP^{2}E consortium. The research team had a constructivist approach[26] to the thematic analysis and viewed the results in light of the WHO Guide to Good Prescribing's Six-step method for problem-based pharmacotherapy education[27] and the framework for the EuroP^{2}E platform[6].

DATA AVAILABILITY

The datasets generated during and/or analysed during the current study are available in the Open Science Framework repository, https://osf.io/62u8a/ [28].

ACKNOWLEDGMENTS

We would like to thank A. de la Croix and R.A. Kusurkar. Their knowledge of and experience with qualitative research has been of great help in setting up this study and writing the paper. This study was funded by the European Union under Erasmus + grant 2020-1-NL01-KA203-083098.

AUTHOR CONTRIBUTIONS

Conceptualization: M.J.B., B.J.L., M.C.R., P.P., R.L., E.J.S., T.C., J.N.C., L.D., F.d.P., C.K., J.v.S., M.A.v.A. and J.T.; Formal Analysis: M.J.B., B.J.L. and J.T.; Investigation: M.J.B., B.J.L. and J.T.; Methodology: M.J.B., B.J.L., M.C.R., P.P., R.L., E.J.S., T.C., J.N.C., L.D., F.d.P., C.K., J.v.S., M.A.v.A. and J.T.; Project administration: M.A.v.A. and J.T.; Supervision: M.A.v.A. and J.T.; Visualization: M.J.B.; Writing—original draft: M.J.B., B.J.L. and J.T.; Writing—review and editing: M.J.B., B.J.L., M.C.R., P.P., R.L., E.J.S., T.C., J.N.C., L.D., F.d.P., C.K., J.v.S., M.A.v.A. and J.T.

COMPETING INTERESTS

The authors declare no competing interests

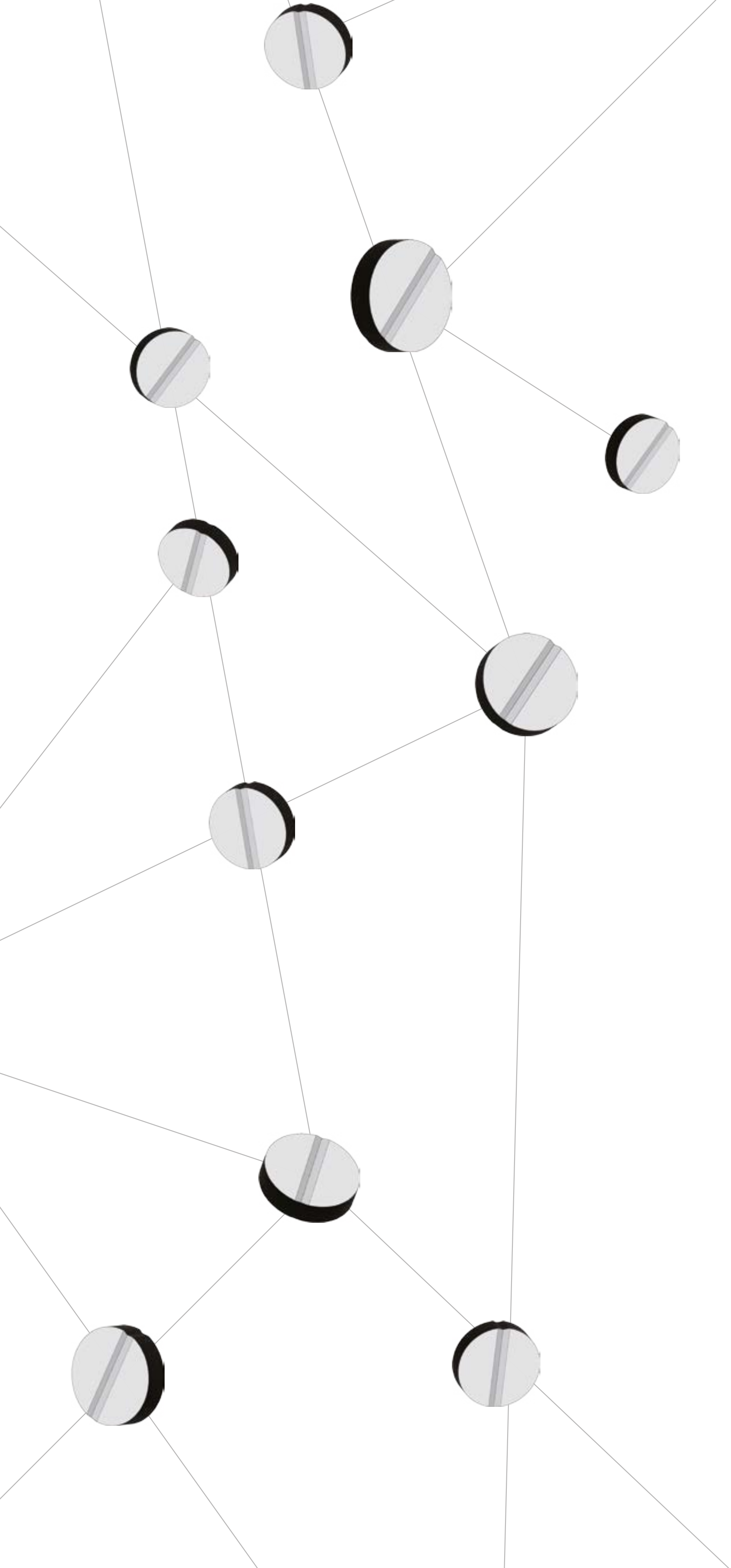
ETHICAL APPROVAL

The medical ethics board of Amsterdam UMC, VU University decided that this study did not fall within the scope of the Medical Research Involving Humans Act (2021.0501), and the Ethics Review Board of the Dutch Society for Medical Education (NVMO) approved this study (2021.5.3). All participants provided written informed consent to take part in this study.

REFERENCES

1. Brinkman DJ, Tichelaar J, Okorie M, et al. Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries. *Clin Pharmacol Ther*. Nov 2017;102(5):815-822. doi:10.1002/cpt.682
2. Heaton A, Webb DJ, Maxwell SR. Undergraduate preparation for prescribing: the views of 2413 UK medical students and recent graduates. *Br J Clin Pharmacol*. Jul 2008;66(1):128-34. doi:10.1111/j.1365-2125.2008.03197.x
3. Brinkman DJ, Tichelaar J, Schutte T, et al. Essential competencies in prescribing: A first european cross-sectional study among 895 final-year medical students. *Clin Pharmacol Ther*. Feb 2017;101(2):281-289. doi:10.1002/cpt.521
4. Dornan T, Ashcroft D, Heathfield H, et al. An in-depth investigation into causes of prescribing errors by foundation trainees in relation to their medical education: EQUIP study.
5. Bakkum MJ, Tichelaar J, Wellink A, Richir MC, van Agtmael MA. Digital Learning to Improve Safe and Effective Prescribing: A Systematic Review. *Clin Pharmacol Ther*. Dec 2019;106(6):1236-1245. doi:10.1002/cpt.1549
6. Bakkum MJ, Richir MC, Papaioannidou P, et al. EurOP^{2}E–the European Open Platform for Prescribing Education, a consensus study among clinical pharmacology and therapeutics teachers. *European Journal of Clinical Pharmacology*. 2021:1-10.
7. Bakkum MJ, Tichelaar J, Papaioannidou P, et al. Harmonizing and improving European education in prescribing: An overview of digital educational resources used in clinical pharmacology and therapeutics. *Br J Clin Pharmacol*. Mar 2021;87(3):1001-1011. doi:10.1111/bcp.14453
8. Brinkman DJ, Tichelaar J, Mokkink LB, et al. Key Learning Outcomes for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study. *Clin Pharmacol Ther*. Aug 2018;104(2):317-325. doi:10.1002/cpt.962
9. Shaw E, Walpole S, McLean M, et al. AMEE Consensus Statement: Planetary health and education for sustainable healthcare. *Medical Teacher*. 2021/03/04 2021;43(3):272-286. doi:10.1080/0142159X.2020.1860207
10. Tun S, Wellbery C, Teherani A. Faculty development and partnership with students to integrate sustainable healthcare into health professions education. *Medical Teacher*. 2020/10/02 2020;42(10):1112-1118. doi:10.1080/0142159X.2020.1796950
11. Bakkum MJ, Richir MC, van Agtmael MA, Tichelaar J. Sustainable medicines use in clinical practice-It is time to help the teacher. *Br J Clin Pharmacol*. Jul 2022;88(7):3030-3031. doi:10.1111/bcp.15340
12. Bakkum M, Verdonk P, Muntinga M, Tichelaar J. Onderscheid maken op basis van huidskleur? *Nederlands Tijdschrift voor Geneeskunde*. 2021;165:D5835.
13. Stoehr F, Müller L, Brady A, et al. How COVID-19 kick-started online learning in medical education—The DigiMed study. *PLOS ONE*. 2021;16(9):e0257394. doi:10.1371/journal.pone.0257394
14. Langlois S, Xyrichis A, Daulton BJ, et al. The COVID-19 crisis silver lining: interprofessional education to guide future innovation. *Journal of Interprofessional Care*. 2020/09/02 2020;34(5):587-592. doi:10.1080/13561820.2020.1800606
15. Hammick M, Olckers L, Campion-Smith C. Learning in interprofessional teams: AMEE Guide no 38. *Medical Teacher*. 2009/01/01 2009;31(1):1-12. doi:10.1080/01421590802585561
16. Reumerman MO, Richir MC, Domela Nieuwenhuis PM, et al. The clinical and educational outcomes of an inter-professional student-led medication review team, a pilot study. *European Journal of Clinical Pharmacology*. 2021/01/01 2021;77(1):117-123. doi:10.1007/s00228-020-02972-3

17. Sultan R, van den Beukel TO, Reumerman MO, et al. An Interprofessional Student-Run Medication Review Program: The Clinical STOPP/START-Based Outcomes of a Controlled Clinical Trial in a Geriatric Outpatient Clinic. *Clinical pharmacology and therapeutics*. Apr 2022;111(4):931-938. doi:10.1002/cpt.2475
18. McLean M, Cilliers F, Van Wyk JM. Faculty development: Yesterday, today and tomorrow. *Medical Teacher*. 2008/01/01 2008;30(6):555-584. doi:10.1080/01421590802109834
19. Steinert Y, Mann K, Anderson B, et al. A systematic review of faculty development initiatives designed to enhance teaching effectiveness: A 10-year update: BEME Guide No. 40. *Medical teacher*. 2016;38(8):769-786.
20. ten Cate OTJ, Kusurkar RA, Williams GC. How self-determination theory can assist our understanding of the teaching and learning processes in medical education. AMEE Guide No. 59. *Medical Teacher*. 2011/12/01 2011;33(12):961-973. doi:10.3109/0142159X.2011.595435
21. van der Burgt SME, Kusurkar RA, Wilschut JA, Tjin A Tsoi SLNM, Croiset G, Peerdeman SM. Medical specialists' basic psychological needs, and motivation for work and lifelong learning: a two-step factor score path analysis. *BMC Medical Education*. 2019/09/05 2019;19(1):339. doi:10.1186/s12909-019-1754-0
22. Donker E, Brinkman D, Richir M, et al. European List of Essential Medicines for Medical Education: a protocol for a modified Delphi study. *BMJ Open*. 2021;11(5):e045635. doi:10.1136/bmjopen-2020-045635
23. Humphrey-Murto S, Varpio L, Gonsalves C, Wood TJ. Using consensus group methods such as Delphi and Nominal Group in medical education research. *Medical Teacher*. 2017/01/02 2017;39(1):14-19. doi:10.1080/0142159X.2017.1245856
24. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative Research in Psychology*. 2006/01/01 2006;3(2):77-101. doi:10.1191/1478088706qp063oa
25. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007;19(6):349-357. doi:10.1093/intqhc/mzm042
26. Strauss A, Corbin J. *Basics of qualitative research techniques*. Citeseer; 1998.
27. De Vries T, Henning RH, Hogerzeil HV, Fresle D, World Health Organization. *Guide to good prescribing: a practical manual*. 1994.
28. Bakkum MJ. Novel teaching resources for the European Open Platform for Prescribing Education (EurOP2E) – a nominal group technique study. http://osf.io/62u8a



6

CAN STUDENTS CREATE THEIR OWN EDUCATIONAL ESCAPE ROOM? LESSONS LEARNED FROM THE OPIOID CRISIS ESCAPE ROOM

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2021, oct; 15;31(6):1739-1745
doi: 10.1007/s40670-021-01425-5

ABSTRACT

Educational escape rooms (EERs) are live-action, team-based games used to teach content-related and generic knowledge and skills. Instead of students just playing the EER, we believed that giving them the opportunity to create their own EERs would augment the learning effects of this teaching method. We report on the feasibility, evaluation and lessons learned of our assignment on an opioid epidemic based EER. This original teaching method appealed to most students, but the workload was evaluated to be too high. Our lessons learned include the need for sufficient (extrinsic) motivation; careful explanation of the assignment and small group sizes.

INTRODUCTION

The prescription and misuse of opioids has become a problem in many countries[1,2]. In order to mitigate opioid abuse, we thought it important to teach students about the dangers of opioid dependency and the important preventive role of prescribers. Given the topicality and international relevance of the subject, we aimed to create an engaging and widely usable learning experience for undergraduate and graduate medical students, nurses, non-medical prescribers etc. that could be easily shared (as open educational resource) with colleagues in the international network of teachers in pharmacotherapy via the EurOP^{2}E platform (www.prescribingeducation.eu).

Escape rooms are live-action, team-based games in which players discover clues, solve puzzles, and accomplish tasks in one or more rooms in order to achieve a specific goal (usually escaping from the room) in a limited amount of time[3]. There are more than 10,000 recreational escape rooms worldwide[4]. The success of these games has prompted teachers in all levels and types of education, including medical education, to recreate these games for educational purposes[5]. Educational escape rooms (EERs) are based on experiential, game-based, and team-based learning principles to increase the intrinsic motivation to learn. This is best explained by the self-determination theory (SDT), which states that humans are self-determined to grow and learn and that this growth is fostered by fulfilling three psychological needs: autonomy, competence and relatedness[6]. Gamified, team-based learning methods, such as EERs are attractive because they allow students to satisfy these three needs – autonomy via freedom of choice (e.g. to approach puzzles in multiple ways); competency via direct feedback on the progress (e.g. locks that open) and relatedness via a common cause (to escape the room) that requires teamwork[7]. A greater intrinsic motivation is associated with better learning and conceptual understanding[6].

The use of EERs in medical and pharmacy education is rising for a variety of purposes[7], ranging from team-building exercises[8] and research[9] to learning and assessing knowledge, skills and attitudes[10-12]. A recent review found that while EERs appeal to students, helping them to consolidate existing knowledge and skills, they appear to be less effective for teaching new concepts[13]. Another often reported drawback of EERs is that they are challenging and labor-intensive to produce. In an international survey among creators of recreational escape rooms (n=175), almost 50% found creating puzzles and balancing the difficulty of puzzles to be "very challenging"[3], as is the case for EERs[14]. We believed that we could use these apparent drawbacks of EERs to our advantage. Asking the students to create the tasks and puzzles for their own EER would provide them with a challenging assignment that could improve the learning effects whilst possibly limiting the time commitment of teaching staff. According to the SDT principles, we aimed to give the students full autonomy in the development of the puzzles, make this a team exercise and enhance the purpose of this assignment beyond that of a single lesson. Therefore, we implemented the following interrelated aspects that were previously shown to enhance motivation in student-led education (SLE): an authentic context with authentic responsibility (to create a real educational resource for use in national and international pharmacotherapy education) and collaboration between students and professionals[15,16]. This is alike our previous and ongoing student-led education (SLE) projects, wherein students run several outpatient clinics[17,18], a pharmacovigilance program[19] and a medication review team[20] - all with supervision but full responsibility for the actual care of patients. These SLE projects were shown to have great learning effects, as well as clinical results and consistently very good evaluations[17-21].

6

With the goal to inform and inspire teachers, this article describes the pedagogical background, feasibility, implementation, evaluation and lessons learned from our assignment for year 3 medical students at the Amsterdam University Medical Center to create an EER about the opioid epidemic.

ACTIVITY

Learning goals

Coinciding with the development of the EER, the Dutch Ministry of Health started a program to reduce inappropriate use of opioids[22]. This program is led by the Dutch Institute for Rational Use of Medicines (IVM) in close collaboration with scientific societies of prescribers and pharmacists. With the aim of creating a uniformly usable EER, we collaborated with the IVM to establish learning goals for the EER (and the assignment to create the EER), namely, 1) Recognizing and treating opioid addiction; 2) Preventing legal and illegal access to prescription opioids; 3) Patient education on safe use of opioids; 4) Treating a patient with an acute opioid overdose; and 5) Safe and effective prescribing of opioids.

General design of the EER

The EER was path-based according to the definition by Nicholson[3], meaning that several (simultaneously playable) sets of puzzles and tasks ("paths") provided essential clues for the final ("meta") puzzle (***figure 1***). Only by completing all the puzzle paths, the players received sufficient information to solve the meta-puzzle and then escape the room. In line with the intrinsic integration theory of Van der Linden et. al[23], the paths and meta-puzzle each taught information related to one of the learning goals. In a path-based EER, the most effective strategy to escape the room is to divide the work (e.g. student A tries to solve path 1 while student B works on path 2 etc.), therefore a drawback of this design is that individual students do not play all the paths (and learn about all learning goals).

The assignment to create the EER

Thirty-nine year 3 (pre-clinical, bachelor) medical students, who were taking an elective course on internal medicine at the Amsterdam Medical Center, VU University, were (alphabetically) divided into three groups (n=13). Each group was asked to make a prototype EER. The assignment was scheduled over a 4-week period and started with a 15 minute plenary briefing during which the students received information about the general design of the EER (see above) and plan for the assignment. The groups of students were subdivided into four teams (3-4 students) and each team was given the task to create one of the paths (***figure 1***). The teachers (M.B. and J.C., two junior doctors who are PhD students and teachers in clinical pharmacology) developed the meta-puzzles (one for each prototype EER). During the four weeks, students could schedule guidance sessions with one of the teachers, for example to discuss whether a task would be too difficult or if they could use specific items (ranging from simple office supplies to food dye to be used in IV-bags). The teachers forbade nothing, but sometimes motivated students to come up with more creative puzzles or more practical solutions. On account of the late deadline (day before playing the rooms), the teachers were unable to check the puzzles for inaccuracies. Teams were free to shape their paths, for example they could create one large puzzle or a sequence of multiple smaller puzzles – the only requirement was that the path could be solved in approximately 10 minutes. Students were encouraged to create cross-linking hints with other teams in their group (***figure 1***), meaning that one team's puzzle would provide a (non-essential but helpful) clue towards solving the other team's path. The students were free to decide how to give substance to the learning goals, and could use any trustworthy source of information at their disposal. In terms of difficulty, the students were told that the ability to progress in the puzzle path should not

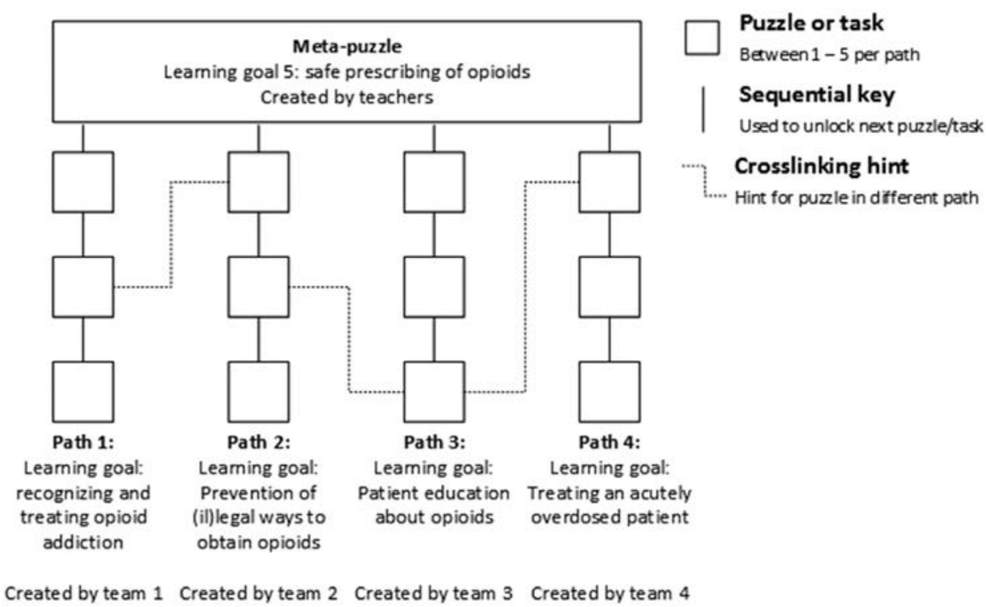


Figure 1. Design schematic. The puzzle was path-based according to the definition by Nicholson, meaning that several (simultaneously playable) sets of puzzles and tasks ("paths") would provide essential clues for the final ("meta") puzzle . Each of the paths and the meta-puzzle were associated with one of the learning goals

be dependent on prior knowledge or experience, but rather on the ability to deduce or find essential information. This was done to make the EER fun and challenging for a wide audience with various backgrounds and levels of education. Lastly, because we wanted the game to be portable and easy to share internationally, students could only use small, every-day, and preferably digital materials (such as padlocks, QR-codes etc.) They were not given a fixed budget but could submit a shopping list of reasonably priced materials for the teachers to acquire. To further increase student motivation, a professional jury (with the dean of medicine and a representative from the IVM) was selected and the team with the most creative, challenging, and educational path was given a visit to a recreational escape room as prize. Examples and a video-impression of the assignment can be viewed at http://www.prescribingeducation.eu/opioid-crisis-escape-room

Playing the EERs

On the last day of the assignment, the prototypes were set up in three separate classrooms. The groups of students rotated the classrooms where they played and tested the EERs. Each rotation lasted 40 minutes, 30 minutes to escape the room and 10 minutes to reset the puzzles and have short debrief. In their "own" room, students did not play (as they knew the answers). Instead they explained their path to the jurors. Before playing the EER, most chairs and tables were set aside and the puzzles were installed across the room by the teachers. Items such as clocks and bins were left in place and at times used as hiding places for parts of a puzzle. No "red herrings" (false clues or objects with the purpose to distract) were used. The EERs were themed around the (rather spooky) "Poppy Fields Nursing Home" and the task of the meta-puzzle was to prescribe the correct treatment (suitable alternative to an opioid analgesic) for the right patient before time ran out. The four puzzle paths revealed which patient was to be treated, a list of patients problems, the current medication of the patient and a (mock) treatment guideline – all of this information was necessary to solve the meta puzzle. The prescription had to be entered in a javascript-based computer program, which validated the answer and showed a congratulatory message with the time it took to "escape" the room. The door was never actually locked. Other than the slightly decorated puzzle items, no decorations were used to make the classrooms look like a nursing home. The EERs were played by a full group (n=13) of students at a time. Cellphones were allowed for specific purposes only, for example to scan QR-codes or to send or receive clues via text message. The teacher monitored time and provided hints as necessary. For some puzzle-paths teachers were required to act as game masters, for example, asking questions in a quiz-like setting.

Ethical considerations

Playing and creating the room were ungraded assignments, and the opioid-themed learning goals were not part of the final exam. The assignment was part of the normal curriculum of the elective course and under Dutch law the evaluation does not fall within the Medical Research Involving Humans Act (WMO), therefore no ethical approval was required. Participation in the assignment was compulsory but the evaluation was voluntary. Students who appear in the promotional video provided informed consent to our communications department

RESULTS

Students' evaluations

Thirty-eight students answered the anonymous voluntary survey about playing the EER; 2 failed to complete the survey about creating the room. Results for the 5-point Likert-type questions about *creating* the escape room are shown in ***table 1***. 47.2% of students agreed (or completely agreed) that they liked this assignment and 44.4% (completely) agreed that they learned a lot. 56.9% (completely) agreed that the assignment was too much work, only 31.9% did not mind this because of the learning effects. Recurring themes on the open-ended question "what did you learn from *creating* the room?" were opioid-related learning goals (e.g. "The importance of preventing an opioid crisis, treatment of acute overdoses, and rehab medicine", 7 times); creative thinking (4 times); and teamwork (2 times). Freedom and creative thinking were the most (10 times) appreciated aspects of the assignment, followed by creating a puzzle (4 times). On the last question "how could we improve the assignment?", 8 students answered that clearer instructions should be provided, 4 that too little time was available, 2 that the overall workload was too high,

Table 1. Students' evaluations about creating the EER (n=36)

	Completely disagree (%)	Disagree (%)	Neutral (%)	Agree (%)	Completely Agree (%)
I liked creating the EER	-	16.7	36.1	27.8	19.4
I learned a lot from creating the EER	2.8	33.3	19.4	36.1	8.3
The opioid-related learning goals are now clear to me	-	6.9	34.7	5-	8.3
The assignment is better than a traditional lecture or practical	2.8	15.3	25.0	37.5	19.4
Creating the EER was too much work	-	27.8	15.3	45.8	11.1
I did not mind the work, because I learned a lot	8.3	38.9	20.8	20.8	11.1
The assignment was clearly explained	2.8	19.4	44.4	30.6	2.8
It was nice to have support from the teacher	-	-	25.0	5-	25.0
The quality of the support was good	-	11.4	25.7	51.4	11.4
Next year, the course should have a similar assignment	5.6	19.4	25.0	25.0	25.0
The plan to use my work in an international EER was motivating	2.8	16.7	13.9	30.6	36.1
Creating the EER was one of the better assignments in the course	2.8	19.4	30.6	30.6	16.7

EER = educational escape room. 36 students answered questions about creating the EER, 38 about playing the EER. When two adjacent answers were provided for one statement (e.g. neutral and agree), each was counted as half.

and 2 that the timing in relation to other assignments was poor. While only 1 student made a written comment, we heard that students were not highly motivated because the assignment was not graded.

Results for the 5-point Likert-type questions about *playing* the escape room are shown in ***table 2***. 80.3% agreed (or completely agreed) that they liked playing the escape room, 26.3% agreed that they learned a lot from playing the room. 67.1% of the students believed the EERs to be a little too difficult. The majority of students (60.5%) believed that the rooms were suited for 7-9 players at a time. On the questions "what did you learn from *playing* the room?", 12 students answered teamwork, 10 opioid-related learning goals, and 2 performing under pressure; however, 4 said they had learned "nothing" or "too little", with explanation that the group was too large. Aspects students liked about playing the room were the actual puzzles (8 times), teamwork and brainstorming together (6 times), and the creative and original teaching method (4 times). On the question "what can we improve?", 11 students answered problems with specific puzzles, such as them being too difficult, too basic (simple crosswords), or containing errors. Four students answered that smaller groups would improve the experience. Lastly, 4 students disliked how independent the four puzzle paths were and suggested improving connections between these paths.

DISCUSSION

Overall, this invention provided a fun, interactive, and stimulating way to teach students about the dangers of prescription opioid abuse and how to prevent it. The jurors were impressed by the engaging puzzles the students had created, some of them not unlike those in recreational escape rooms. These puzzles provide a strong foundation for the EER that we aim to further develop with the students, for use in national and international education. The students' evaluations, however, were not uniformly positive, leaving room for improvement for future assignments and for anyone aiming to implement a comparable teaching method.

First, we had overestimated the motivation of the students in relation to the workload. We expected the fun, creative, and original method of learning would be motivating in itself, combined with the competitive elements and the fact that the students would be contributing to a lasting, internationally used educational experience. While almost two-thirds of students agreed that the international plans for the EER helped motivate them, not all the students seemed to appreciate the potential impact of their work. We even overheard them discussing how the teachers were using them to do their (the teachers') work. This feedback surprised us, because it has never been mentioned in our student-run clinics, which also rely heavily on context-based learning with real responsibilities[15,16]. Two important differences may explain this discrepancy. First, for medical students, treating a patient is probably a context they can relate to, in contrast to creating an educational experience. Secondly, the clinics are run by students who are actively looking for learning opportunities, either during their clinical rotations, or because they have

Table 2. Students' evaluations about playing the EER (n=38)

	Completely disagree (%)	Disagree (%)	Neutral (%)	Agree (%)	Completely Agree (%)
I liked playing the EER	-	-	19.7	59.2	21.1
I learned a lot from playing the EER	-	30.3	43.4	22.4	3.9
The opioid-related learning goals are now clear to me	2.7	18.9	37.8	36.5	4.1
Playing the EER is better than a traditional lecture or practical	2.6	18.4	31.6	28.9	18.4
The students' puzzles were of sufficient quality	5.3	5.3	43.4	38.2	7.9
The teachers' puzzles were of sufficient quality	-	-	10.5	57.9	31.6
Next year, the course should have an EER to play	-	10.5	28.9	34.2	26.3
Playing the EER was one of the better assignments in the course	5.3	15.8	22.4	25.0	31.6
	Too easy (%)	**A little too easy (%)**	**Right difficulty (%)**	**A little too difficult (%)**	**Too difficult (%)**
How difficult was playing the EER?	-	-	26.3	67.1	6.6
	5 or less players (%)	**5-6 players (%)**	**7-8 players (%)**	**8-9 players (%)**	**10 or more players (%)**
How many players can the rooms accommodate?	-	23.7	31.6	28.9	15.8

signed up voluntarily. However, this assignment was compulsory, which possibly explains why students found the workload high and poorly planned in relation to other, graded, learning activities. We believe that motivation, and not the actual limited workload of 8–12 hours, was the problem. We suggest that, in the future, the assignment should be graded or that its learning objectives should be constructively aligned with a test.

Secondly, given the problem of motivation, it is not surprising that some students put minimal effort into the assignment, handing in basic crosswords and unclear or even unsolvable puzzles. This directly affected the learning experience of other students, who were annoyed by the poor design and lack of progress. Students also disliked the lack of cohesion between the different paths. While we aimed to improve this by introducing cross-linking hints, the assignment was difficult to properly explain and, in hindsight, it was insufficiently understood by the students.

Lastly, due to a fixed schedule, we were forced to play and test the EERs with relatively large groups of 13 students. This meant that individual students played less than half of the available puzzles, reducing the experience and learning effects of the EER. The majority of students believed that the EERs were suitable for maximally 7–9 players.

From a teacher's perspective, the assignment was also challenging. Tutoring the teams, getting their shopping lists in time, buying the diverse items on these lists, properly understanding all paths, joining them together in playable prototypes, and creating the meta-puzzles were all time-consuming (estimated to be at least two full-time weeks for a single teacher) and at times stressful activities. That said, the teachers found it very fulfilling that three playable prototypes were created.

While the majority of students liked playing the EER, they were less positive about the educational yield of this part of the assignment. One of the biggest challenges of creating EERs is to balance the learning effects with fun. Puzzles that are packed with content are often quite dull (e.g. a quiz-like puzzle or crossword), whereas more creative puzzles tend to lose learning effects (e.g. time spent counting green and blue pills, is time not spent on the opioid-related learning goals). Both the students and teachers had difficulties to find this balance, and we believe that all puzzles need improvement and further testing before they can be used in the final EER. The limited educational yield, however, is a common critique of EERs[13,14]. In order to create the puzzles, students need a deeper understanding of the learning goals. Indeed, the students evaluated the learning effects of creating the room more positively. Therefore, we believe that adding the assignment to create the EER is a promising way to increment the learning effects of an EER whilst maintaining the positive effects of (playing) EERs.

This article shows the feasibility of having students create the tasks and puzzles for an EER. This novel teaching method was well-evaluated and improved the student-reported learning effects towards our opioid-related learning goals as compared to playing the EER. With minor modifications (see lessons learned), we believe that this method could provide a valuable addition to the teaching repertoire of healthcare teachers.

Limitations

Investigating the learning-effects of creating the EER in an objective (i.e. more than student-reported) manner was beyond the scope of this project and should be subject to further investigation.

Lessons learned

To our knowledge we are the first to publish about this promising teaching method. With the aim to assist teachers elsewhere in creating similar assignments, we have summarized our lessons learned:

1. Learning objectives for the assignment should have an authentic and relatable context.
2. Learning objectives should be paired with puzzle paths; limiting the number of paths may help to unite the puzzles into an EER.
3. It should be clear to the students why they are asked to create the puzzles and paths. That is to enhance the educational effects via peer-teaching.
4. The assignment should be properly explained and include background information on the effects and design of EERs, preferably with examples of educational puzzles.
5. The assignment should be constructively aligned in the course. Grading the activity could help to improve student motivation, especially if participation is compulsory.
6. Costs for materials can be kept low. However, the assignment may become costly in terms of man-hours.
7. Sufficient time should be given for the students to create the paths; early deadlines and sufficient coaching may help to avoid last-minute stress.
8. Team sizes during creating and playing the EERs should be kept small. This may make it logistically challenging to accommodate large numbers of students.

ACKNOWLEDGEMENTS

The authors would like to thank the students that participated in this project for their helpful evaluations and useful contributions to the escape room.

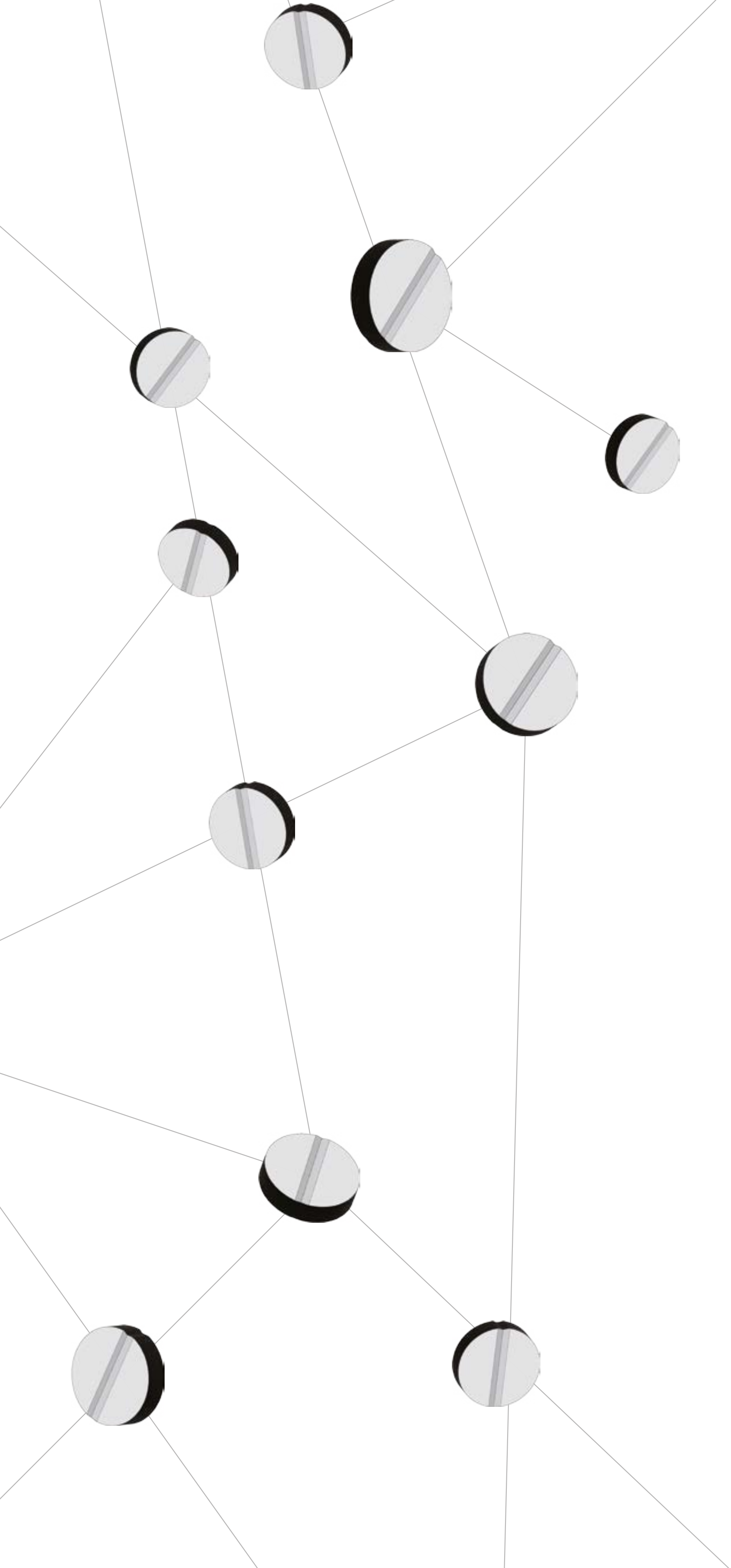
COMPLIANCE WITH ETHICAL STANDARDS

Funding: No funding was received for this study.
Conflict of interest: All other authors declared no competing interests for this work
Ethical Approval: Not required under Dutch law.
Informed consent: Not required for the evaluation; obtained for the video-impression.

REFERENCES

1. Smith BH, Fletcher EH, Colvin LA. Opioid prescribing is rising in many countries. *BMJ*. 2019;367:l5823. doi:10.1136/bmj.l5823
2. Skolnick P. The Opioid Epidemic: Crisis and Solutions. *Annual Review of Pharmacology and Toxicology*. 2018/01/06 2018;58(1):143-159. doi:10.1146/annurev-pharmtox-010617-052534
3. Nicholson S. Peeking behind the locked door: A survey of escape room facilities. 2015;
4. Solveprague.cz. How many escape rooms are there in the world? https://solveprague.cz/blog/2019/02/26/how-many-escape-rooms-are-there-in-the-world/
5. Veldkamp A, Daemen J, Teekens S, Koelewijn S, Knippels M-CPJ, van Joolingen WR. Escape boxes: Bringing escape room experience into the classroom. *British Journal of Educational Technology*. 2020;51(4):1220-1239. doi:10.1111/bjet.12935
6. Ten Cate TJ, Kusurkar RA, Williams GC. How self-determination theory can assist our understanding of the teaching and learning processes in medical education. AMEE guide No. 59. *Med Teach*. 2011;33(12):961-73. doi:10.3109/0142159x.2011.595435
7. Guckian J, Eveson L, May H. The great escape? The rise of the escape room in medical education. *Future Healthc J*. 2020;7(2):112-115. doi:10.7861/fhj.2020-0032
8. Gordon SK, Trovinger S, DeLellis T. Escape from the usual: Development and implementation of an 'escape room' activity to assess team dynamics. Article. *Currents in Pharmacy Teaching and Learning*. 2019;11(8):818-824. doi:10.1016/j.cptl.2019.04.013
9. Guckian J, Sridhar A, Meggitt SJ. Exploring the perspectives of dermatology undergraduates with an escape room game. Article in Press. *Clinical and Experimental Dermatology*. 2019;doi:10.1111/ced.14039
10. Caldas LM, Eukel HN, Matulewicz AT, Fernández EV, Donohoe KL. Applying educational gaming success to a nonsterile compounding escape room. Article in Press. *Currents in Pharmacy Teaching and Learning*. 2019;doi:10.1016/j.cptl.2019.06.012
11. Eukel HN, Frenzel JE, Cernusca D. Educational Gaming for Pharmacy Students - Design and Evaluation of a Diabetes-themed Escape Room. *American Journal of Pharmaceutical Education*. 2017;81(7):1-5.
12. Zhang XC, Diemer G, Lee H, Jaffe R, Papanagnou D. Finding the 'QR' to Patient Safety: Applying Gamification to Incorporate Patient Safety Priorities Through a Simulated 'Escape Room' Experience. *Cureus*. Feb 5 2019;11(2):e4014. doi:10.7759/cureus.4014
13. Veldkamp A, van de Grint L, Knippels MCPJ, van Joolingen WR. Escape education: A systematic review on escape rooms in education. *Educ Res Rev-Neth*. Nov 2020;31 doi:ARTN 10036410.1016/j.edurev.2020.100364
14. Fotaris P, Mastoras T. Escape rooms for learning: A systematic review. Academic Conferences and publishing limited Denmark; 2019:
15. Schutte T, Tichelaar J, Donker E, Richir MC, Westerman M, van Agtmael MA. Clarifying learning experiences in student-run clinics: a qualitative study. *BMC medical education*. Oct 26 2018;18(1):244. doi:10.1186/s12909-018-1352-6
16. Tichelaar J, van Kan C, van Unen RJ, Schneider AJ, van Agtmael MA, de Vries TP, Richir MC. The effect of different levels of realism of context learning on the prescribing competencies of medical students during the clinical clerkship in internal medicine: an exploratory study. *European journal of clinical pharmacology*. Feb 2015;71(2):237-42. doi:10.1007/s00228-014-1790-y
17. Schutte T, Tichelaar J, Reumerman MO, et al. Feasibility and Educational Value of a Student-Run Pharmacovigilance Programme: A Prospective Cohort Study. *Drug safety*. May 2017;40(5):409-418. doi:10.1007/s40264-016-0502-1

18. Schutte T, Tichelaar J, van Agtmael M. Learning to prescribe in a student-run clinic. *Medical Teacher*. 2016/04/02 2016;38(4):425-425. doi:10.3109/0142159X.2015.1072145
19. Reumerman MO, Tichelaar J, Richir MC, van Agtmael MA. Medical students as junior adverse drug event managers facilitating reporting of ADRs. *British journal of clinical pharmacology*. May 5 2021;doi:10.1111/bcp.14885
20. Reumerman MO, Richir MC, Domela Nieuwenhuis PM, et al. The clinical and educational outcomes of an inter-professional student-led medication review team, a pilot study. *European journal of clinical pharmacology*. Jan 2021;77(1):117-123. doi:10.1007/s00228-020-02972-3
21. Reumerman M, Tichelaar J, Richir MC, van Agtmael MA. Medical students as adverse drug event managers, learning about side effects while improving their reporting in clinical practice. *Naunyn-Schmiedeberg's archives of pharmacology*. Mar 5 2021;doi:10.1007/s00210-021-02060-y
22. medicijngebruik Ivv. opiaten.nl. https://www.opiaten.nl/
23. van der Linden A, van Joolingen WR, Meulenbroeks RF. Designing an intrinsically integrated educational game on newtonian mechanics. Springer; 2018:123-133.



7

A CLINICAL PHARMACOLOGY AND THERAPEUTICS TEACHER'S GUIDE TO RACE-BASED MEDICINE, INCLUSIVITY, AND DIVERSITY

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Clinical Pharmacology & Therapeutics
2023, Mar; 113(3):600-606.
doi: 10.1002/cpt.2786.

ABSTRACT

The relationship between race and biology is complex. In contemporary medical science, race is a social construct that is measured via self-identification of study participants. But even though race has no biological essence, it is often used as variable in medical guidelines (e.g. treatment recommendations specific for Black people with hypertension). Such recommendations are based on clinical trials in which there was a significant correlation between self-identified race and actual, but often unmeasured, health-related factors such as (pharmaco)genetics, diet, sun-exposure etc.. Many teachers are insufficiently aware of this complexity. In their classes, they (unintentionally) portray self-reported race as having a biological essence. This may cause students to see people of shared race as biologically or genetically homogeneous, and believe that race-based recommendations are true for all individuals (rather than reflecting the average of a heterogeneous group). This medicalizes race and reinforces already existing healthcare disparities. Moreover, students may fail to learn that the relation between race and health is easily biased by factors such as socio-economic status, racism, ancestry, and environment and that this limits the generalizability of race-based recommendations. We observed that the clinical case vignettes that we use in our teaching contain many stereotypes and biases, and do not generally reflect the diversity of actual patients. This guide, written by clinical pharmacology and therapeutics teachers, aims to help our colleagues and other health professions teachers to reflect on and improve our teaching on race-based medical guidelines and to make our clinical case vignettes more inclusive and diverse.

INTRODUCTION

Race is often considered an essential biological variable in diagnostic algorithms and treatment decisions. Examples of race-based medicine can be found in the clinical practice guidelines of virtually all medical specialties[1,2]. Many of these race-based recommendations directly or indirectly influence the choice of drug therapy, for instance the race-based corrections for estimating the glomerular filtration rate (GFR)[3-5], the specific treatment recommendations for hypertension in Black patients[6-8], and the diverse medicines for which human leukocyte antigen (HLA)-typing is advised, often only for people with a certain ethnic background (e.g. HLA-B*5801 in patients of southeast Asian or African American descent[9]). These and other race-based recommendations are increasingly criticized for being biased[10,11], unscientific[12], and increasing rather than reducing healthcare disparities[1,2].

As teachers in clinical pharmacology and therapeutics (CPT), we endeavour to equip medical and other healthcare students (such as nursing, pharmacy and dental students) with appropriate prescribing knowledge and skills in order for them to be able to prescribe medicines safely, effectively, and responsibly. Besides the required knowledge about pharmacology, side-effects, and drug-drug interactions, this also entails teaching students to adopt an informed and critical attitude towards clinical practice guidelines and evidence based medicine in general[13,14]. The controversies regarding race-based recommendations, however, are rarely explained by CPT and other "core medical science" lecturers. Medical students increasingly take issue with how their teachers explain the relationship between race and health, in particular because often, race is presented as a biological variable which may obfuscate issues of racism and historical oppression as root causes for ill-health[15]. One analysis found that 96% of preclinical lecture slides that mentioned race, presented it as risk factor for disease without explaining that race is not a biological but a social construct that is prone to bias[16]. Unfortunately, this situation reflects our own teaching experience at eleven academic institutions in seven EU countries and the United Kingdom where we, until recently, taught about race-based medical guidelines without discussing the controversies or considering the nuanced relationship between race and health. We suspect that the same is true for (CPT) teaching in the rest of Europe.

Teachers are insufficiently knowledgeable about the concept of race in relation to healthcare and insufficiently aware of their own bias and the potential harmful consequences of passing this bias on to the next generation of health professionals[17]. Yet, in talking with our (predominantly white) colleagues, we often experience reluctance to discuss these matters openly and believe that this is because fear for being called out as a racist is a barrier. Rather than critically considering that what we teach may be rooted in a racist history, we perceive it as offending our pure intentions and instinctively refute it. This response is known as white fragility[18] and underlies other often heard responses such as that "you can't say anything anymore these days" or that the attention for inclusion and diversity ("wokeness") restricts academic freedom[19].

This guide aims to help us as CPT and other health professions teachers to examine our personal roles in propagating racial bias through race-based guidelines and clinical case vignettes. We first explore the concept of race, history of race-based medicine and the fallacies and consequences thereof. We then provide practical ideas for teaching this knowledge to students. Lastly, we provide practical guidance towards creating more inclusive and diverse case vignettes. The guide is based on a review of the literature and consensus among an international consortium of CPT teachers established for the European Open Platform for Prescribing Education (EurOP^{2}E) project.

What is race and how is it used in medical literature and guidelines?

Many systems have been used to classify humans into groups based on their physical appearance, the most controversial being that of Johann Friedrich Blumenbach (1752-1840). He divided the human species into five races, based mainly on the phenotypical appearance of the skull: Caucasian, Negroid, Mongoloid, American, and Malayan[20]. While reportedly holding markedly anti-racist views for his time, Blumenbach's classification formed the basis of ideologies claiming the superiority of the Caucasian race over other races[21]. Because of the historic burden of this nomenclature, it has been abandoned and should be discouraged[22]. Although it remains commonly used in both daily and scientific language, the word Caucasian is not exempt from these controversies[23,24].

Since Blumenbach, race essentialism (i.e. the belief in a genetic or biological essence that defines all members of a racial category) has been widely discredited[25]. However, the concept of race remained in use and now reflects a social definition that is based on an individual's self-identification with a racial category. This contemporary use of 'race' is intertwined with 'ethnicity'. According to the United Nations' recommendations on statistical data gathering regarding ethnicity: *"Ethnicity can be measured using a variety of concepts, including ethnic ancestry or origin, ethnic identity, cultural origins, nationality, race, colour, minority status, tribe, language, religion or various combinations of these concepts. The subjective nature of the term requires that information on ethnicity be acquired through self-declaration of a respondent and also that respondents have the option of indicating multiple ethnic affiliations"*[26]. If, and how, countries gather data on race and ethnicity for census and/or scientific purposes varies[27]. In Europe these data are usually confined to the national identity or country of birth (of oneself and parents)[28], as recording race or more complex definitions of ethnicity is (historically) considered prone to abuse[29]. While the concept of race is intrinsically inclusive of colour and physical characteristics and ethnicity not (per se)[30], both are measured by self-identification on the basis of subjective, personal and overlapping criteria (such as ancestry and culture)[17,31]. Therefore, we view these concepts as inseparable and use "race/ethnicity" for the remainder of the article.

For both race and ethnicity, any classification may be used and the UN recommends to use precise and inclusive categories (e.g. regional, local and self-perceived groups)[26]. However, the most commonly used division in medical literature is based on the U.S. Government Office of Management and Budget's (OMB) Census Bureau definitions. They use a social definition, in which people self-identify with one or more of the following five racial categories: White; Black or African American; American Indian or Alaska Native; Asian; and Native Hawaiian or Other Pacific Islander. Additionally, and independent of race, people are asked to self-identify with one of two ethnicities: Hispanic or Latino and non-Hispanic or Latino. The OMB emphasizes the social nature of this classification and specifically states that it is not aimed at defining race anthropologically, biologically, or genetically[32]. Genomic research has confirmed that social definitions of race are not supported by genetic data [25,33].

Because of concerns that ethnic differences affect the safety, efficacy and/or dosing of medicines, some governing medical bodies require racial data for drug authorization. The FDA mandates reporting of effectiveness and safety data for racial subgroups according to the OMB's classification and additionally recommends reporting data separately for Hispanic or Latino and non-Hispanic or Latino populations[34]. The EMA accepts foreign clinical safety and efficacy data in their evaluation of new drugs if the pharmacokinetics of a drug are comparable across the most prevalent (self-declared) racial groups in the original country and Europe[35]. Because governing bodies require these data, it has become standard practice to report them in clinical trials. Many medical journals now have reporting guidelines that encourage authors to report data by race and ethnicity[36-38].

The way in which data on race/ethnicity are collected and evaluated is based on (fluid and socially determined) self-identification and therefore unlikely to have inherent biological consequences. Yet, there are numerous situations in which pharmacokinetics, drug efficacy, and/or drug safety differ across groups. For example, race/ethnicity has been found to be correlated with a number of health-related factors, such as (pharmaco) genetics (e.g. cytochrome P450 polymorphisms), environmental factors (e.g. related to sun exposure) and diet (e.g. related to salt-intake). Moreover, race/ethnicity is intertwined with socio-economic status and both these factors are associated with health and known to influence access to healthcare. Because the relationship between race/ethnicity and the actual health-related factors is often multifactorial and the underlying reasons are almost never completely understood (or even properly investigated), race/ethnicity is used as a proxy for these health factors in race-based guidelines and algorithms[11].

So, what is the problem?

In theory, using race/ethnicity as a marker of risk is not much different from using any other diagnostic marker. Race/ethnicity may help to predict outcomes, whether that is the likelihood of a diagnosis, treatment response, or estimation of a physical parameter (e.g. glomerular filtration rate), so what is wrong with this practice? Like other risk factors, correlations between race/ethnicity and outcome reflect different *average* results and it is difficult to translate these findings into *individual* patient decisions. Too often, the race-based distinction is considered as an absolute, whereas in reality it fails to correctly identify all patients and incorrectly identifies others. This is explained in a Venn diagram (***figure 1***). When the results of investigative tests are misinterpreted, this may cause potential harm and problems with race-based medicine come to light. ***Table 1*** shows examples of possible harm due to race-based guidelines. Harm may befall both those patients who are incorrectly identified by the race-based diagnostic and those who remain undetected. Both the probability and severity of harm differ in these populations and therefore race-based recommendations tend to reinforce racial inequity[1,2].

Additionally, using race/ethnicity as a diagnostic marker implies it to be a risk factor in itself rather than a marker of underlying risk factors. This pathologizes race and thereby facilitates racial bias and stereotyping. Being exposed to racism negatively impacts health outcomes[41-43], leading to a vicious cycle whereby the incorrect portrayal of race as a risk factor actually contributes to health disparities[12,16,31].

Even when there evidently is a correlation between race and certain medical outcomes, we advise caution in applying race-based guidelines; however, this is rarely the case. It is beyond the scope of this guide to discuss the evidence behind the individual race-based recommendations, but three common fallacies limit the applicability of race/ethnicity as a diagnostic tool.

First, much of the research behind race-based recommendations in guidelines is biased. Groups that have historically been marginalized, such as Black people in the United States, are much more likely to have their race linked to pathology than other groups[10]

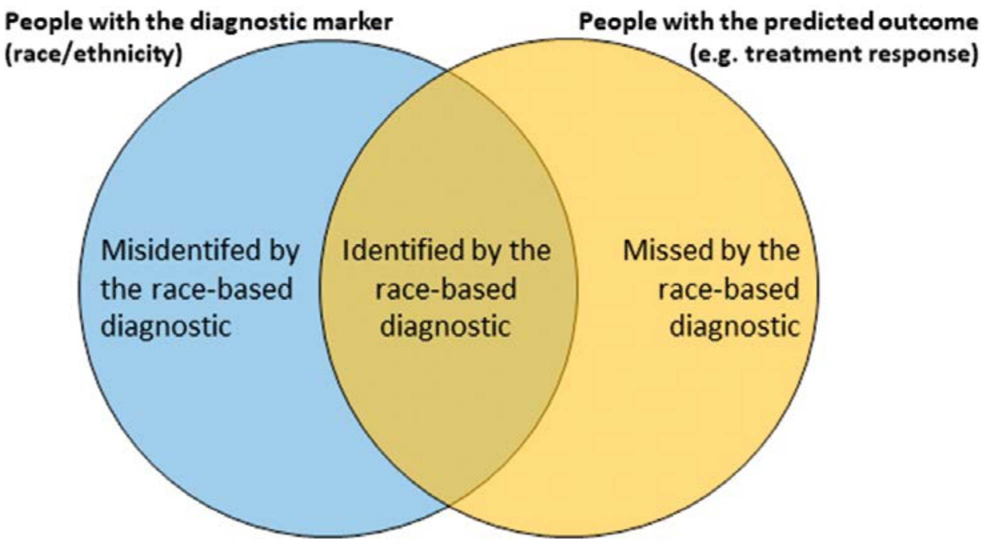


Figure 1. (In)accuracy of race-based diagnostic (schematic). The left circle represents people sharing the racial identifcation used as diagnostic marker (e.g. Black), the right circle represents people with the predicted outcome (e.g. people who respond better to calcium channel blockers or diuretics than ACE-inhibitors or angiotensin receptor blockers. Only people in the overlapping part are correctly identified by the race-based diagnostic, those in blue are misidentified (the race-based recommendation is incorrectly applied) and those in yellow are missed (the race-based recommendation is incorrectly not applied). The sizes of the respective areas vary depending on the diagnostic used and are often difficult to estimate / investigate.

Table 1. Examples of potential harm caused by race-based guidelines.

Guideline / Algorithm	Rationale	How it is used in practice	Potential harm for identified patients	Potential harm for other patients
MDRD and (previous) CKD-EPI formulas for estimating GFR[3,5]	Applying the correction for patients identifying as Black was shown to a improve agreement between measured and estimated GFR.	The correction factor is applied to all Black patients	Kidney function of Black patients more likely to be overestimated (possibly leading to delayed diagnosis and referral for treatment)	Kidney function of patients of other race more likely to be underestimated (possibly leading to over-diagnosis and overtreatment)
Hypertension treatment guidelines[6-8]	In patients identifying as Black, greater blood-pressure reductions were observed on diuretics and CCBs compared to ACEi and ARB.	Only CCBs or diuretics are given to Black patients.	Less likely to be treated with ACEi/ARB (even if this is the best treatment option).	More likely to be treated with ACEi/ARB (even if this is **not** the best treatment option).
CPIC Guidelines[39,40]	CYP2C19 poor metabolizer phenotypes are more frequent in Asian subpopulations compared to Europeans.	Reduced dosages or alternative medicines are advised for all Asian patients	Asian patients are more likely to receive subtherapeutic dosages or less effective medicines (insufficient effect)	Patients of other race are more likely to receive supratherapeutic dosages (adverse effects).

MDRD = Modification of Diet in Renal Disease; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; GFR = Glomerular Filtration Rate; CPIC = Clinical Pharmacogenetics Implementation Consortium; CCB = Calcium Channel Blocker; ACEi = ACE-inhibitor; ARB = Angiotensin Receptor Blocker.

and even under the best circumstances, research methodology cannot always correct for confounders such as socioeconomic status, racism and discrimination[11].

Secondly, race-based associations are often falsely generalized. Correlations found in one part of the world do not necessarily apply to patients of the same race/ethnicity living elsewhere as they are likely to have a widely dissimilar ancestry[44] and/or environment (impacting lifestyle, diet etc.)[45]. This is schematically shown in ***figure 2***. Moreover, the whole concept of race/ethnicity is viewed differently depending on geography, as do the used categories[28]. Therefore the reasons for self-identification (and groups that result of it) are largely incomparable[1]. For example, the apparent greater effectiveness of calcium channel blockers and thiazide diuretics as opposed to renin-angiotensin-system inhibiting agents that was observed in Black American and African patients could not be reproduced in Black patients living in the United Kingdom[46].

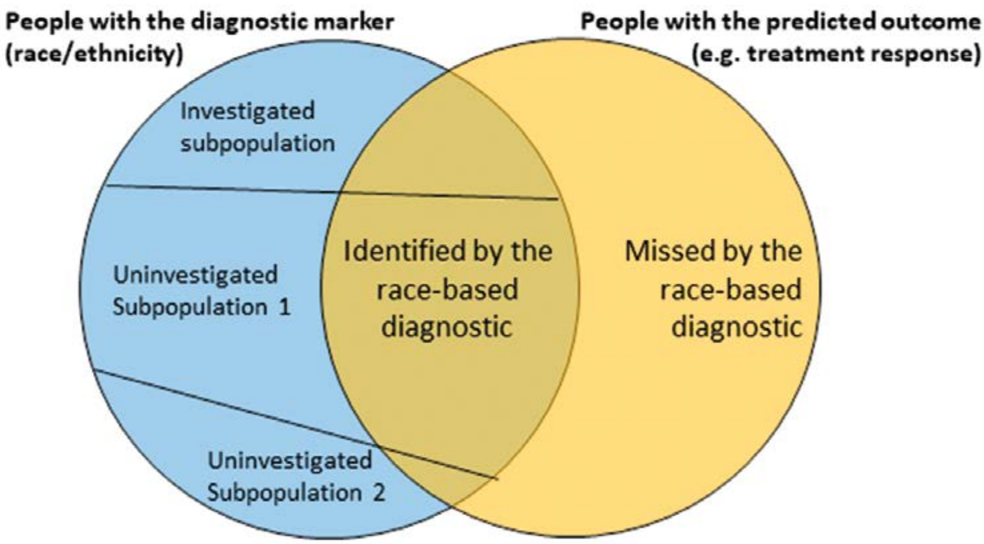


Figure 2. False generalization of race-based recommendations (schematic). As in figure 1, the blue circle represents people sharing the racial identifcation used as diagnostic marker (e.g. Black). However, this schematic shows that the accuracy as observed in one subpopulation (e.g. Black people in the U.S.) cannot be generalized to other subpopulations (e.g. Black people in Europe). The sizes of the respective areas vary depending on the diagnostic used and are often difficult to estimate / investigate.

Lastly, in applying race-based recommendations, caregivers are faced with a false dichotomy. They must decide whether their patient fits the guideline category or not, even if the reality is more nuanced, for example because the patient identifies as multiracial[2]. A further mismatch occurs because caregivers usually "guesstimate" the race/ethnicity of their patient based on observations (of physical appearance, language, name etc.), sometimes combined with limited questions of geographic ancestry[47,48].

What should we do instead?

We must not forget that race-based recommendations were implemented in guidelines with a view to improve care. White (middle-aged, male) patients are overrepresented in clinical studies and most of what we consider evidence is not, or insufficiently, studied in other groups. If we look again at the example of race-based corrections for estimating GFR, and if it is true that a correction factor is required for Black patients on average, then not using the correction factor may lead to underestimation of the GFR, putting many of them at risk of inadequate dosage of medication and subsequent adverse effects. Moreover, denying differences between people (or "racial colour blindness") is just as problematic as oversimplifying or exaggerating the differences, because we avert our eyes to any health inequities that arise from racism[49]. This is also the reason why it is important that research into racial (health) inequities continues. While ideally, we should not need to use proxies for pathology as rough and flawed as race/ethnicity, we must face the fact that they often remain the best markers of risk we have currently available. We therefore argue that we cannot simply stop using race/ethnicity-based guidance, but rather that we need to apply it with more care and respect for the aforementioned drawbacks.

There is no harm in trying calcium channel blockers or thiazides first in Black hypertensive patients, but there is potential harm in failing to understand that this may be a suboptimal treatment option for your individual patient. Likewise, there is no harm in applying the race-based correction for estimating GFR, but there is potential harm in not considering that this estimation may be wildly off. Cerdeña and colleagues advocated abandoning all race-based guidelines and replacing them with what they call race-conscious alternatives[1]. Sometimes, these are very suitable alternatives, such as the 2021 version of the CKD-EPI formula, which provides a widely validated race-independent estimation of GFR[50]. Unfortunately, many of the other alternatives are not evidence-based solutions, but mere pragmatic approaches in which treatment is started independent of race/ethnicity and adjusted on the basis of effect and safety parameters. Of course, treatment should always be evaluated in this manner, and therefore we argue that this does not differ much from applying race-based guidelines while acknowledging their drawbacks.

How should we change our teaching?

Diversity and inclusion are key concerns in higher education. In a recent survey among European higher education institutions (n=159), nearly all respondents reported either having (85%) or developing (13%) strategies or policies to improve diversity, equity, and/or inclusion[51]. An increasing number of medical schools now offer lectures and/or elective courses on health equity, race and bias[16,52]. However, these improvements have little effect when other ("core science") teaching continues to portray race as an important risk factor for disease with insufficient context[17]. We, as CPT teachers, cannot simply ignore the issue. When teaching about race-based guidelines, we should – at the very least – be nuanced about the value of race as marker of risk and explain the potential for harm and difficulties to translate study results into clinical practice. Additionally, we recommend consulting institutional diversity officer(s) (i.e. person(s) tasked with diversity and inclusion) to help examine your teaching and learn whether knowledge and attitudes towards the use of race in medicine is (or could become) part of the medical curriculum. We have good experience with interactive small-group discussions (both online and in-class) in which we discuss the questions posed in the heading of this guide. We suggest a 'bottom-up' approach to curriculum content development and delivery methods, which encourages transparency and co-production with students.

Diversity and inclusion in clinical case vignettes

CPT is frequently taught using case vignettes debated amongst a small group of students[13]. Unfortunately, these vignettes are often stereotypical and full of (implicit) bias[53,54]. In this part of the guide, we look beyond race and ethnicity, because sex, gender and religious or political beliefs may also relate to sickness and health, and just as with race or ethnicity, it may be difficult to decide what information, and how much, to provide about a patient's background when making clinical cases to use in medical education[55].

Stereotyping is a big problem in case vignettes. Too often, the race (or sexual orientation etc.) of a patient is stereotypically connected to their disease or a direct and oversimplified clue to the "correct" answer in case-based examinations or exercises[56]. By designing our assignments in this manner, we reward our students for their bias and teach them to see such characteristics as markers – markers that may ultimately prove harmful (lead to delayed diagnosis or suboptimal treatment etc.) in real patient care. We should therefore be reflective of our own bias when making cases. More importantly, we must consider that our cases are about *individual* patients and that they do not always have to reflect the epidemiological *average* patient. In fact, we argue that it is better to make cases about patients that do not fit the norm, because this challenges pre-existing ideas/opinions and because it is a more adequate reflection of clinical practice (as no individual is average in all respects)[53]. Stereotyping may not only be problematic in relation to diagnosis and treatment, but also in relation to other aspects of a clinical case. For example, when a job description is provided in the case, care must be taken that this is not gender-biased (e.g. high positions more often allocated to male patients). Likewise, bias in terms of risk behaviour, lifestyle, or employment should be avoided when treating immigrant patients (or patients with a 'foreign-sounding' name).

Patients in simulated case scenarios should reflect the diversity of actual patients with respect to their gender, sexual orientation, race, ethnicity, disabilities, religion, political beliefs, and any other aspects that may shape their identity, as well as the intersection of these dimensions (intersectionality)[52,57]. Therefore, when creating cases, it is advisable to add diversifying traits and characteristics to your patients. Care must be taken that this is done regardless of the teaching topic (e.g. not only in relation to sexual health problems or lifestyle diseases), avoiding stereotypical associations with other health-related aspects. Moreover, it is important to use inclusive and respectful language (e.g. when the patient is trans or gender non-conforming, make sure to consistently address them by their preferred pronouns)[58].

An important aspect of being inclusive is to avoid using descriptors of gender, sexual orientation, religion etc. in ways that are irrelevant to the story. For example, mentioning a patient's religion (e.g. Christian, Buddhist or Muslim) may be irrelevant for the treatment of a fractured leg and because there is no clear purpose for providing this information, it easily gets a discriminatory connotation. Creating inclusive cases whilst avoiding such unwanted connotations is difficult. However, rather than explicitly stating that the patient is, for example, Muslim, you can make the case more inclusive and avoid unwanted connotations with subtext, for instance by mentioning that he broke his leg in a fall down some steps at the mosque.

Lastly, it is important to be aware of implicit bias (at both your own and the reader's end) and avoid to (inadvertently) communicating this bias. This is best achieved by being very specific with the information you provide[53,58]. For example, in a case about a possible sexually transmitted infection (STI), the information that the patient is gay may imply that he is having unsafe sex with other men, whereas he may be sexually abstinent or having (monogamous) safe sex. It is therefore better to state whether he had unsafe sex or not, and whether his sexual partner(s) had an increased risk of STIs. Likewise, in a case about sickle cell disease, the information that the patient is Black is less informative than the information that his/her birthparents come from a malaria-endemic region in Kenya.

Final remarks

We have tried to provide a nuanced, scientific, and two-sided view of the issues that surround race-based medicine, diversity and inclusion in medical teaching. We hope that this approach convinces CPT and other "core medical science" teachers that they have an important role in reducing the propagation of bias via medical guidelines and case vignettes, and that doing so is not at odds with academic freedom. However, we realize that it is impossible to write a guide that is not biased by our own opinions and the spirit of our times. Therefore, we see this guideline as a starting point for an evolving discussion aimed at improving education. On the European Open Platform for prescribing Education (EurOP^{2}E, www.prescribingeducation.eu), we aim to keep the discussion alive and provide more ready-to-use open (free to re-use, revise and redistribute) teaching materials about race-based medicine and practical tools to improve diversity and inclusion.

REFERENCES

1. Cerdeña JP, Plaisime MV, Tsai J. From race-based to race-conscious medicine: how anti-racist uprisings call us to act. *The Lancet*. 2020;396(10257):1125-1128. doi:10.1016/S0140-6736(20)32076-6
2. Vyas DA, Eisenstein LG, Jones DS. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. *New England Journal of Medicine*. 2020;383(9):874-882. doi:10.1056/NEJMms2004740
3. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med*. Aug 15 2006;145(4):247-54. doi:10.7326/0003-4819-145-4-200608150-00004
4. Levin A, Stevens PE, Bilous RW, et al. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney international supplements*. 2013;3(1):1-150.
5. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. May 5 2009;150(9):604-12. doi:10.7326/0003-4819-150-9-200905050-00006
6. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens*. Oct 2018;36(10):1953-2041. doi:10.1097/hjh.0000000000001940
7. Boffa RJ, Constanti M, Floyd CN, Wierzbicki AS. Hypertension in adults: summary of updated NICE guidance. *BMJ*. 2019;367:l5310. doi:10.1136/bmj.l5310
8. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *Jama*. Feb 5 2014;311(5):507-20. doi:10.1001/jama.2013.284427
9. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. *Arthritis Rheumatol*. Jun 2020;72(6):879-895. doi:10.1002/art.41247
10. Cooper RS, Kaufman JS, Ward R. Race and Genomics. *New England Journal of Medicine*. 2003;348(12):1166-1170. doi:10.1056/NEJMsb022863
11. Osborne NG, Feit MD. The Use of Race in Medical Research. *JAMA*. 1992;267(2):275-279. doi:10.1001/jama.1992.03480020085037
12. Kaufman JS, Cooper RS. In search of the hypothesis. *Public Health Rep*. Nov-Dec 1995;110(6):662-666.
13. De Vries T, Henning RH, Hogerzeil HV, Fresle D, Policy M, Organization WH. *Guide to good prescribing: a practical manual*. 1994. *{UNESCO, #54}*.
14. Brinkman DJ, Tichelaar J, Mokkink LB, et al. Key Learning Outcomes for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study. *Clin Pharmacol Ther*. 2018;104(2):317-325. doi:10.1002/cpt.962
15. Nieblas-Bedolla E, Christophers B, Nkinsi NT, Schumann PD, Stein E. Changing How Race Is Portrayed in Medical Education: Recommendations From Medical Students. *Academic Medicine*. 2020;95(12)
16. Tsai J, Ucik L, Baldwin N, Hasslinger C, George P. Race Matters? Examining and Rethinking Race Portrayal in Preclinical Medical Education. *Academic Medicine*. 2016;91(7):916-920. doi:10.1097/acm.0000000000001232
17. Amutah C, Greenidge K, Mante A, et al. Misrepresenting Race — The Role of Medical Schools in Propagating Physician Bias. *New England Journal of Medicine*. 2021;384(9):872-878. doi:10.1056/NEJMms2025768
18. DiAngelo R. *White fragility: Why it's so hard for white people to talk about racism*. Beacon Press; 2018.

19. Pearce R. Academic freedom and the paradox of tolerance. *Nature Human Behaviour*. 2021/11/01 2021;5(11):1461-1461. doi:10.1038/s41562-021-01214-5
20. Blumenbach JF. Handbuch der Vergleichenden Anatomie und Physiologie. *Göttingen Search in*. 1804;
21. Bhopal R. The beautiful skull and Blumenbach's errors: the birth of the scientific concept of race. *BMJ*. 2007;335(7633):1308-1309. doi:10.1136/bmj.39413.463958.80
22. American Psychological Association. Bias free language - Racial and Ethnic Identity. Accessed 30 March, 2022. https://apastyle.apa.org/style-grammar-guidelines/bias-free-language/racial-ethnic-minorities
23. Freedman BJ. For debate...Caucasian. *Br Med J (Clin Res Ed)*. Mar 3 1984;288(6418):696-8. doi:10.1136/bmj.288.6418.696
24. Popejoy AB. Too many scientists still say Caucasian. *Nature*. 2021;596(7873):463-463.
25. ASHG Denounces Attempts to Link Genetics and Racial Supremacy. *Am J Hum Genet*. 2018;103(5):636-636. doi:10.1016/j.ajhg.2018.10.011
26. Commission E, Justice D-Gf, Consumers, Farkas L. *Analysis and comparative review of equality data collection practices in the European Union : data collection in the field of ethnicity*. Publications Office; 2020.
27. Routen A, Akbari A, Banerjee A, et al. Strategies to record and use ethnicity information in routine health data. *Nature Medicine*. 2022/07/01 2022;28(7):1338-1342. doi:10.1038/s41591-022-01842-y
28. Helberg-Proctor A, Meershoek A, Krumeich A, Horstman K. Ethnicity in Dutch health research: situating scientific practice. *Ethnicity & Health*. 2016/09/02 2016;21(5):480-497. doi:10.1080/13557858.2015.1093097
29. Boyd KM. Ethnicity and the ethics of data linkage. *BMC Public Health*. 2007/11/08 2007;7(1):318. doi:10.1186/1471-2458-7-318
30. Merriam-Webster. Difference between 'race' and 'ethnicity'. Accessed 30 March, 2022. https://www.merriam-webster.com/words-at-play/difference-between-race-and-ethnicity
31. Grubbs V, Cerdeña JP, Non AL. The misuse of race in the search for disease-causing alleles. *The Lancet*. 2022;399(10330):1110-1111. doi:10.1016/S0140-6736(22)00488-3
32. United States Office of Management and Budget Census Bureau. About the topic of race. Accessed 30 March, 2022. https://www.census.gov/topics/population/race/about.html
33. Mersha TB, Abebe T. Self-reported race/ethnicity in the age of genomic research: its potential impact on understanding health disparities. *Hum Genomics*. Jan 7 2015;9(1):1. doi:10.1186/s40246-014-0023-x
34. Food U, Administration D. Collection of race and ethnicity data in clinical trials. 2019.
35. EMA. Note for guidance on ethnic factors in the acceptability of foreign clinical data. European Medicines Agency London; 1998.
36. Striving for Diversity in Research Studies. *New England Journal of Medicine*. 2021;385(15):1429-1430. doi:10.1056/NEJMe2114651
37. Flanagin A, Frey T, Christiansen SL, Committee AMoS. Updated Guidance on the Reporting of Race and Ethnicity in Medical and Science Journals. *JAMA*. 2021;326(7):621-627. doi:10.1001/jama.2021.13304
38. Lancet. Information for authors. Accessed 31 March, 2022. https://thelancet.com/pb/assets/raw/Lancet/authors/tlrm-info-for-authors.pdf
39. Lo C, Nguyen S, Yang C, et al. Pharmacogenomics in Asian Subpopulations and Impacts on Commonly Prescribed Medications. *Clin Transl Sci*. Sep 2020;13(5):861-870. doi:10.1111/cts.12771
40. Clinical Pharmacogenetics Implementation Consortium. Guidelines. Accessed 23 August 2022, https://cpicpgx.org/guidelines/

41. Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. *Lancet*. Apr 8 2017;389(10077):1453-1463. doi:10.1016/s0140-6736(17)30569-x

42. Pallok K, De Maio F, Ansell DA. Structural Racism — A 60-Year-Old Black Woman with Breast Cancer. *New England Journal of Medicine*. 2019;380(16):1489-1493. doi:10.1056/NEJMp1811499

43. Paradies Y, Ben J, Denson N, et al. Racism as a Determinant of Health: A Systematic Review and Meta-Analysis. *PLOS ONE*. 2015;10(9):e0138511. doi:10.1371/journal.pone.0138511

44. Goodman CW, Brett AS. Race and Pharmacogenomics—Personalized Medicine or Misguided Practice? *JAMA*. 2021;325(7):625-626. doi:10.1001/jama.2020.25473

45. Agyemang C, Meeks K, Beune E, et al. Obesity and type 2 diabetes in sub-Saharan Africans - Is the burden in today's Africa similar to African migrants in Europe? The RODAM study. *BMC Med*. Oct 21 2016;14(1):166. doi:10.1186/s12916-016-0709-0

46. Sinnott S-J, Douglas IJ, Smeeth L, Williamson E, Tomlinson LA. First line drug treatment for hypertension and reductions in blood pressure according to age and ethnicity: cohort study in UK primary care. *BMJ*. 2020;371:m4080. doi:10.1136/bmj.m4080

47. Kaplan JB, Bennett T. Use of race and ethnicity in biomedical publication. *Jama*. May 28 2003;289(20):2709-16. doi:10.1001/jama.289.20.2709

48. Boehmer U, Kressin NR, Berlowitz DR, Christiansen CL, Kazis LE, Jones JA. Self-reported vs administrative race/ethnicity data and study results. *Am J Public Health*. 2002;92(9):1471-1472. doi:10.2105/ajph.92.9.1471

49. Okah E, Thomas J, Westby A, Cunningham B. Colorblind Racial Ideology and Physician Use of Race in Medical Decision-Making. *Journal of Racial and Ethnic Health Disparities*. 2021/09/07 2021;doi:10.1007/s40615-021-01141-1

50. Inker LA, Eneanya ND, Coresh J, et al. New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. *New England Journal of Medicine*. 2021;385(19):1737-1749. doi:10.1056/NEJMoa2102953

51. Claeys-Kulik AL, Jørgensen TE, Stöber H. Diversity, equity and inclusion in European higher education institutions. *Results from the INVITED Project Brussel: European University Association Asil, 51p*. 2019;

52. Muntinga ME, Krajenbrink VQE, Peerdeman SM, Croiset G, Verdonk P. Toward diversity-responsive medical education: taking an intersectionality-based approach to a curriculum evaluation. *Adv Health Sci Educ Theory Pract*. 2016;21(3):541-559. doi:10.1007/s10459-015-9650-9

53. Krishnan A, Rabinowitz M, Ziminsky A, Scott SM, Chretien KC. Addressing Race, Culture, and Structural Inequality in Medical Education: A Guide for Revising Teaching Cases. *Acad Med*. Apr 2019;94(4):550-555. doi:10.1097/acm.0000000000002589

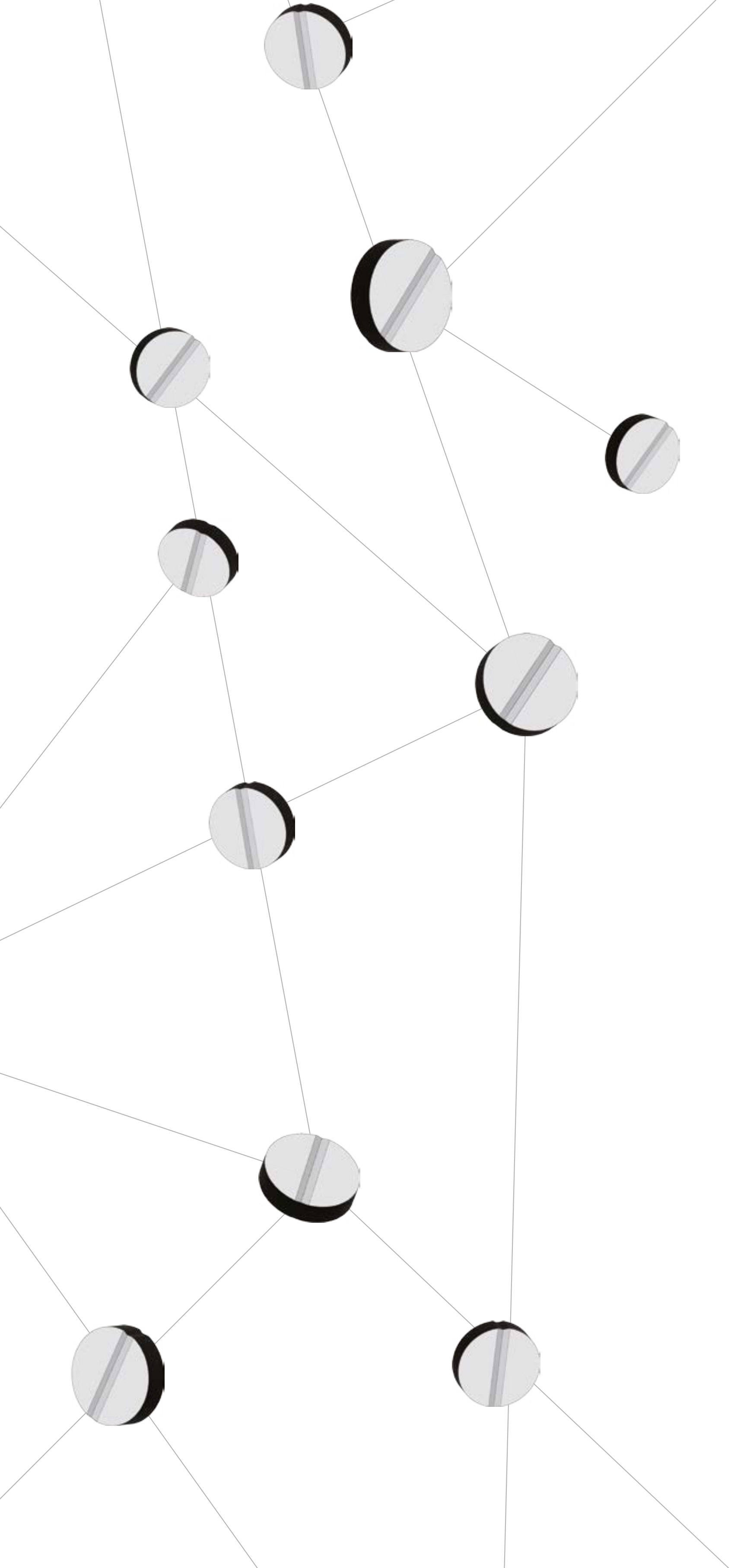
54. Muntinga M, Beuken J, Gijs L, Verdonk P. Are all LGBTQI+ patients white and male? Good practices and curriculum gaps in sexual and gender minority health issues in a Dutch medical curriculum. *GMS J Med Educ*. 2020;37(2):Doc22. doi:10.3205/zma001315

55. Verdonk P, Benschop YW, de Haes HC, Lagro-Janssen TL. From gender bias to gender awareness in medical education. *Adv Health Sci Educ Theory Pract*. Mar 2009;14(1):135-52. doi:10.1007/s10459-008-9100-z

56. Ripp K, Braun L. Race/Ethnicity in Medical Education: An Analysis of a Question Bank for Step 1 of the United States Medical Licensing Examination. *Teach Learn Med*. Apr-Jun 2017;29(2):115-122. doi:10.1080/10401334.2016.1268056

57. Verdonk P, Muntinga M, Leyerzapf H, Abma T. From Gender Sensitivity to an Intersectionality and Participatory Approach in Health Research and Public Policy in the Netherlands. In: Hankivsky O, Jordan-Zachery JS, eds. *The Palgrave Handbook of Intersectionality in Public Policy*. Springer International Publishing; 2019:413-432.

58. American Psychological Association. Bias free language - General. Accessed 26 April, 2022. https://apastyle.apa.org/style-grammar-guidelines/bias-free-language/



8

SUSTAINABLE MEDICINES USE IN CLINICAL PRACTICE – IT IS TIME TO HELP THE TEACHER

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British Journal of Clinical Pharmacology
2022, Jul;88(7):3030-3031
doi: 10.1111/bcp.15340.

We read the invited review on sustainable medicines use in clinical practice by Adeyeye et al[1] and would like to congratulate the authors with the captivating way in which they used scientific facts combined with very practical solutions to convey their call to action. This call is primarily addressed to the NHS, which the authors suspect will resonate with other health systems. While we fully agree with necessity of this top-down approach, we additionally believe that there is much to be gained by making future prescribers more knowledgeable and aware about the impact they have on planetary health. The article remains very brief about next generation of healthcare professionals by quoting the General Medical Council's statement that "newly qualified doctors must be able to apply the principles, methods and knowledge of population health and the improvement of health and sustainable healthcare to medical practice"[2]. However, the underlying question - how we effectively train future healthcare professionals in these attitudes underpinned by knowledge – is not addressed.

The Association for Medical Education in Europe's (AMEE) recent consensus statement provides a clear global, collaborative, representative and inclusive vision on how to educate an interprofessional workforce that can provide sustainable healthcare and promote planetary health[3]. It includes examples of learning activities and assessment methods that can be included in daily teaching, such as roleplaying exercises and objective structured clinical examinations (OSCEs) in which the students discuss the most environmentally sustainable intervention (e.g. dry powder inhalers instead of metered-dose inhalers) with a patient and literature based research assignments (e.g. about the environmental impact of specific drug classes). However, the cornerstone of improving planetary health education is faculty engagement, and it is here that we foresee difficulties for sustainable clinical pharmacology and therapeutics (CPT) education. Like many other medical teachers, CPT teachers often have to balance their teaching tasks with clinical duties and in many countries there is a shortage of clinical pharmacologists. To incorporate sustainable prescribing in their teaching is something that most teachers simply do not have time for and even if they have the time, they may feel that there are more urgent improvements to be made. For example, CPT education in many countries is still very traditional (i.e. lecture and textbook-based) whereas problem-based teaching is more effective[4]. Moreover, the teachers may not be as invested in the issues of planetary health as the current young doctors and students and they may not feel confident that they have the expertise to teach about it[5].

If we want large numbers of students to learn about sustainable prescribing, it is of utmost importance to make the job of the teacher as easy as virtually possible. That means not expecting everyone to single-handedly invent the wheel, but to collaboratively create standpoints, teaching materials and faculty development (or "teach the teacher") materials and to share them openly. That is free (without cost or copyright restrictions) and easy to re-use, revise (e.g. to local standards if necessary) and redistribute (e.g. local versions, improvements or translations). This is the goal of the European Open Platform for Prescribing Education (EurOP^{2}E). Aimed at improving and harmonizing international

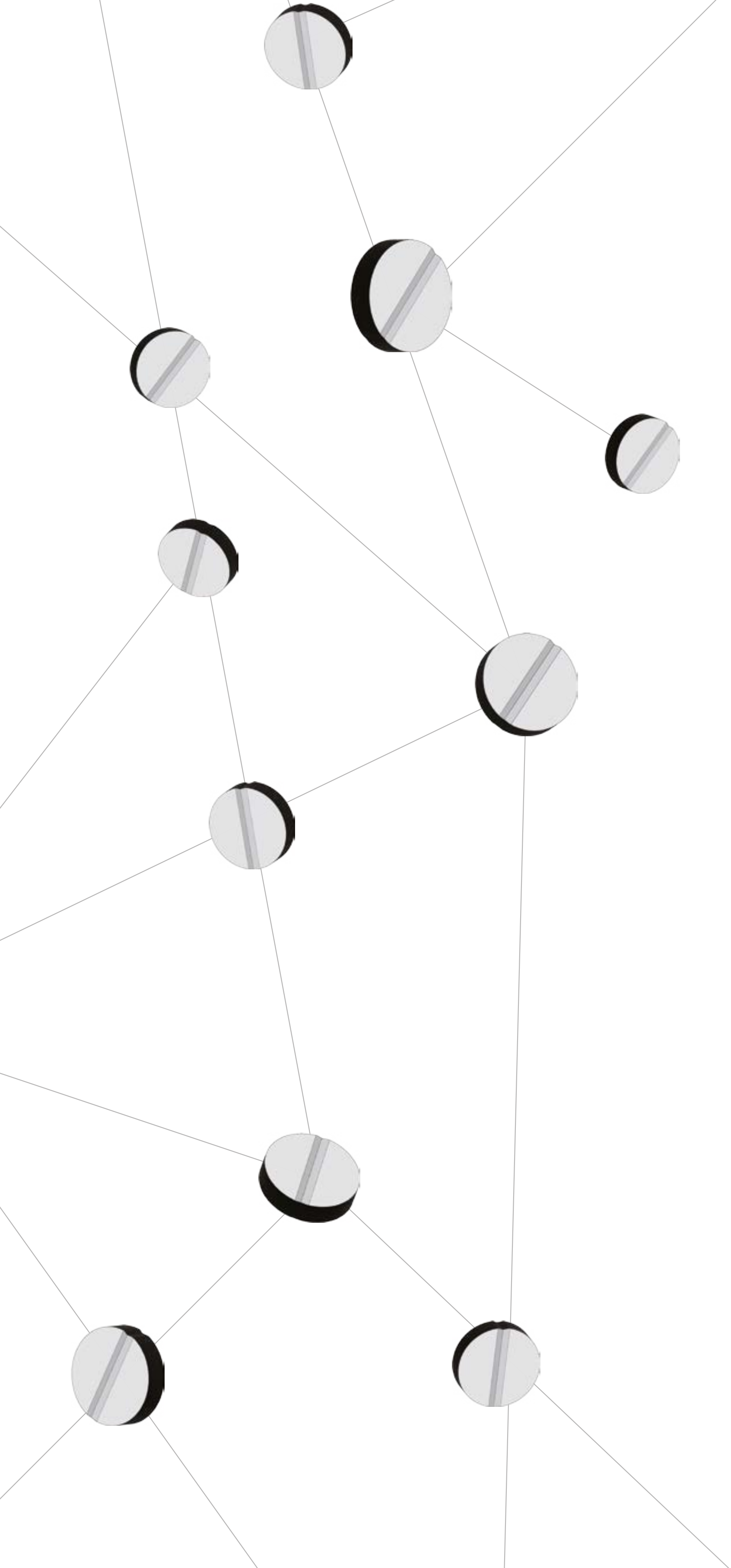
CPT education, EurOP²E is an online environment for CPT teachers to collaborate and to share and create open educational resources. The framework for the platform was recently published[6], and it is set to go live in the spring of 2022 (www.prescribingeducation.eu).

Planetary health should be a cross-cutting theme throughout the whole of medical education[7]. Within medical education, prescribing is likely to have the most impact, as human pharmaceuticals not only account for an estimated 25% of all medical greenhouse gas emissions, but also exert direct ecotoxicological effects via sewage systems[8]. Moreover, prescribers may directly influence their environmental impact through individual treatment decisions. Therefore, while any ready-to-use teaching materials will provide a welcome start, planetary health must be incorporated in the basics of pharmacotherapy education. The six-step model of the WHO guide to good prescribing and the accompanying teacher's guide to good prescribing are currently under revision[9] (http://www.guidetogoodprescribing.org). Aside from pharmaceutical advances, globalization of information and digitization of both the prescribing process and medical education, the revision will include sustainable medicines use. We expect that specifically step 3(b) of the six-step process – to verify the suitability of a (standard) treatment and adapt it to the individual needs of a patient – will be updated so that prescribers learn to take the environmental impact of their treatment decisions into account. The exact nature of the update will be decided in a consensus meeting with its users.

The authors of this letter are involved in both the development of EurOP²E and the revision of the WHO Guide to Good Prescribing and actively looking for collaborators with an interest in sustainable medicines use. Interested readers may apply via the aforementioned webpages of the respective projects.

REFERENCES

1. Adeyeye E, New BJM, Chen F, Kulkarni S, Fisk M, Coleman JJ. Sustainable medicines use in clinical practice: A clinical pharmacological view on eco-pharmaco-stewardship. *Br J Clin Pharmacol*. Nov 15 2021;n/a(n/a)doi:10.1111/bcp.15140
2. General Medical Council. Outcomes for graduates. 2020. . Accessed 28-12-2021, https://www.gmc-uk.org/education/standards-guidance-and-curricula/standards-and-outcomes/outcomes-for-graduates/outcomes-for-graduates
3. Shaw E, Walpole S, McLean M, et al. AMEE Consensus Statement: Planetary health and education for sustainable healthcare. *Med Teach*. Mar 2021;43(3):272-286. doi:10.1080/0142159X.2020.1860207
4. Brinkman DJ, Tichelaar J, Okorie M, et al. Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries. *Clin Pharmacol Ther*. Nov 2017;102(5):815-822. doi:10.1002/cpt.682
5. Tun S, Wellbery C, Teherani A. Faculty development and partnership with students to integrate sustainable healthcare into health professions education. *Med Teach*. Oct 2020;42(10):1112-1118. doi:10.1080/0142159X.2020.1796950
6. Bakkum MJ, Richir MC, Papaioannidou P, et al. EurOP(2)E - the European Open Platform for Prescribing Education, a consensus study among clinical pharmacology and therapeutics teachers. *Eur J Clin Pharmacol*. Aug 2021;77(8):1209-1218. doi:10.1007/s00228-021-03101-4
7. Tun S. Fulfilling a new obligation: Teaching and learning of sustainable healthcare in the medical education curriculum. *Med Teach*. Oct 2019;41(10):1168-1177. doi:10.1080/0142159X.2019.1623870
8. Fent K, Weston AA, Caminada D. Ecotoxicology of human pharmaceuticals. *Aquat Toxicol*. Feb 10 2006;76(2):122-59. doi:10.1016/j.aquatox.2005.09.009
9. Tichelaar J, Richir MC, Garner S, Hogerzeil H, de Vries T. WHO guide to good prescribing is 25 years old: quo vadis? *Eur J Clin Pharmacol*. Apr 2020;76(4):507-513. doi:10.1007/s00228-019-02823-w



EDUCATIONAL VALUE OF INTERNATIONAL AND INTERCULTURAL DIFFERENCES IN PRESCRIBING: THE INTERNATIONAL AND INTERPROFESSIONAL STUDENT-RUN CLINIC PROJECT

9

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On behalf of the Erasmus+ consortia European Prescribing Exam, European Open Platform of Prescribing Education and Clinical Pharmacology and Therapeutics Teach the Teacher program, and the EACPT Education Working Group.

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European Journal of Clinical Pharmacology
2023, Apr;79(4):571-574.
doi: 10.1007/s00228-023-03465-9.

Treatment guidelines differ significantly, not only between Europe and North America but also among European countries[1-4]. Reasons for these differences include antimicrobial resistance patterns, accessibility to and reimbursement policies for medicines, and culturally and historically determined prescribing attitudes. The European Association of Clinical Pharmacology and Therapeutics' Education Working Group has launched several initiatives to improve and harmonize European pharmacotherapy education, but international differences have proven to be a major barrier to these efforts[5-7]. While we have taken steps to chart these differences[6,8], it will probably not be possible to fully resolve them. Rather than viewing these differences as a barrier, we should perhaps see them as an opportunity for intercultural learning by providing students and teachers a valuable lesson in the context-dependent nature of prescribing medication and the different interpretations of evidence-based medicine. Here, we extend our experience with interprofessional student-run clinics[9,10], to report on our first experiences with the "International and Interprofessional Student-run Clinic".

We organized three successful video meetings with medical and pharmacy students of the Amsterdam UMC, location VU University (the Netherlands), and the University of Bologna (Italy). During these meetings, one of the students presented a real-life case of a patient on polypharmacy. Then, in a 45-minute session, the students split into smaller groups (break-out rooms) to review the patient's medication, using the prescribing optimization method and STOPP/START criteria[11,12]. The teachers rotated between the different rooms and assisted the students when necessary. Teachers and students reconvened for 60 minutes for debriefing, with students presenting their findings and suggestions to revise the medication list and teachers stimulating discussion and indicating how they would alter the medication list. Participation was voluntary and the meetings were held in the evenings to accommodate students in clinical rotations.

Third-to-final year medical and pharmacy students participated in the three meetings (n=17, n=20, n=12, respectively). They reported learning a lot from each other, gaining an international and interprofessional perspective. Moreover, they learned to always consider the patient's perspective, that evidence-based medicine is context-dependent, and that guidelines should be adapted to the patient's situation.

There were marked differences in prescribing guidelines and use and accessibility of medicines (***table 1***). In both countries, national societies develop guidelines based on international standards, but in the Netherlands most hospitals have their own local guidelines as well, resulting in different prescribing preferences (e.g. use of different low-molecular-weight heparins). Differences in prescribing preferences exist in Italy, but are based on regional, not local, formularies. For instance, the Emilia-Romagna region has a periodically revised formulary, whereas the Lombardy region does not. Moreover, while in the Netherlands physicians are allowed to prescribe almost all marketed drugs, even if their costs are not always reimbursed, in Italy certain drugs may only be prescribed by a specialist (e.g. new glucose lowering drugs, until January 2022)[13].

Table 1. Examples of differences between clinical practice guidelines and use of medicines in the Netherlands and Italy.

Subject:	Dutch situation[a]:	Italian situation[b]:
Acetylsalicylic acid	Almost exclusively used in low dosages as anti-platelet therapy (41.7 DDD/1000 inhabitants/day).	Commonly used as over-the-counter nonsteroidal anti-inflammatory drug[c] and as anti-platelet therapy (46.1 user DDD/1000 inhabitants/day).
Direct oral anticoagulants[d]	Commonly prescribed by medical specialists and general practitioners (18.6 DDD/1000 inhabitants/day)[14].	Almost exclusively prescribed by medical specialists due to prescribing restrictions that were lifted only recently (15.2 DDD/1000 inhabitants/day)[15].
Vitamin D supplements	Advised as primary prevention for osteoporosis in postmenopausal women and men aged 70 years or older (65.3 DDD/1000 inhabitants/day). Selective reimbursement since 2019, possibly lead to increase of over-the-counter use[c]. Per 2023 no reimbursement at all (over-the-counter use promoted).	In adults, reimbursement was recently restricted to selected conditions because of its potentially inappropriate use (142.9 DDD/1000 inhabitants/day).
Gastric ulcer prophylaxis[e]	Very directive guidelines intended to avoid under- and overuse of PPIs (126.8 DDD/1000 inhabitants/day).	Guidelines aimed at preventing gastric ulcers/bleeding, but not at reducing overuse (79.8 DDD/1000 inhabitants/day).
Osmotic laxatives with opioids[f]	Prophylactic treatment with laxatives is advised when opioids are started (18.9 DDD/1000 inhabitants/day).	Laxatives are reactively given when constipation develops (2.2 DDD/1000 inhabitants/day).
Type II diabetes mellitus	SU derivates[g] remain second-line treatment (for patients without prior cardiovascular or renal disease) (24.6 DDD/1000 inhabitants/day).	SU derivates virtually abandoned since introduction of SGLT2-inhibitors and GLP1-agonists (7.1 DDD/1000 inhabitants/day).
Angina pectoris prophylaxis	Long-acting nitrates usually administered orally	Long-acting nitrates usually administered either via skin patches or oral tablets

DDD= Defined daily dose; PPI = proton pump inhibitor; SU = sulfonylurea; SGLT2 = sodium/glucose cotransporter-2; GLP = glucagon-like peptide-1. [a] Data based on figures of the Dutch National Health Care Institute [16]; [b] Data based on figures of OSMED report - Italian Medicines Agency (AIFA) [17]; [c] No data about over-the-counter use available; [d] Apixaban, rivaroxaban, edoxaban, dabigatran; [e] Omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole; [f] Macrogol, lactulose; [g] Glibenclamide, tolbutamide, gliclazide, glimepiride

These first experiences with international and interprofessional case discussions during the COVID pandemic have taught us that geographical distance no longer needs to be an obstacle to organizing educational events. This, together with the earlier finding that an interprofessional student-run medication review program could optimize pharmacotherapy and reduce adverse drug events, is a promising development[18,19]. We intend to expand the scope of these case discussions by including different universities and larger (intra-curricular) assignments. Five other European universities monitored the last two meetings and want to participate in future meetings. The European Open Platform of Prescribing Education (EurOP^{2}E) provides a meeting place for international teachers wishing to organize such meetings and helps to facilitate them. Interested teachers can apply via www.prescribingeducation.eu.

FUNDING

This work was supported by Erasmus+, grant numbers 2019-1 - NL01 - KA203-060492, 2020-1-NL01-KA203-083098, and2022-1-NL01-KA220-HED-000088069

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by MB, ED, CAMH, PST. The first draft of the manuscript was written by MB and ED and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

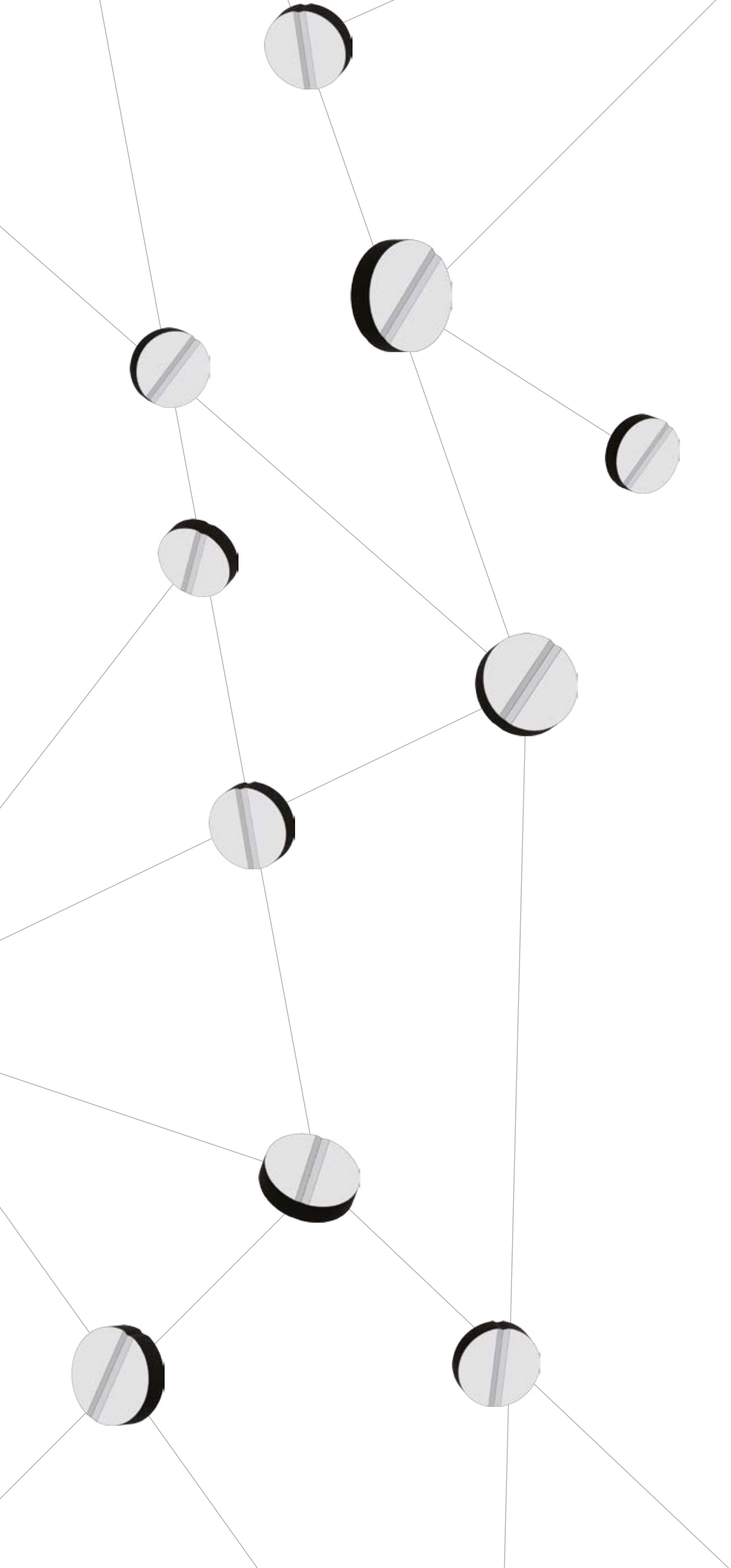
ETHICS APPROVAL

Not applicable

REFERENCES

1. van der Meer P, Gaggin HK, Dec GW. ACC/AHA Versus ESC Guidelines on Heart Failure: JACC Guideline Comparison. *Journal of the American College of Cardiology*. 2019/06/04/ 2019;73(21):2756-2768. doi:https://doi.org/10.1016/j.jacc.2019.03.478
2. Youssef A, Vermeulen N, Lashley EELO, Goddijn M, van der Hoorn MLP. Comparison and appraisal of (inter)national recurrent pregnancy loss guidelines. *Reproductive BioMedicine Online*. 2019/09/01/ 2019;39(3):497-503. doi:https://doi.org/10.1016/j.rbmo.2019.04.008
3. Mohan GC, Lio PA. Comparison of Dermatology and Allergy Guidelines for Atopic Dermatitis Management. *JAMA Dermatology*. 2015;151(9):1009-1013. doi:10.1001/jamadermatol.2015.0250
4. Becker M, Breuing J, Nothacker M, et al. Guideline-based quality indicators—a systematic comparison of German and international clinical practice guidelines. *Implementation Science*. 2019/07/09 2019;14(1):71. doi:10.1186/s13012-019-0918-y
5. Bakkum MJ, Richir MC, Papaioannidou P, et al. EurOP(2)E - the European Open Platform for Prescribing Education, a consensus study among clinical pharmacology and therapeutics teachers. *Eur J Clin Pharmacol*. Aug 2021;77(8):1209-1218. doi:10.1007/s00228-021-03101-4
6. Brinkman DJ, Tichelaar J, Mokkink LB, et al. Key Learning Outcomes for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study. *Clinical pharmacology and therapeutics*. Aug 2018;104(2):317-325. doi:10.1002/cpt.962
7. Donker EM, Brinkman DJ, Richir MC, et al. The European Prescribing Exam: assessing whether European medical students can prescribe rationally and safely. *Eur J Clin Pharmacol*. Jun 2022;78(6):1049-1051. doi:10.1007/s00228-022-03301-6
8. Donker E, Brinkman D, Richir M, et al. European List of Essential Medicines for Medical Education: a protocol for a modified Delphi study. *BMJ Open*. May 4 2021;11(5):e045635. doi:10.1136/bmjopen-2020-045635
9. Schutte T, Tichelaar J, van Agtmael M. Learning to prescribe in a student-run clinic. *Med Teach*. Apr 2016;38(4):425. doi:10.3109/0142159x.2015.1072145
10. Dekker RS, Schutte T, Tichelaar J, Thijs A, van Agtmael MA, de Vries TP, Richir MC. A novel approach to teaching pharmacotherapeutics--feasibility of the learner-centered student-run clinic. *Eur J Clin Pharmacol*. Nov 2015;71(11):1381-7. doi:10.1007/s00228-015-1916-x
11. Drenth-van Maanen AC, van Marum RJ, Knol W, van der Linden CMJ, Jansen PAF. Prescribing Optimization Method for Improving Prescribing in Elderly Patients Receiving Polypharmacy. *Drugs & Aging*. 2009/08/01 2009;26(8):687-701. doi:10.2165/11316400-000000000-00000
12. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age and Ageing*. 2014;44(2):213-218. doi:10.1093/ageing/afu145
13. *Agenzia Italiana del Farmaco (2022) NOTA 100.* https://www.aifa.gov.it/documents/20142/1728125/nota-100.pdf
14. de Jong LA, Koops M, Gout-Zwart JJ, Beinema MJ, Hemels MEW, Postma MJ, Brouwers J. Trends in direct oral anticoagulant (DOAC) use: health benefits and patient preference. *Neth J Med*. Dec 2018;76(10):426-430.
15. *Agenzia Italiana del Farmaco (2020) NOTA 97.* https://www.aifa.gov.it/documents/20142/1728116/nota-97.pdf
16. Zorginstituut Nederland / GIPdatabank. https://www.gipdatabank.nl/
17. *Italian Medicines Agency (2022) The Medicines Utilisation Monitoring Centre. National Report on Medicines use in Italy. Year 2021.*

18. Sultan R, van den Beukel TO, Reumerman MO, et al. An Interprofessional Student-Run Medication Review Program: The Clinical STOPP/START-Based Outcomes of a Controlled Clinical Trial in a Geriatric Outpatient Clinic. *Clinical pharmacology and therapeutics*. Apr 2022;111(4):931-938. doi:10.1002/cpt.2475
19. Reumerman MO, Richir MC, Sultan R, et al. An inter-professional student-run medication review programme. Reducing adverse drug reactions in a memory outpatient clinic: a controlled clinical trial. *Expert Opin Drug Saf*. Apr 28 2022:1-10. doi:10.1080/14740338.2022.2069748



10

USING ARTIFICIAL INTELLIGENCE TO CREATE DIVERSE AND INCLUSIVE MEDICAL CASE VIGNETTES FOR EDUCATION

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British Journal of Clinical Pharmacology
2024, Mar; 90(3):640-648.
doi: 10.1111/bcp.15977

ABSTRACT

Introduction

Medical case vignettes play a crucial role in medical education, yet they often fail to authentically represent diverse patients. Moreover, these vignettes tend to oversimplify the complex relationship between patient characteristics and medical conditions, leading to biased and potentially harmful perspectives among students. Displaying aspects of patient diversity, such as ethnicity, in written cases proves challenging. Additionally, creating these cases places a significant burden on teachers in terms of labor and time. Our objective is to explore the potential of AI-assisted computer-generated clinical cases to expedite case creation and enhance diversity, along with AI-generated patient photographs for more lifelike portrayal.

Methods

In this study, we employed chatGPT (OpenAI, GPT 3.5) to develop diverse and inclusive medical case vignettes. We evaluated various approaches and identified a set of eight consecutive prompts that can be readily customized to accommodate local contexts and specific assignments. To enhance visual representation, we utilized Adobe Firefly beta for image generation.

Results

Using the described prompts, we consistently generated cases for various assignments, producing sets of 30 cases at a time. We ensured the inclusion of mandatory checks and formatting, completing the process within approximately 60 minutes per set.

Discussion

Our approach significantly accelerated case creation and improved diversity, though prioritizing maximum diversity compromised representativeness to some extent. While the optimized prompts are easily reusable, the process itself demands computer skills not all educators possess. To address this, we aim to share all created patients as Open Educational Resources (OER), empowering educators to create cases independently.

INTRODUCTION

Medical case vignettes are widely used for educational purposes; however, they often fall short in representing the diverse patient population encountered in clinical practice[1,2]. The process of clinical reasoning begins the moment healthcare professionals access a patient's electronic health record. The patient's name may lead us to make assumptions about their ethnicity, while their prior medical history provides information about their condition and healthcare utilization. Even during the short walk back from the waiting room, we may form subconscious assumptions about the patient's gender identity, mobility, health literacy, and more. In the best scenarios, these assumptions can enhance patient care by allowing personalized medical approaches. However, in less favorable situations, they can contribute to implicit provider bias[3]. To accurately reflect this reality and ensure that students gain experience with and an awareness of these complexities, it is vital that simulated case scenarios incorporate patients who mirror the diversity commonly encountered in real clinical settings. This includes considering factors such as gender, sexual orientation, race (viewed as a societal construct, determined by the patient's self-identification), ethnicity, disabilities, and other aspects that shape patient identity (social identities). However, it is important to acknowledge that patients rarely fit neatly into predefined categories and conveying the complexity of patient characteristics within text-based cases can be challenging.

Comparable to medicine in general, medical case vignettes often oversimplify the relationship between patients' social identities, such as race or sexual orientation, and their corresponding diseases[4]. Instances vary from relatively benign scenarios, such as a forester visiting a healthcare provider's office, leading students to consider tick-borne illnesses, to more harmful situations where HIV cases are disproportionately associated with men who have sex with men. While it is important to educate students about relative risk factors, these oversimplified and stereotypical connections can inadvertently reinforce essentialist biases and foster the mistaken belief that these characteristics have a direct one-to-one association with disease[5,6]. Such an approach can have detrimental effects on real patient care, resulting in delayed diagnosis and suboptimal treatment[7]. Additionally, the persistence of race-based medicine, which considers race as an essential factor in diagnostic algorithms and clinical practice guidelines, remains prevalent. In our previous publication, a clinical pharmacology and therapeutics teachers guide, we provided insights into effectively teaching about such guidelines without oversimplifying the relationship between race and illness[8]. Awareness of these biases is crucial during the creation of cases. However, attempting to eliminate them may inadvertently introduce new biases. Achieving the delicate balance between promoting diversity and mitigating stereotyping proves challenging, as human creators are inherently constrained in their capacity to develop truly diverse cases.

The process of manually creating high-quality cases, even without attention for diversity, is a labor-intensive task. This is particularly true for (objective structured) clinical examinations, where a substantial number of cases must be generated to prevent fraudulent practices. Policies that require publishing these cases after their initial use may restrict their reusability in subsequent years. During a study focused on determining the specific needs of clinical pharmacology and therapeutics teachers in terms of Open Educational Resources (OERs), it was observed that a repository of reusable clinical case scenarios was the most frequently desired resource on the European Open Platform for Prescribing Education (EurOP²E, http://prescribingeducation.eu)[9].

Introducing computer-generated case generation with randomized patient characteristics holds promise in theoretically enhancing diversity while simultaneously simplifying the case creation process. However, our previous attempts at computer-randomized case generation highlighted certain challenges. Completely randomized cases often led to the emergence of implausible scenarios, such as ethnically inappropriate names and biologically impossible combinations of diversity (e.g., a 70-year-old individual being pregnant). While introducing extreme forms of diversity can be beneficial in encouraging students to question preconceived notions, we recognized the need to strike a balance that avoids the creation of scenarios that would undermine credibility or risk unintended ridicule.

The emergence of user-friendly artificial intelligence (AI), such as ChatGPT, has presented an opportunity to explore whether it can address the issues of limited diversity and stereotype-driven content found in human-generated cases, as well as the limitations of completely random computer-generated scenarios[10]. This innovative approach aims to utilize an AI-powered chatbot (OpenAI chatGPT), to randomize patient characteristics in a manner that ensures broad inclusivity and maintains ethnical and biological appropriateness. Furthermore, it seeks to convey a significant portion of this information without relying on predefined categories, while preserving nuance similar to real-life clinical scenarios. This is achieved through the integration of AI image generation techniques (Adobe Firefly). The primary objective of this approach is to create a significant quantity of authentic and diverse cases that can be reused and customized as OER within local educational contexts. Furthermore, it strives to enhance the accessibility of case creation using AI for all medical educators, particularly those teaching clinical pharmacology and therapeutics who are connected via EurOP²E.

METHODS

To assess the feasibility of this approach, we conducted initial tests to determine if chatGPT could generate medical cases. Initially, we prompted chatGPT to create complete medical cases using a single prompt. While chatGPT demonstrated the ability to generate cases, the results lacked diversity, and customizing the output proved challenging. We observed that longer prompts often led chatGPT to disregard certain parts of our instructions. Based on these findings, we determined that generating cases through small, incremental portions of patient characteristics at a time yielded more favorable outcomes.

We utilized chatGPT to generate a table of fictive patients by prompting it to first generate their names and ethnicities (to reflect the diversity of Amsterdam). Subsequently, we added additional columns, one at a time, for characteristics such as age, BMI, lifestyle, and medicine use. This method yielded improved results as it allowed us to introduce more diversity and provide specific limitations in the prompts. For instance, we discovered that not specifying the desired age range led chatGPT to predominantly create relatively young patients. However, this was not ideal when aiming to create a hypertension case where a broader age range was needed. We encountered two challenges when employing this approach. Firstly, regenerating the tables after each prompt became time-consuming due to their increasing size, resulting in longer waiting times and occasionally caused chatGPT to lose track of the original prompt. Secondly, combining prompts in this manner occasionally led to the creation of stereotypical combinations of diversity. Although these examples were relatively harmless, our intention was to counteract stereotypes rather than reinforce them. Notably, we observed associations such as the occupation "cook" being linked to a high BMI and the French ethnicity being associated with the occupation "wine connoisseur".

To mitigate stereotypical associations, we next aimed to randomize patient characteristics independently. However, it was not feasible to randomize all characteristics independently, as certain attributes were inherently interconnected. For instance, ensuring ethnically and gender-appropriate names required simultaneous consideration of the name, gender, and ethnicity. Nonetheless, characteristics such as BMI, lifestyle, and occupation could be randomized independently. To systematically organize the desired characteristics and their interrelationships, we initially created an overview (***Figure 1***) as a reference. This overview served as a guide to ensure comprehensive coverage of relevant patient attributes and facilitated the identification of interconnected characteristics that needed to be randomized together. Not all patient attributes were intended to be directly displayed as text within the case scenarios due to the risk of oversimplification and the loss of nuanced information. To address this, we employed the concept of "dummies" for certain attributes, which served as underlying variables influencing other characteristics. For instance, ethnicity was treated as a dummy variable that influenced the selection of appropriate names and the AI image.

In the end, we were able to generate all relevant patient information in eight short chatGPT prompts (***table 1***). These prompts can be further tailored and expanded to suit local contexts and the specific focus of the assignment. For instance, if the aim is to simulate a scenario in a different city or country, the requirement to match the ethnicities of the fictional individuals with that of Amsterdam can be substituted accordingly. Moreover, when exploring a case study on type 2 diabetes mellitus, adjustments might be needed to accommodate different age ranges and weight distributions and for a case study on urinary tract infections, the addition of a randomization prompt for urinalyses may be beneficial. The patient presentation and physical examination findings can be randomized as desired, and the manner in which they present their symptoms can be customized as

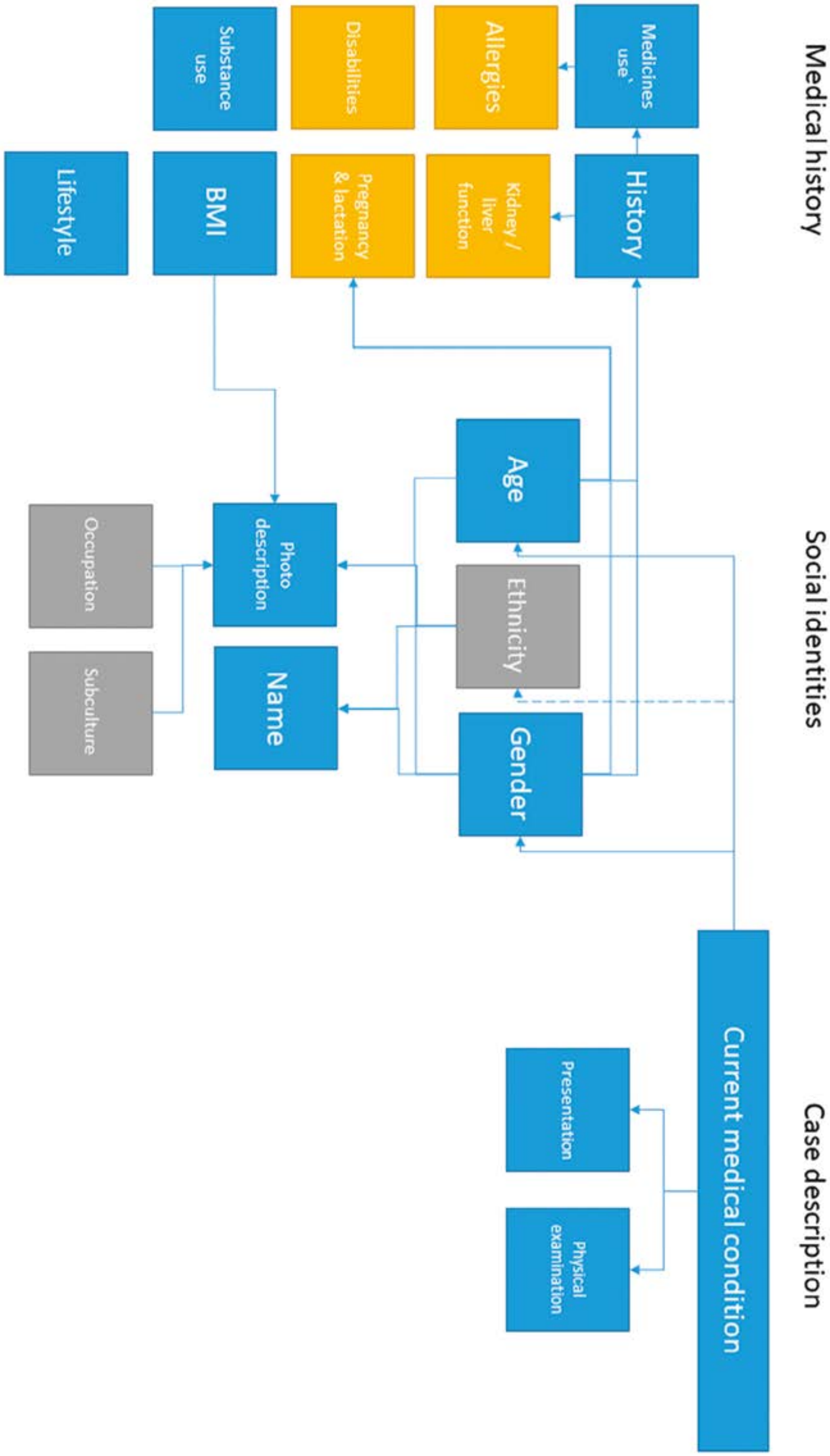
Medical history
Social identities
Case description
Medicines use
History
Allergies
Kidney / liver function
Disabilities
Pregnancy & lactation
Substance use
BMI
Lifestyle
Age
Ethnicity
Gender
Photo description
Name
Occupation
Subculture
Current medical condition
Presentation
Physical examination

Figure 1. Overview of randomized characteristics and their interconnections**.** The patient characteristics generated by chatGPT. In blue: randomized characteristics displayed as text; in grey: dummy variables used for influencing other characteristics and in yellow: characteristics to be combined in medical alerts and disabilities.

Table 1. ChatGPT prompts to generate all relevant patient information for case vignettes

Characteristics	Prompt	Notes
Name Gender Ethnicity	Make 30 fictive people for use in medical case vignettes. Make their **ethnicity reflect the diversity of Amsterdam.** **Make 4 have a trans <use transman or transwoman> or non-binary gender.** Output in table with columns first name, last name, gender, ethnicity.	Limiting ethnic diversity to reflect Amsterdam helped create a more representative population. By specifying gender diversity, the 30 cases included a diverse range of gender identities. Without this specification, there would be fewer non-binary patients and no mention of transgender individuals.
Age Date of birth Occupation Subculture	For use in medical case vignettes randomize 30 **birthdates, so that the fictive patients are between 18 and 98 years old.** Also randomize their **occupation, be inclusive of pensioners and jobless people**. Also randomize their **subculture, be inclusive of all possibilities including none.** Output as table with columns age, date of birth (in dd-mm-yyyy), occupation and subculture.	Specifying the age-limit ensured a more accurate representation of disease prevalence (in this example infectious diseases). Without it, ChatGPT primarily generated responses related to individuals aged 20-60. Both occupation and subculture served as dummy variables in the photograph, showcasing relatively diverse examples such as student, bus driver, barista, graphic designer, as well as punk, gamer, and sports fan subcultures.
BMI Length Weight Alcohol intake Tobacco use Drug use Lifestyle	For use in medical case vignettes randomize 30 **BMI's, to reflect a diverse population of individuals. Be inclusive of thin, healthy weight, obese and morbidly obese individuals.** Also randomize **lifestyle**, **alcohol** (in average units/day) , **tobacco use** (as either active, with number of packs/ per day; stopped with the number of pack-years smoked; or never) and **recreational drug use** (with explanation of what drugs and the frequency). Output as table with columns length (in meters); weight (in kilograms) and BMI (one decimal), lifestyle, alcohol intake, tobacco use and recreational drug-use.	Specifying body metrics is crucial for representing diversity accurately. Without it, ChatGPT tends to generate responses predominantly depicting individuals with a healthy weight. However, it can be further customized by prompting to make it typical for patients with a specific condition, such as diabetes type II.

Table 1. (continued)

Characteristics	Prompt	Notes
Medical history	For use in medical case vignettes randomize medical history for the following fictive patient's age and gender: **<paste list of patient age and gender>** **Make it include between two and four of the following chronic conditions.** Be inclusive of all options. pain <replace with specific example, like ankle fracture, osteoarthritis and more>, Hypertension, Diabetes type 2, Contraceptive use, Acne, Eczema, Allergies <replace with specific example like allergic rhinitis, conjunctivitis>, hypothyroidism, Acid reflux, Gastric ulcer disease, Atrial fibrillation, Ischemic heart disease, Heart failure, depression **And between two and four of the following minor ailments.** Be inclusive of all options**.** Headache, Common cold, Sore throat, Cough, Fever, Nausea, Upset stomach, Diarrhea, Heartburn, Indigestion, Muscle ache, Backache, Minor cuts <use example like cut finger>, Bruises, Sprains, Minor burns <use example like burned hand> etc.* **Avoid conditions that are untypical for age and gender** In total the lists must be between 3 and 7 conditions long. Randomize the order. in format <year of onset> - <condition>. Output as table with a new column, with linebreaks between the conditions.	Addressing medical history can be challenging since it intertwines with various biological factors. However, we discovered that providing comprehensive lists of potential conditions is necessary. Without such specificity, ChatGPT tends to rely on a limited range of options. Differentiating between chronic and minor illnesses is vital for accuracy and relevance, especially considering the diseases that students have previously learned to diagnose and treat. The "avoid conditions that are untypical for age and gender" prompt feature may occasionally experience malfunctions. Therefore, we highly recommend manually reviewing the lists to ensure accuracy and appropriateness. *Table shortened for presentation; actual list of minor conditions is longer.

Table 1. (continued)

Characteristics	Prompt	Notes
Current medicine use	For use in medical case vignettes. Please randomize the **current medicine lists** for patients with the following conditions. Output as table, one fictive patient per row as below. indicate linebreaks within a cell. **<paste list of medical histories>** **Use generic drug names, not brand names, nor group names. Use only drugs available in the Netherlands.** **Minor conditions <2021 must not be treated.** **Avoid clinically relevant drug-drug interactions and medicine contra-indicated by comorbidty.** Use format: drug name, dosage, daily use. (e.g. lisinopril, 10mg. 1 tablet per day) Output as table, with new column with linebreaks between the medicines.	Creating accurate medical lists can be challenging for ChatGPT. While the prompt to use generic names and output in the given format is effective, it may not account for local availability of medicines, contra-indications, and drug-drug interactions. Due to these limitations, it is crucial to manually review and verify the lists for accuracy.
Pregnancy Lactation Allergies	For use in medical case vignettes, randomize the **allergies, pregnancy and lactations status** for fictive patients with the following ages and genders. <paste list of patient ages and genders> **40% of female, transman (not transwoman) or non-binary patients aged 18-46 should be pregnant or lactating (not both).** Write pregnancies including duration in weeks+days notations (e.g. pregnant 34+5). Write lactating as "lactating". Leave empty if not applicable.	Randomizing medical contra-indications poses challenges, particularly when it comes to specifying pregnancy and lactation. ChatGPT may not fully comprehend transgender pregnancies or reproductive age-limits. Therefore, it becomes necessary to explicitly define who can be pregnant and lactate in order to ensure accurate and inclusive information. The pregnancy/ lactation rate was set higher to offer students ample training opportunities. However, it can be adjusted for a more representative experience in line with real-world scenarios.

Table 1. (continued)

Characteristics	Prompt	Notes
	25% of all patients should have one or more allergies to medicinal products (specific drugs, latex, bandages etc). make it diverse. Other allergies should not be listed (leave empty). The most common medicinal allergies are for penicillin, NSAIDS and ACE-inhibitors, but use others too. Output as table with a new columns allergies and pregancy/lactation.	Specifying allergies is essential to include only medically relevant ones. We extensively experimented with combining it so that ChatGPT avoids allergic reactions to medications already present in the current medications list, but unfortunately, we were unable to make this feature work reliably. As a result, manual correction is necessary to ensure accuracy in handling allergies and medications.
Disability Renal insufficiency	For use in medical case vignettes randomize fictive patients. <paste list of patient ages> **Make one in ten of these people have a disability, consider prevalence in relation to age**. Leave empty if not applicable. Pick from : Visual impairment, Hearing loss, Mobility impairment, Cognitive impairment, Autism spectrum disorder, Speech and language disorder, Developmental delay, Attention deficit hyperactivity disorder (ADHD), Learning disability , Intellectual disability , Dyslexia, Down syndrome, Cerebral palsy, amputee (right foot) **Make one in ten of these people have a renal insufficiency warning, consider prevalence in relation to age.** Write as: renal insufficiency (eGFR <randomly generated 20-60>). Leave empty if not applicable. Output as table with new columns for disability and kidney insufficiency.	Randomizing disability, along with the last medical contra-indication of renal insufficiency, can be treated as separate characteristics during the generation process. However, combining these factors with the previously generated ages may enhance the ability to generate more age-appropriate results.

Table 1. (continued)

Characteristics	Prompt	Notes
AI image prompt	Provide a **visual description** for each of the following fictive patients: Use format: A <age> year old <gender description> who is <BMI description>, <pregnancy description>, <disability description>, <occupation> <subculture description> <paste table with aforementioned parameters> Output as new column in the table	To generate four images, you can copy these prompts into Adobe Firefly and manually select the best one. For optimal results, we suggest using "photo" settings rather than "art" or "graphic" settings to ensure a more realistic representation and avoid caricature-like images.

in bold, the dimensions of diversity and their distributions, which can be modified based on the specific context and requirements. To capture the outputs effectively, we propose employing a follow-up prompt: "Output as .csv with semicolon separators, preserving line breaks." This prompt will generate text that can be conveniently copied and saved as a .csv file using software like Notepad or pasted into a spreadsheet program, aided by the text-to-column wizard. Given that csv files do not support line breaks, it is crucial to substitute them with a concise code, such as
 in this case, which can be subsequently replaced with an actual line break using the find and replace function in your preferred text processing software.

was previously demonstrated by Benoit[11]. However, for the purpose of this example, we deliberately ensured that each patient was designed to exhibit a highly similar manner of presentation. This placed emphasis on the diverse patient characteristics, allowing learners to focus on the intricacies and complexities of individual patient profiles. The process of generating AI images involves utilizing the eight prompt to generate a textual description of the patient. This description is then copied and pasted into Adobe Firefly, which produces four photographs based on the provided details. From these generated images, the most appropriate one can be manually selected for use.

Through our observations, we have found that generating 30 cases strikes a balance between diversity and loading times. Creating too few cases may lead to an overrepresentation of certain ethnicities and gender identities, while generating too many can unnecessarily increase loading time and occasionally lead to malfunctions. To capture the outputs, we recommend making chatGPT output them as .csv files (as explained in table caption) and copying the responses into one spreadsheet. While transforming this spreadsheet into nicely formatted cases can be done manually, we suggest exploring the mail merge option in MS Word as a way to automate the process. By utilizing mail merge, data from the spreadsheet can be seamlessly merged into predefined templates, resulting in time and effort savings by eliminating the need for individual case formatting.

While the authors have access to a ChatGPT Plus subscription, which proved helpful during peak usage times for non-paying users, for the sake of repeatability, all prompts were conducted using GPT-3.5, the freely accessible version of OpenAI's ChatGPT (https://chat.openai.com/). All images were generated using Adobe Firefly's (beta) free text to image generator (https://firefly.adobe.com/)

RESULTS

Utilizing this approach, we have successfully expedited the process of creating cases, whilst taking steps to improve the representation of diversity within these cases. ***Figure 2*** presents four case vignettes about cellulitis, supplement 1 shows the 30 unedited vignettes generated for urinary tract infections. The optimization of prompts required considerable time and effort; however, having completed this process, the generation of 30 cases, including formatting, manual checks for appropriateness, and other necessary tasks, could be accomplished within approximately one hour.

Our objective is to implement a trial using these cases in our educational setting, where students will evaluate and provide feedback on them. This feedback will be utilized to further refine and enhance the case generation process. We envision a lesson where each student is presented with a patient who presents in a similar manner, but with patients themselves demonstrating substantial diversity. Through team-based learning[12], students will engage in discussions to identify and analyze the distinct factors that differentiate the patients and explore how these variations impact their diagnostic and treatment approaches. This interactive approach fosters critical thinking and promotes a deeper understanding of the influence of diversity on healthcare decision-making.

DISCUSSION

Our approach has successfully achieved its goal of expediting the case-creation process, enhancing diversity through computer-randomization of patient characteristics. Nevertheless, it is important to acknowledge a trade-off when it comes to representativeness. In the real world, patients do not possess a randomized set of characteristics; instead, they have multiple social identities that intersect and mutually shape one another (known as intersectionality)[13,14]. While we believe chatGPT to be quite capable of giving ethnically appropriate names, this was not verified through name databases. Moreover, it insufficiently takes other intersections into account. For instance, chatGPT generated a case where a 61-year-old Moroccan patient had an Arabic first name and a Dutch last name (Mohamed van der Berg). While this combination is not impossible, it is uncommon, as most 61-year-old Moroccan males living in the Netherlands are first-generation migrants, and such name combinations are more likely in later generations. Another example is the case vignette of Fatima Rahman in Figure 2, who consumes an atypical amount of alcohol (1.8 units per day) considering her pregnancy. Our current approach aimed to minimize stereotypes, prioritizing diversity over representativeness. Whether this balance is optimal is a topic that should be explored in future research and subject to debate.

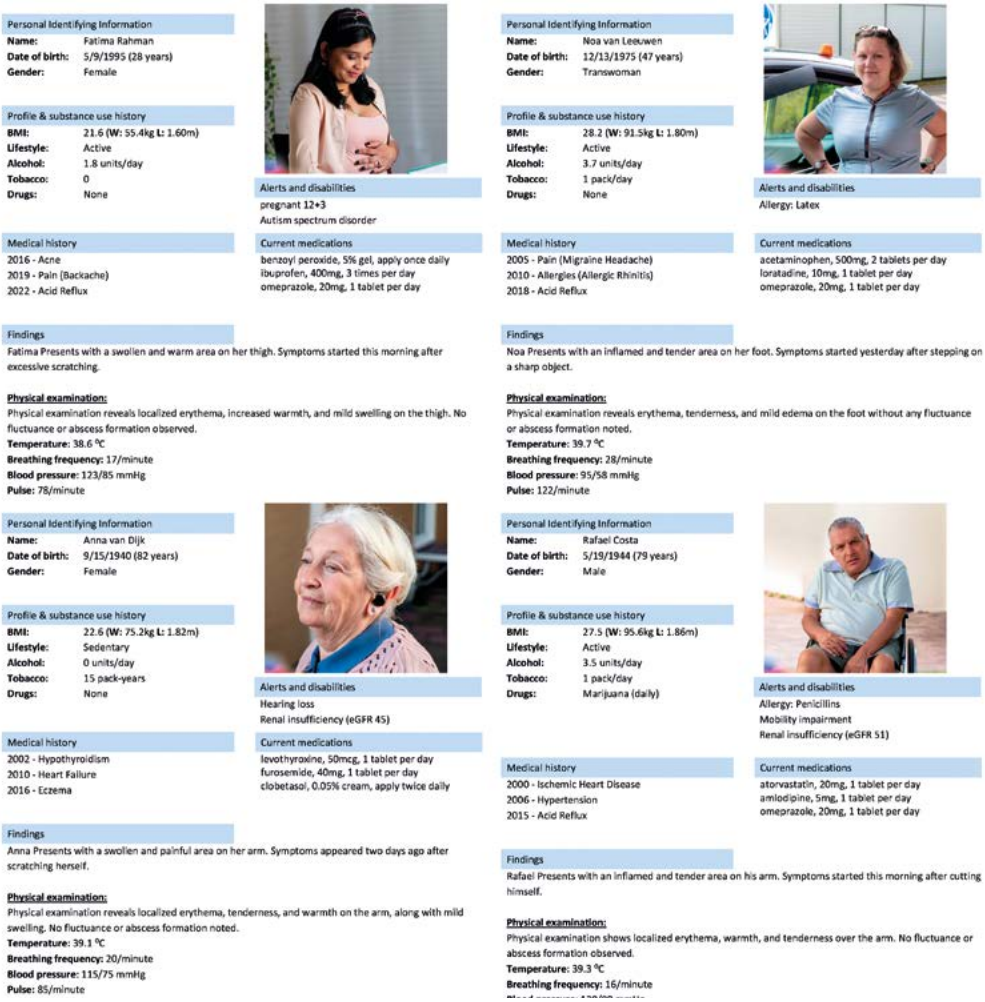

Figure 2. Examples of case descriptions. Four examples of cases generated for a case-based clinical pharmacology & therapeutics assignment about cellulitis.

The same is true for the choice of what characteristics to include in the vignettes and how to display them. By incorporating a wide range of patient characteristics, students gain insights into the factors that influence their clinical decision-making, distinguishing between relevant and irrelevant information across different clinical scenarios. Case vignettes should avoid providing clues about relevance by selectively including or excluding certain details. Currently, dimensions of diversity such as religion, political beliefs, and sexual preference were not encompassed in the cases. This decision was made to focus on the most commonly relevant factors in medical scenarios and to align with real-life patient care practices. For instance, parameters like BMI and smoking history hold relevance across various medical scenarios and are typically documented in medical records.

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Conversely, religion seldom holds relevance, nor is a routinely recorded parameter in such contexts. Ethnicity can be significant in relation to disease prevalence and therapeutic response[15]. However, capturing ethnicity as a single categorical label poses challenges due to its multifaceted nature, encompassing concepts such as ancestry, nationality, and culture[16,17]. Moreover, in real clinical settings, ethnicity is seldom objectified but rather inferred from a patient's phenotype, name, and cultural expressions[18,19]. To reflect this reality and encourage students to recognize and challenge(!) their assumptions, we made the decision to convey information about ethnicity (as well as (sub)culture and occupation) through a photograph of the patient, rather than a label. Utilizing AI image generation to create lifelike photographs of non-existing individuals offers several advantages over using real photographs, eliminating the need for extensive searches for suitable images that match the fictional patient's profile while addressing privacy, portrait and intellectual property law concerns. Images generated through Adobe Firefly can be freely reused for non-commercial purposes. In situations where a sexual history is relevant, such as in cases related to sexually transmitted diseases or potential pregnancy, we recognize that it cannot be simply captured through a single categorical label (e.g., man having sex with men). Instead, it necessitates a comprehensive explanation within the patient presentation. This detailed information can also be generated by AI. If this information is included in a case, it is essential to approach it without normativity by ensuring equal detail in the display of information[2,20]. For example, the sexual history of patients with one primary sex partner should be described as thoroughly as that of patients with multiple sex partners, and the details of heterosexual relations should be presented with the same level of depth as that of bisexual and homosexual relations.

ChatGPT functions by accurately predicting word order, enabling it to generate responses that may appear knowledgeable. However, it is crucial to remember that ChatGPT does not possess actual medical, biological or social knowledge. Furthermore, it is essential to emphasize that chatGPT was trained using a vast collection of texts sourced from the internet, including webpages and books and mostly texts from the Global North. Although the exact details of the training dataset have not been publicly disclosed, it is improbable for the materials to be completely free from biases. Therefore, it is essential to acknowledge that chatGPT inherently reflects the same biases that we are already familiar with, such as a tendency towards favoring young and white individuals, for example[21,22]. Consequently, certain limitations arise when employing it for the development of medical cases, such as BMI's not being calculated accurately from length and weight, genders and ethnicities not generating according to the requested distribution, patients having allergies to currently prescribed medications etc. Some of these limitations can be mitigated by including explicit specifications in the prompts or regenerating the response several times until it has the correct format and level of diversity. However, addressing other limitations necessitates manual refinement. To ensure precision and consistency, we highly recommend conducting comprehensive manual reviews of all cases to identify any potential inconsistencies.

While our optimized prompts have significantly facilitated the process of creating cases, we acknowledge that making these cases with chatGPT still requires a certain level of computer skills. For instance, saving chatGPT outputs to a .csv file and creating a template for mail merge in MS Word can be challenging. Exploring the possibilities of utilizing the chatGPT API code to streamline the process is an avenue worth considering, although it may require expertise beyond our current capabilities. As an alternative approach, we intend to make the diverse fictional individuals we generate accessible on EurOP^{2}E as OER. This will allow teachers to access the patient information and manually input the cases for various medical subjects themselves. Moreover, we have plans to develop a comprehensive guide on crafting these cases detailing the challenges and opportunities, and establish a discussion board where teachers can engage in conversations about the prompts, share their experiences, and collectively enhance their quality.

A scientific evaluation of our efforts, including students' reactions and evaluations was not included in the current manuscript. We are committed to conducting such an evaluation and reporting the findings separately.

ACKNOWLEDGEMENTS

The authors acknowledge the assistance of chatGPT in copy-editing the text of this article. It is important to note that chatGPT was solely used as a tool for editing purposes (prompt: *improve writing*), and no content was generated by chatGPT.

FUNDING INFORMATION

Erasmus+ grant 2020-1-NL01-KA203-083098

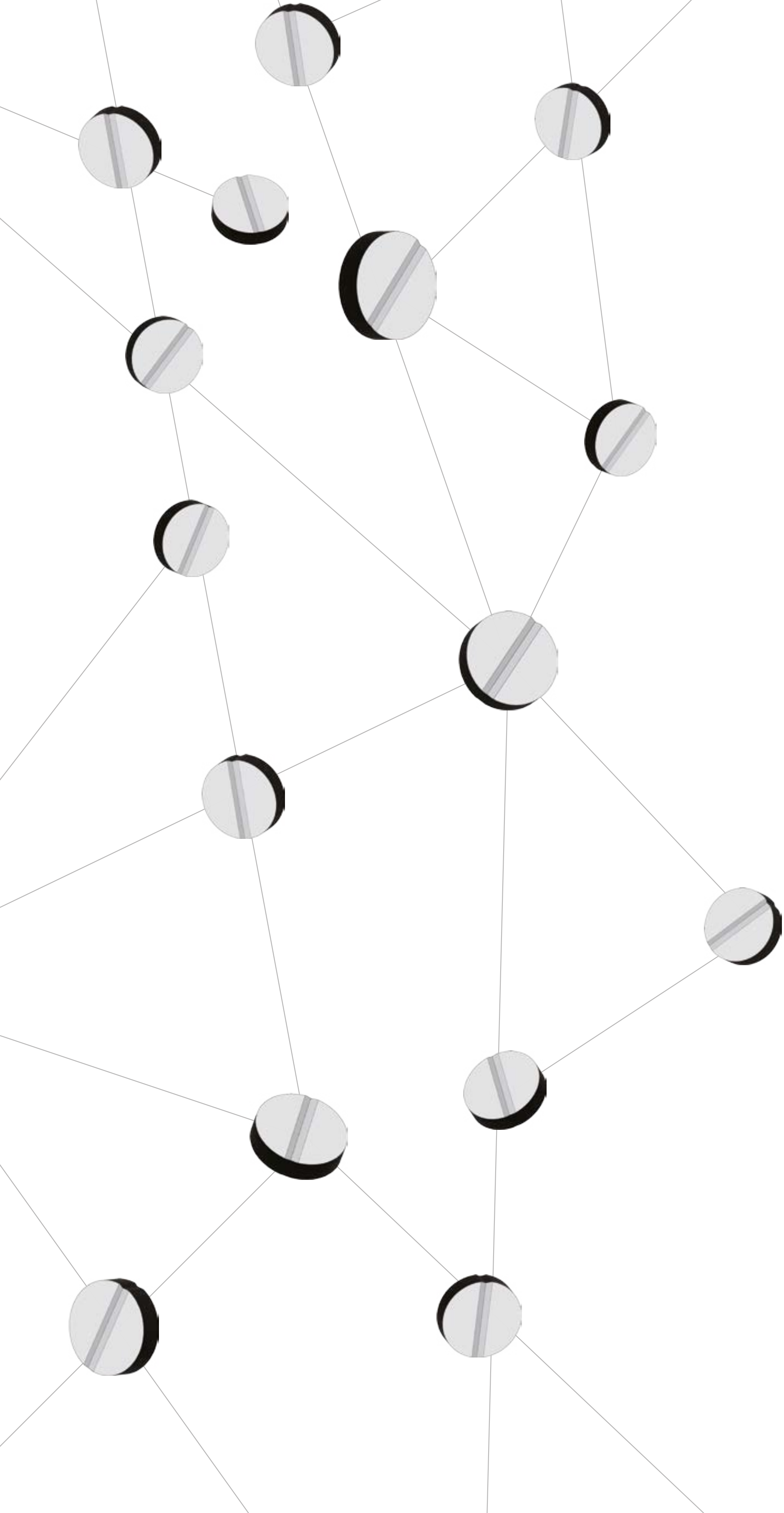
AUTHOR CONTRIBUTIONS

Michiel J. Bakkum: Conceptualization, formal analysis, writing draft, visualization. Mariëlle G. Hartjes, Joost D. Piët, Erik M. Donker: Conceptualization, formal analysis, writing – review and editing. Robert Likic, Emilio Sanz, Fabrizio de Ponti, Petra Verdonk, Milan C. Richir, Michiel A. van Agtmael: Conceptualization, writing – review and editing. Jelle Tichelaar: Conceptualization, writing – review and editing, supervision.

REFERENCES

1. Lee CR, Gilliland KO, Beck Dallaghan GL, Tolleson-Rinehart S. Race, ethnicity, and gender representation in clinical case vignettes: a 20-year comparison between two institutions. *BMC Medical Education*. 2022/07/30 2022;22(1):585. doi:10.1186/s12909-022-03665-4
2. Muntinga M, Beuken J, Gijs L, Verdonk P. Are all LGBTQI+ patients white and male? Good practices and curriculum gaps in sexual and gender minority health issues in a Dutch medical curriculum. *GMS J Med Educ*. 2020;37(2):Doc22. doi:10.3205/zma001315
3. Oxtoby K. How unconscious bias can discriminate against patients and affect their care. *BMJ*. 2020;371:m4152. doi:10.1136/bmj.m4152
4. Ripp K, Braun L. Race/Ethnicity in Medical Education: An Analysis of a Question Bank for Step 1 of the United States Medical Licensing Examination. *Teach Learn Med*. Apr-Jun 2017;29(2):115-122. doi:10.1080/10401334.2016.1268056
5. Nieblas-Bedolla E, Christophers B, Nkinsi NT, Schumann PD, Stein E. Changing How Race Is Portrayed in Medical Education: Recommendations From Medical Students. *Academic Medicine*. 2020;95(12)
6. Tsai J, Ucik L, Baldwin N, Hasslinger C, George P. Race Matters? Examining and Rethinking Race Portrayal in Preclinical Medical Education. *Academic Medicine*. 2016;91(7):916-920. doi:10.1097/acm.0000000000001232
7. Cerdeña JP, Plaisime MV, Tsai J. From race-based to race-conscious medicine: how anti-racist uprisings call us to act. *The Lancet*. 2020;396(10257):1125-1128. doi:10.1016/S0140-6736(20)32076-6
8. Bakkum MJ, Verdonk P, Thomas EG, et al. A Clinical Pharmacology and Therapeutics Teacher's Guide to Race-Based Medicine, Inclusivity, and Diversity. *Clin Pharmacol Ther*. Mar 2023;113(3):600-606. doi:10.1002/cpt.2786
9. Bakkum MJ, Loobeek BJ, Richir MC, et al. Teaching resources for the European Open Platform for Prescribing Education (EurOP(2)E)-a nominal group technique study. *NPJ Sci Learn*. Sep 30 2022;7(1):23. doi:10.1038/s41539-022-00141-y
10. Sallam M. ChatGPT Utility in Healthcare Education, Research, and Practice: Systematic Review on the Promising Perspectives and Valid Concerns. *Healthcare (Basel)*. Mar 19 2023;11(6) doi:10.3390/healthcare11060887
11. Benoit JRA. ChatGPT for Clinical Vignette Generation, Revision, and Evaluation. *medRxiv*. 2023:2023.02.04.23285478. doi:10.1101/2023.02.04.23285478
12. Parmelee D, Michaelsen LK, Cook S, Hudes PD. Team-based learning: a practical guide: AMEE guide no. 65. *Med Teach*. 2012;34(5):e275-87. doi:10.3109/0142159x.2012.651179
13. Muntinga ME, Krajenbrink VQ, Peerdeman SM, Croiset G, Verdonk P. Toward diversity-responsive medical education: taking an intersectionality-based approach to a curriculum evaluation. *Adv Health Sci Educ Theory Pract*. Aug 2016;21(3):541-59. doi:10.1007/s10459-015-9650-9
14. Verdonk P, Muntinga M, Leyerzapf H, Abma T. From Gender Sensitivity to an Intersectionality and Participatory Approach in Health Research and Public Policy in the Netherlands. In: Hankivsky O, Jordan-Zachery JS, eds. *The Palgrave Handbook of Intersectionality in Public Policy*. Springer International Publishing; 2019:413-432.
15. Vyas DA, Eisenstein LG, Jones DS. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. *New England Journal of Medicine*. 2020;383(9):874-882. doi:10.1056/NEJMms2004740
16. Commission E, Justice D-Gf, Consumers, Farkas L. *Analysis and comparative review of equality data collection practices in the European Union : data collection in the field of ethnicity*. Publications Office; 2020.

17. Routen A, Akbari A, Banerjee A, et al. Strategies to record and use ethnicity information in routine health data. *Nature Medicine*. 2022/07/01 2022;28(7):1338-1342. doi:10.1038/s41591-022-01842-y
18. Kaplan JB, Bennett T. Use of race and ethnicity in biomedical publication. *Jama*. May 28 2003;289(20):2709-16. doi:10.1001/jama.289.20.2709
19. Boehmer U, Kressin NR, Berlowitz DR, Christiansen CL, Kazis LE, Jones JA. Self-reported vs administrative race/ethnicity data and study results. *Am J Public Health*. 2002;92(9):1471-1472. doi:10.2105/ajph.92.9.1471
20. Krishnan A, Rabinowitz M, Ziminsky A, Scott SM, Chretien KC. Addressing Race, Culture, and Structural Inequality in Medical Education: A Guide for Revising Teaching Cases. *Acad Med*. Apr 2019;94(4):550-555. doi:10.1097/acm.0000000000002589
21. Singh S. Is ChatGPT Biased? A Review. 2023;
22. Stypinska J. AI ageism: a critical roadmap for studying age discrimination and exclusion in digitalized societies. *AI & SOCIETY*. 2023/04/01 2023;38(2):665-677. doi:10.1007/s00146-022-01553-5



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SUMMARY AND GENERAL DISCUSSION

SUMMARY AND GENERAL DISCUSSION

Medical education and training often fall short in adequately equipping medical students and young doctors with the competence to prescribe medications safely[1,2]. The art of prescribing medicines necessitates hands-on training under clinical supervision, facilitated by case scenarios or similar problem-based learning approaches, as opposed to mere lectures and textbooks[3,4]. Despite this, a considerable number of European medical schools adhere to conventional teaching methods[5]. This situation accentuates substantial global disparities in the extent and quality of education in clinical pharmacology and therapeutics.

In this thesis, our hypothesis poses that improving international collaboration among teachers in clinical pharmacology and therapeutics will contribute to the improvement and harmonization of prescribing education standards across Europe and other regions. Digital educational resources are promising because of their broad applicability across diverse educational frameworks, requiring only a single investment of time and resources. As such, our studies started with the following primary research questions: **What is the present scope of digital education in clinical pharmacology and therapeutics, and what are its outcomes?**

Chapter 2 was devoted to addressing these questions by methodically examining the existing literature. To this end, we reviewed 65 articles, each assessing a minimum of one digital educational resource, not necessarily online, for the teaching of prescribing skills. Our analysis suggests that digital resources are effective in transferring essential knowledge required for safe prescribing. While some studies reported that digital resources had a positive impact on prescribing quality, as assessed with chart reviews or prescribing simulations, other did not. The body of research investigating direct effects of these resources on patient outcomes remains limited, preventing a definitive conclusion about direct patient benefits stemming from these interventions. Undergraduate and postgraduate students uniformly expressed satisfaction with the digital resources. Distilling recurring themes from user evaluations, we formulated ten recommendations concerning elements or topics that should be incorporated in future digital resources. These include features such as on-demand accessibility and direct feedback, as presented in Chapter 2, Table 3.

Limitations to this study must be acknowledged. First, the search yielded a diverse array of digital resources and study frameworks, making direct comparisons difficult. The scarcity of studies that compared digital resources with non-digital alternatives further hindered the ability to establish the effects of digital education compared with traditional approaches. A fundamental limitation of this study lay in the likelihood of incomplete reporting. Not many teachers subject their teaching materials to scientific assessment and subsequently publish research articles on the topic. Thus, while this study design was the optimal approach for addressing the latter aspect of the research question — the impact of digital resources—it may not have been the most suitable methodology for addressing the initial question—investigating how digital resources are used in clinical pharmacology and therapeutics education.

In **Chapter 3**, our focus was on addressing this question. We carried out a survey among our network of pharmacotherapy teachers. The aim was to gain insight into the digital learning resources used in their curricula.

Ninety-nine teachers from 95 medical schools across 26 out of the then 28 EU member states participated. Of these, 66 schools (70%) used digital resources in their teaching programmes. We identified 89 distinct resources, with a variety of formats: e-learning (23.9%), pharmacokinetics/pharmacodynamics simulation (10.2%), virtual patient modules (8.0%), electronic prescribing system simulation (2.3%), and other types (Chapter 3, Table 2). We reviewed these resources in detail and evaluated their learning objectives. This showed that slightly less than 40% of the resources were oriented towards problem-based learning, and that nearly 70% of the resources were subject to access restrictions. Restrictions were either commercial in nature, requiring payment for personal or institutional access, or non-commercial with resources being limited to students enrolled at the respective institution for unclear reasons. Of the 89 resources, only 2 had licenses that permitted unrestricted adaptation and non-commercial redistribution of the resources.

Like any voluntary survey, the outcomes of this study might have been affected by participation bias. Thus, achieving an all-encompassing compilation of every digital educational resource used in the teaching of clinical pharmacology and therapeutics is exceedingly challenging (and not particularly enlightening). Consequently, it is more appropriate to regard this article as a compendium of potential avenues and best practices of digital educational resources.

On the basis of the findings of these two studies, we concluded that a diverse array of digital educational resources are currently used in prescribing education. These resources effectively supplement the teaching of clinical pharmacology and therapeutics. However, we also found areas that could be improved. Although we identified several problem-based resources, the majority concentrated solely on knowledge outcomes. A more crucial observation was the underutilization of the potential of digital resources to disseminate knowledge.

What remained elusive was understanding why international clinical pharmacology and therapeutics teachers so rarely shared their resources. We lacked insight into their willingness to collaborate more intensively and how to facilitate this collaboration. Therefore, our second research question was: **How can we enhance international collaboration in digital education?**

In **Chapter 4**, we combined the findings of an international survey, sent out together with the survey presented in Chapter 3, with those of an international consensus meeting held during the bi-annual EACPT conference in Stockholm in 2019. The survey targeted participants' motivation for engaging or abstaining from collaboration in digital education. Among the predefined hypotheses explored were the participants' lack of confidence in the efficacy of online education, institutional constraints, and concerns regarding intellectual property laws. We proposed setting up an online platform for sharing open educational resources and collaboration and asked participants about perceived opportunities and obstacles to this.

The survey was completed by 99 teachers from 26 EU member states. They reported benefits of resource sharing, such as potential cost reduction, broader student outreach, and mutual learning. They reported a lack of networking opportunities, technical problems, and translation difficulties as being major barriers (Chapter 4, Supplementary Table 1). The participants thought that digital resources were more effective than in-person instruction in teaching knowledge, but less effective in teaching skills and attitudes. With regard to setting up an online platform, they anticipated positive effects such as accessing high-quality resources, drawing inspiration, improving teaching quality, and more (Chapter 4, Table 2). Yet, they also foresaw obstacles, such as language problems, differences in guidelines and teaching styles, time and financial investment, technological challenges, quality control, ownership and responsibility concerns for the platform, and difficulties dissemination of this project.

Subsequently, a consensus meeting was held during the 2019 EACPT conference in Stockholm, attended by 47 international teachers in clinical pharmacology, therapeutics, and (basic) pharmacology. The mission statement, aimed at establishing a network of pharmacology and clinical pharmacology teachers to improve and standardize teaching through shared resources, collaboration, and inspiration via an online platform, was unanimously approved. The platform's name, "The European Open Platform for Prescribing Education" (EurOP^{2}E), was officially decided during this meeting. To address the identified obstacles, potential solutions were discussed, culminating in the framework depicted in Figure 1 and explained below.

Foundation: The platform shall be founded in evidence-based education and the pre-existing framework of the World Health Organization's Guide to Good Prescribing. Supported by the large network of teachers in pharmacotherapy.

Resource applicability: To ensure the broad relevance of open educational resources available on the platform, these resources shall be available primarily in English. Nevertheless, considering the predominant use of local languages, it is important that all resources are translatable. Local teachers should be empowered to adapt resources to accommodate disparities in prescribing guidelines, drug availability, and related factors. To facilitate this, editable source files should be provided alongside resources, accompanied by Creative Commons (or equivalent) licenses that permit adaptation and redistribution. Resources with stricter licenses are not consistent with the platform's ethos. A spirit of collaborative improvement is actively promoted, encouraging contributors to re-upload improved versions for collective benefit.

Resource Quality Improvement: To reduce concerns about the potential inadequacy of resources on the platform, we reached consensus on implementing three measures to guarantee content quality. First, we determined that resources to be uploaded onto the platform should first be peer-reviewed. The exact specifications of this review process have yet to be determined. Second, in recognition of the fact that resources must be up to date with regard to evidence-based medicine, and that this might not be assured by the peer-review process, it was agreed that a user review system should be set up. Teachers could provide feedback on the content and, if deemed appropriate, rank the quality of the resources. Lastly, it was decided not to make the entire platform accessible to all. Instead, access to certain segments of the platform would be restricted to teachers. While this necessitates the introduction of a teacher verification system and entails a partial departure from complete openness, its value lies in empowering teachers. This approach enables them to evaluate resources for quality, timeliness, relevance to their local context, and other relevant criteria before incorporating them into their teaching.

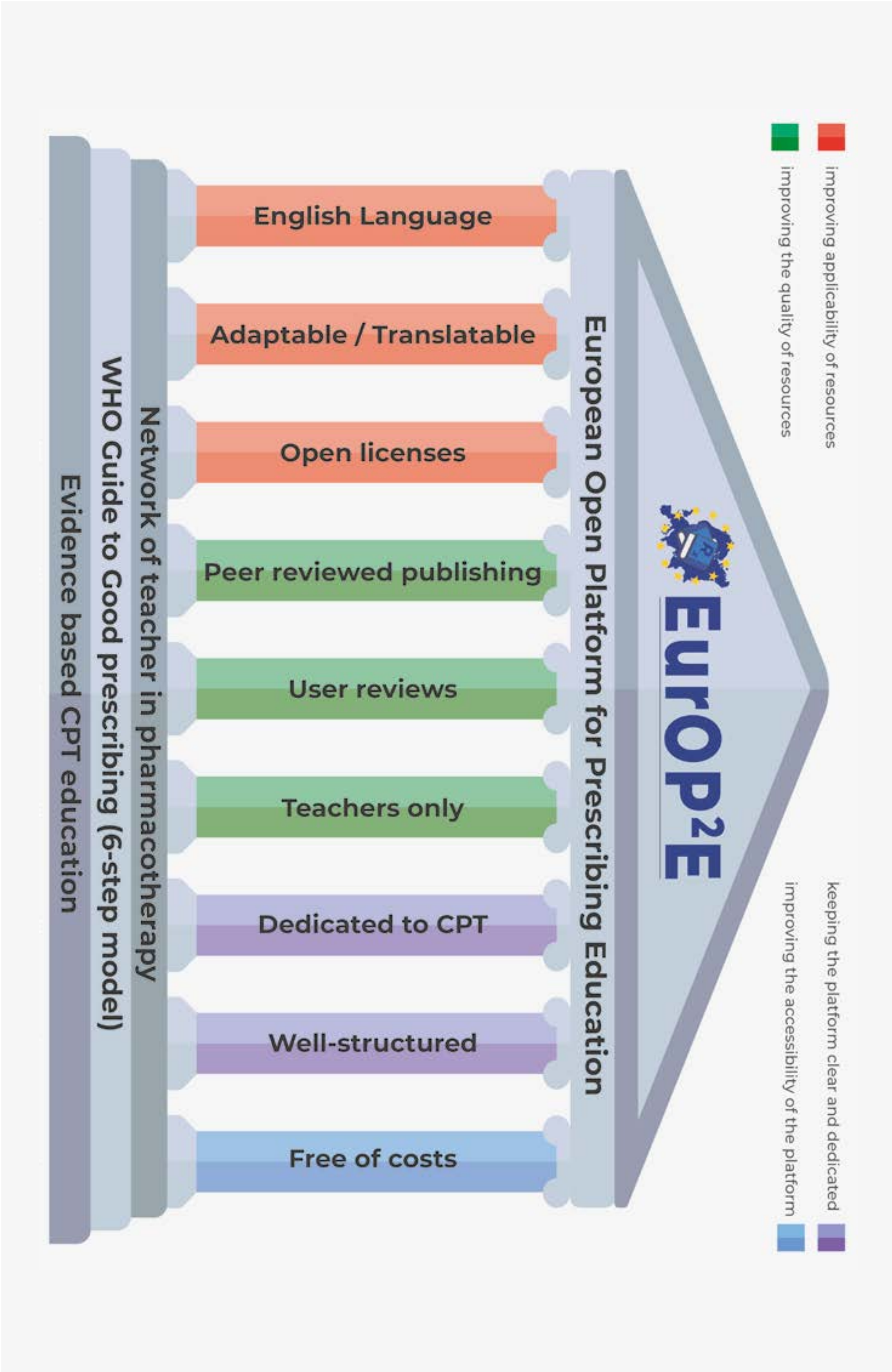
Platform Clarity: Addressing apprehensions about the potential overload of resources as seen on other platforms, we proactively resolved to maintain the platform's distinctiveness. Our aim is to ensure its focus on clinical pharmacology and therapeutics education, thereby avoiding the risk of the platform becoming a repository for indiscriminate resources of questionable quality and relevance.

Accessibility: There was unanimous agreement that the platform's accessibility should always be completely free of any charges.

The study revealed that European teachers in clinical pharmacology and therapeutics are willing to improve collaboration and share educational resources. Our suggestion to use EurOP^{2}E for this purpose was favourably received. While international clinical pharmacology and therapeutics teachers perceive certain obstacles to collaboration, these hindrances can be overcome by adopting appropriate strategies. It is important to acknowledge limitations inherent in this study, which primarily stem from selection bias. The limited willingness of digitally active teachers to participate in our survey, possibly because it took 20–30 minutes to complete, could have influenced the outcomes. Additionally, the consensus meeting was exclusive to EACPT conference attendees in Stockholm, potentially excluding diverse perspectives. Nonetheless, given the substantial participation in both phases of the study, we believe that the findings offer a largely representative insight into the body of European teachers in clinical pharmacology and therapeutics.

Between carrying out the research and publishing the results, the global landscape was shaken by the COVID-19 pandemic. This situation made research complicated–for example, because collaborators had to take on more clinical duties. Furthermore, numerous international conferences were postponed or cancelled. However, amidst the disruptions, the pandemic catalysed a surge in teachers worldwide who embraced online instruction. While navigating the transition from in-person to remote teaching, we encountered difficulties in delivering certain types of education, such as small group

Figure 1. Framework for the European Open Platform for Prescribing Education. CC By 4.0 - Previously published in chapter 4. CPT = clinical pharmacology and therapeutics.


improving applicability of resources
improving the quality of resources
keeping the platform clear and dedicated
improving the accessibility of the platform
EurOP²E
European Open Platform for Prescribing Education
English Language
Adaptable / Translatable
Open licenses
Peer reviewed publishing
User reviews
Teachers only
Dedicated to CPT
Well-structured
Free of costs
Network of teacher in pharmacotherapy
WHO Guide to Good prescribing (6-step model)
Evidence based CPT education

11

discussions, which were less appealing and participatory in the online format. Conversely, we identified the feasibility of prerecording lectures for on-demand consumption and found that conducting one-on-one oral examinations online offered advantages over in-person settings. The COVID-19 pandemic caused us to explore novel avenues, including hosting international student-led medication reviews, as outlined in Chapter 9. Furthermore, it provided an opportunity to secure funding for EurOP^{2}E through the European Union Erasmus+ initiative focused on improving digital educational readiness in response to the pandemic. This funding was granted for the period spanning 1 March 2021 to 31 August 2023.

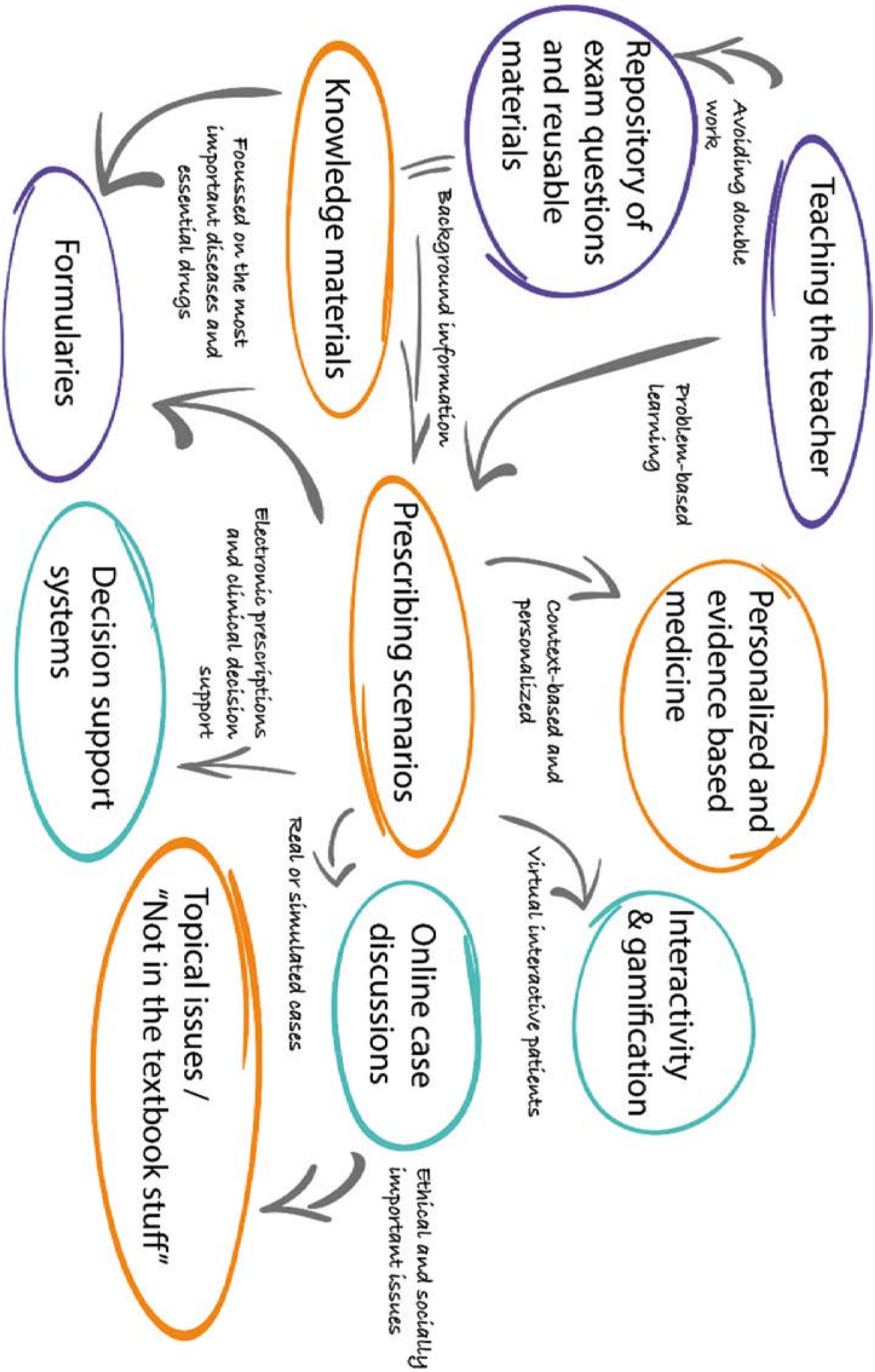
Equipped with a prepared framework and funding, our endeavour to set up EurOP^{2}E was set in motion. Insights gleaned from the studies described in Chapters 2 and 3 underscored the scarcity of problem-based and open access resources across European universities. This realization prompted a dual approach: not only to encourage the sharing of existing materials but also to collectively craft new open educational resources. However, the specific nature and content of these resources was not yet clear.

As a result, in **Chapter 5**, we investigated the most sought-after resources in the European clinical pharmacology and therapeutics teaching community. We did so using nominal group technique style interviews, because of validated effectiveness in reaching consensus and the added advantage of prioritizing various ideas. Thematic analysis of the transcripts enabled us to identify shared concepts across diverse discussions. The study recruited 20 teachers, from universities in 15 European countries, who collectively participated in four group interviews. They proposed a total of 35 unique educational resources. We categorized the suggestions into ten overarching themes across three primary groups, as explained below and illustrated in Figure 2.

<u>Themes related to learning outcomes for Clinical Pharmacology and Therapeutics</u>: Consensus was reached on the need of a repository of prescribing scenarios. Additionally, the participants advocated a dedicated section for fundamental knowledge resources. These materials would serve as a scaffold, equipping students with the essential foundational knowledge underlying the prescribing scenarios. Moreover, consensus emerged on the inclusion of content relating to evidence-based medicine and personalized medicine. Finally, the participants expressed desire for materials addressing contemporary issues that often lie beyond the scope of conventional textbooks and curricula, such as planetary health and diversity and inclusion..

<u>Themes related to the format of teaching:</u> Participants ideas revolved around two themes: interactivity and gamification. The consensus was that the platform should foster highly engaging and gamified instructional methods. Additionally, participants stressed the importance of incorporating clinical decision support tools and electronic prescribing

Figure 2. Visual representation of the thematic analysis. CC By 4.0 - Previously published in chapter 5. Orange = related to learning outcomes for Clinical Pharmacology and Therapeutics; Cyan = related to format of teaching; purple = related to resource and faculty development


Teaching the teacher
Avoiding double work
Repository of exam questions and reusable materials
Problem-based learning
Background information
Knowledge materials
Focussed on the most important diseases and essential drugs
Formularies
Prescribing scenarios
Context-based and personalized
Personalized and evidence based medicine
Virtual interactive patients
Interactivity & gamification
Electronic prescriptions and clinical decision support
Decision support systems
Real or simulated cases
Online case discussions
Ethical and socially important issues
Topical issues / "Not in the textbook stuff"

formats into the platform. Furthermore, teachers advocated establishing innovative forms of international live-teaching experiences. Suggestions encompassed transnational case discussions and webinars aimed at transcending geographical boundaries and facilitating insightful exchanges among teachers and learners worldwide.

Themes related to resource and faculty development: The participants proposed themes focused on streamlining the teacher's experience. For instance, they recommended the creation of a repository of examination questions that could be repurposed in other educational contexts. This resource would expedite the development of assessments, ultimately saving valuable time for teachers. Additionally, participants proposed tailored training sessions designed to boost teaching skills. Moreover, the participants highlighted the potential benefits of establishing international (student) formularies.

This study yielded a well-defined and prioritized overview of resource concepts for collaborative development and availability on EurOP^{2}E. The finding that teachers sought training not only for their students but also for their own professional development led to the conceptualization of the Clinical Pharmacology and Therapeutics Teacher Training Program (CP4T), a sister project designed to facilitate "teach the teacher" events and co-create instructional content in partnership with EurOP^{2}E.

A limitation of this study was the inability to recruit participants from all the countries in the network, including some of the larger ones. Nevertheless, given that EurOP^{2}E is conceived as a dynamic and continuously evolving platform, we anticipate to incorporate their suggestions in the platform's ongoing development.

At this stage, we had finalized the framework for EurOP^{2}E and gained clarity regarding the specific resources teachers would like to see on the platform. Despite this conceptual groundwork, the actual content was not available, and uncertainties lingered about the practicality of generating open educational resources encompassing all the suggestions outlined in Chapter 5. Consequently, for the final segment of this thesis, **our objective was to demonstrate the feasibility of collectively producing open educational resources.**

In **Chapter 6**, we looked into gamifying clinical pharmacology and therapeutics education by developing an educational escape room centred around the opioid epidemic. The intention was to craft a blueprint for this escape room, so that it could serve as an open educational resource. Gamification in education entails the integration of game elements, such as competition, into the teaching process to enhance learner engagement and motivation. Educational escape rooms exemplify this approach – small teams of learners have to unravel clues, solve puzzles, and complete tasks together to reach a predefined objective – typically escaping from the room – whilst learning. Prior research on educational escape rooms showed them to be effective in nurturing soft skills such as teamwork and communication but less suitable for teaching medical skills and knowledge. To increase the pedagogical impact, we introduced an innovative layer by allowing students to design the puzzles and tasks themselves. This approach aimed to encourage deep learning, as compared to merely participating in solving the puzzles. Additionally, this approach aimed to increase students' engagement with the tasks.

Thirty-nine third-year medical students participated in this initiative. Their feedback showed that 47.2% enjoyed crafting the escape room puzzles, and 80.2% enjoyed playing the escape room. As anticipated, students felt they learned more when they created the puzzle (56.9% agreement) than when they only solved the puzzle (26.3% agreement). Notably, the teamwork and creative thinking emerged as highly appreciated aspects of the assignment. Although the overall evaluations fell below our initial expectations, contextual factors probably influenced this outcome. Student workload, including graded assignments, may have curbed enthusiasm for this time-intensive, ungraded task. The quality of puzzles generated by the students varied, ranging from straightforward crosswords to intricate physical puzzles alike those found in recreational escape rooms. Our initial plan to provide a replicable blueprint for the opioid crisis escape room ran into problems , in part because of the COVID-19 pandemic. However, the insights we gained from this initiative are valuable for teachers seeking to craft educational escape rooms or similar projects. These insights are described in a peer-reviewed publication (Chapter 6) and in a teaching tutorial for teachers on EurOP^{2}E.

Chapter 7 grapples with the need for inclusion and diversity within medical guidelines, teaching methods, and examination materials. A prevailing practice across medical specialties involves the recommendation of different diagnostic and treatment strategies depending on a patient's race or ethnicity. Yet, the relationship between biology and race/ethnicity is intricate. In contemporary medical science, both race and ethnicity are captured through the self-identification of study participants. This self-identification serves as a social metric devoid of biological essence. However, the application of this classification as a determinant in medical guidelines can inadvertently propagate the impression of a causal connection between race/ethnicity, biology, and health. Medical teachers, including ourselves prior to the writing of this article, often lack awareness of this complexity, occasionally misrepresenting race as biologically rooted.

In this first international collaborative open educational resource on EurOP^{2}E, we used a literature review to increase awareness among clinical pharmacology and therapeutics teachers regarding the difficulties surrounding race-based medicine. It emphasizes the need for teachers to introspectively improve their teaching methodologies on this subject. The unintentional depiction of self-reported race/ethnicity as being inherently biological may have unintended consequences. For instance, students may perceive individuals of shared race/ethnicity as possessing genetic uniformity, potentially fostering the misconception that race-based recommendations are universally applicable rather than representative of an average within a diverse group. This not only medicalizes race but also amplifies existing healthcare disparities. Additionally, students might overlook the inherent bias that influences the relationship between race/ethnicity and health. Factors such as socioeconomic status, racism, ancestry, and environment can significantly skew this relationship, rendering race-based recommendations less broadly applicable. By highlighting these complexities, teachers can play a pivotal role in reducing misperceptions and nurturing a more comprehensive understanding among future medical practitioners.

"The Clinical Pharmacology and Therapeutics Teacher's Guide to Race-Based Medicine, Inclusivity, and Diversity" is accessible as both a peer-reviewed journal article and an extensive teach-the-teacher course on the platform.

Chapter 8 serves as a plea for the more sustainable use of medicines in clinical practice. A review article published in the British Journal of Clinical Pharmacology[6] urged the UK National Health Service and local health systems to adopt a top-down approach to enhance the sustainability of medicine use. In this chapter, we expand this message by emphasizing the potential benefits of incorporating sustainable prescribing education in the training of future medical practitioners. However, the scarcity of evidence on medicine sustainability is an important obstacle. Within this context, we explored how EurOP^{2}E could play a role in consolidating teaching resources on this topic and providing guidance for teachers. The platform's potential extends to both gathering relevant materials and training teachers to deliver these essential lessons. The first materials on planetary health prescribing are already accessible on the platform. Additionally, this article marked the inception of a new international sister project, PlanED Prescribing (Planetary Health Education in Prescribing), which was recently granted funding through Erasmus+ for the years 2023-2025. The outcomes of this project will be accessible through EurOP^{2}E.

Chapter 9 delves into an another teaching approach proposed in the nominal group technique study featured in Chapter 5—live international discussions. This Chapter presents the feasibility assessment and initial outcomes of online, international, and interprofessional student-led medication reviews

Through Zoom calls, participants from the VU University in Amsterdam (Netherlands) and the University of Bologna (Italy), and, subsequently, students from diverse European backgrounds were presented with cases of polypharmacy. They were tasked with formulating strategies to optimize medication, working together in mixed (international and interprofessional) teams. This collaborative endeavour was followed by a plenary discussion that highlighted disparities in guidelines, medication usage, availability, and educational systems across distinct countries. In addition to an article on this initiative, the platform is used as a hub to start more of these enriching international exchanges.

In **Chapter 10**, we looked into the most sought-after educational materials, as identified in the study described in Chapter 5: case vignettes applicable across various educational contexts. Case vignettes are widely used. However, it takes time and effort to develop high-quality vignettes. We looked into the possibility of mass-producing case vignettes with the assistance of artificial intelligence, particularly OpenAI's chatGPT. We also addressed a longstanding issue in medical education—the lack of inclusivity in case vignettes, which often only incorporate characteristics of diversity when they directly relate to diagnosis or treatment decisions. This practice can inadvertently reinforce stereotyping and misconceptions about the biological implications of markers such as race (as discussed in Chapter 7). To counter this, we sought to improve the diversity of cases through the computerized randomization of a broad spectrum of patient characteristics, including ethnicity, BMI, and occupation. To mirror the nuances of real-life clinical and therapeutic reasoning, some aspects of diversity are conveyed not through text labels but through AI-generated patient images.

We demonstrated the feasibility of this approach and provided step-by-step instructions and the chatGPT prompts necessary to generate these cases. These prompts can be customized by local users to suit specific scenarios. Despite these steps, the case creation process can still be complex. To streamline this, the instructions and the cases themselves have been made available on EurOP^{2}E, thereby allowing teachers to duplicate and tailor them.

The randomization process yielded very diverse cases. However, there appeared to be a trade-off with representativeness. This led to unusual or biologically implausible combinations of characteristics, such as a 70-year-old individual being pregnant. Moreover, it is worth noting that real patients possess interconnected and multifaceted social identities that intersect and mutually influence one another—a concept termed intersectionality. Achieving a realistic level of intersectionality in case vignettes remains a challenge we continue to work on.

A NOTE ON ARTIFICIAL INTELLIGENCE

In discussing digital education in 2024, the role of artificial intelligence can not be left unmentioned. The increasing accessibility of artificial intelligence applications to the general public has created conditions that will reshape our approach to teaching, research, and medical practice. While I recognize the caution and apprehension surrounding the potential for student misconduct facilitated by artificial intelligence applications, I am of the opinion that we should wholeheartedly embrace this evolution (if not only because it is inevitable). Within this context, EurOP^{2}E emerges as an ideal platform to foster consensus among teahers on how best to navigate this shift. As exemplified in Chapter 10, this platform enlightens us on the ways in which artificial intelligence can complement our roles as teachers. A comprehensive study of the precise role of artificial intelligence in academia, along with its associated risks, exceeds the scope of this thesis. However, one notable application of artificial intelligence technology is the utilization of chatbots such as ChatGPT for science communication. Interestingly, both this chapter and Chapter 10 were copy-edited, but not written(!), with the assistance of ChatGPT. Did you notice?

THE EUROPEAN OPEN PLATFORM FOR PRESCRIBING EDUCATION AND THE FUTURE

The outcome of the studies described this thesis resulted in the official launch of the platform during a dedicated symposium held on 1–2 June, 2023. As of 31 August, 2024, the platform has achieved the following milestones:

» Registration of over 3500 users
» Facilitation of online collaboration among more than 70 active teachers specializing in clinical pharmacology and therapeutics

» Offering 7 distinct teacher courses encompassing diverse topics such as race-based medicine, planetary health, objective structured clinical examinations, and artificial intelligence.
» Provision of an additional 7 open educational resources. These resources include clinical case vignettes, medical illustrations, and teaching materials focused on pharmacovigilance. These resources are conveniently accessible for local education purposes.

The platform's overarching objective is to expand substantially in the upcoming years, to become the primary hub for teachers seeking innovative teaching methods in clinical pharmacology and therapeutics. To achieve growth, it crucial to continue improving the content EurOP^{2}E has to offer. Prioritized in Chapter 5 is the need for large numbers of high-quality case vignettes, and our focus should be on collecting them on the platform. However, in our efforts to do so, we found that there is very limited information on what these vignettes should entail, and further studies are needed to achieve international consensus and, specifically, on finding the balance between straightforward and feasible (but perhaps too simple) and authentic and detailed (but perhaps too complex) case vignettes. I suggest that such a study should start with an inventory of the content and characteristics of current international case vignettes, followed by a Delphi study. As detailed in Chapters 7 and 10, it is important to include diversity and inclusivity aspects in this investigation. To further ensure the platform's sustained growth, multiple international initiatives are in progress. I will briefly introduce three of these initiatives here.

UPDATE OF THE WHO GUIDE TO GOOD PRESCRIBING

After more than 25 years, the cornerstone of pharmacotherapy education requires a comprehensive revision to bring it up to date with the contemporary global landscape, integrating new technologies and pedagogical theories of the 21st century. Numerous parallels can be drawn between this endeavour and the platform. The updated Guide to Good Prescribing aims to sensitize its readers to the intricacies of race-based medicine, incorporate considerations of planetary health in treatment decisions, and utilize the platform's case vignettes as practical examples. This synergy prompts a symbiotic relationship with the platform, wherein the teaching community can contribute to the guide's update, while the updated guide, in turn, may facilitate the platform's expansion beyond its European origins. The groundwork for this update started together with the preparation of this thesis and will continue over the coming years.

CLINICAL PHARMACOLOGY AND THERAPEUTICS TEACH THE TEACHER – CP4T

Similar to the initial global teaching sessions that marked the inception of the WHO Guide to Good Prescribing, we are currently engaged in an international "Teach the Teacher" project. This initiative focuses on teachers in clinical pharmacology and therapeutics and covers diverse topics such as crafting improved examination questions and effectively integrating artificial intelligence in the classroom. Beyond live events hosted at various European universities and online teleconferencing sessions, we are in the process of developing on-demand "Teach the Teacher" courses, which will be accessible through the platform.

PLANETARY HEALTH EDUCATION IN PRESCRIBING – PLANED

As previously mentioned, it is imperative to instil in medical students the significance of considering planetary health when prescribing medications. The ongoing goal of the "PlanED" project is to create a comprehensive European curriculum for evidence-based sustainable prescribing. Naturally, the new curriculum will find its home on EurOP^{2}E, thereby fostering the integration of planetary health principles into medical education.

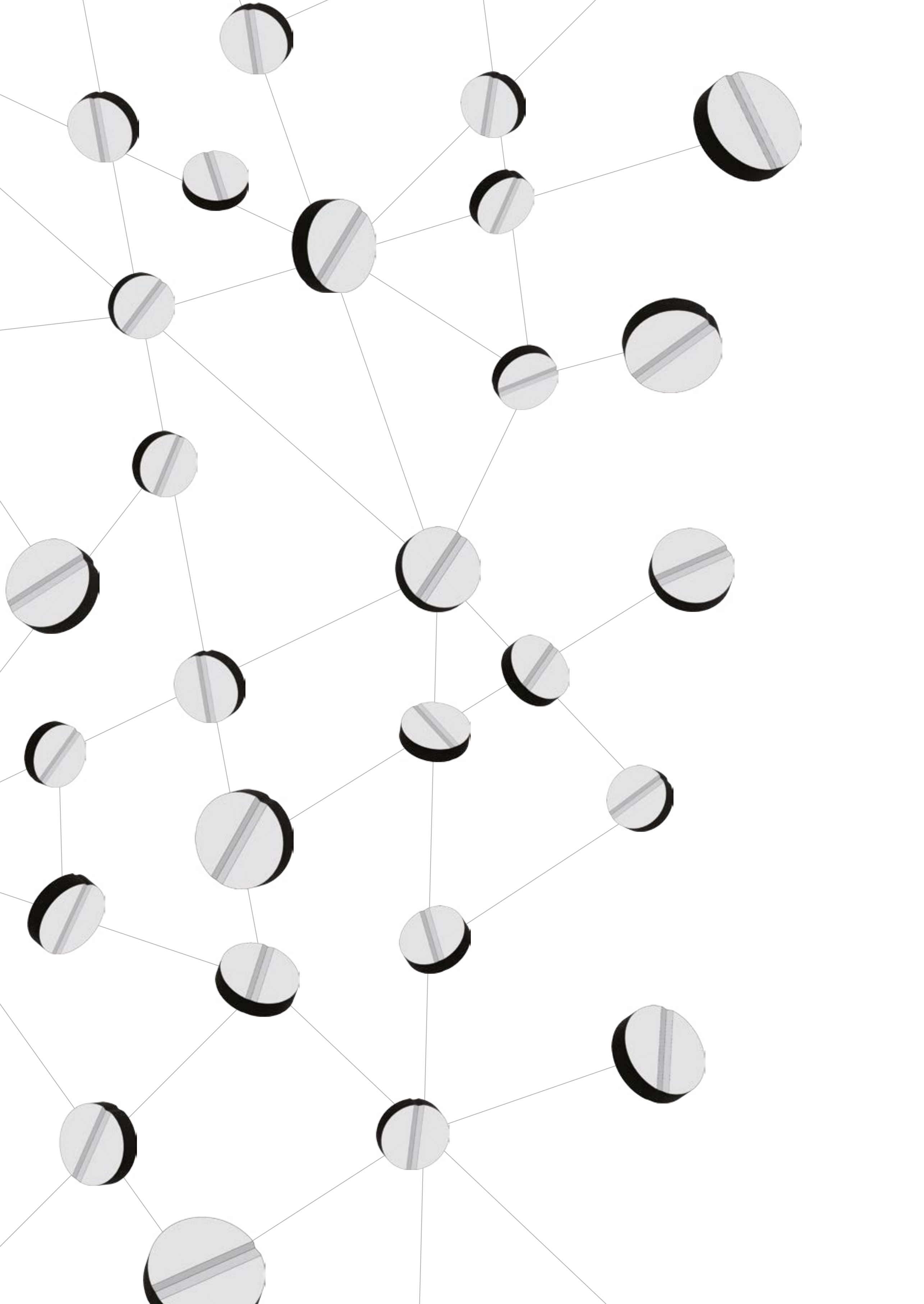
THE FUTURE

With these three concurrent projects in motion, we have achieved the elements essential to the continued development of the platform and secured funding for the foreseeable future. Nevertheless, for the platform to flourish, a significant paradigm shift is required. My aspiration to foster resource sharing has not consistently gathered the enthusiasm I initially anticipated. Interestingly, financial constraints do not seem to be the primary problem, given that European medical schools typically operate without a profit-oriented agenda and lack direct competition for prospective students. A prevalent issue surfaces in the form of misdirected competition among individual teachers within European universities. There is a reluctance to share their finest educational materials, coupled with a hesitancy to contribute more than their colleagues, often driven by a sense of perceived injustice. It is precisely this mindset that serves as the Achilles' heel of the platform and necessitates a transformative shift. The pursuit of excellence should not be misconstrued as an attempt to outshine others. My aspiration is that by setting a precedent, in collaboration with our partner universities, we can instigate a positive ripple effect. This effect will ideally inspire others to follow suit, fostering a culture of mutual support and resource sharing.

As it is too early now to tell whether EurOP^{2}E is effective in harmonizing and improving clinical pharmacology and therapeutics education in Europe and beyond, the project should be thoroughly evaluated in a couple years' time. This investigation should not only focus on improving the platform itself, but also study whether the platform has changed the overall opinion of clinical pharmacology and therapeutics teachers about open education and whether they are more willing to share their educational materials. Hopefully, findings will confirm the strength of the framework (Chapter 4), which is focused on providing dedicated, high-quality resources and a strong sense of community. Ultimately, this could provide potential for translating our findings into other fields of education.

REFERENCES

1. Brinkman DJ, Tichelaar J, Schutte T, et al. Essential Competencies in Prescribing: A First European Cross-Sectional Study Among 895 Final-Year Medical Students. *Clinical Pharmacology & Therapeutics*. Feb 2017;101(2):281-289. doi:10.1002/cpt.521
2. Brinkman DJ, Tichelaar J, Graaf S, Otten RHJ, Richir MC, van Agtmael MA. Do final-year medical students have sufficient prescribing competencies? A systematic literature review. *British Journal of Clinical Pharmacology*. Apr 2018;84(4):615-635. doi:10.1111/bcp.13491
3. De Vries T, Henning RH, Hogerzeil HV, Fresle D, Policy M, World Health Organization. *Guide to good prescribing: a practical manual*. 1994.
4. World Health Organization. *Teacher's guide to good prescribing Hans V. Hogerzeil (editor)...[et al.]*. 2001.
5. Brinkman DJ, Tichelaar J, Okorie M, et al. Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries. *Clinical Pharmacology & Therapeutics*. Nov 2017;102(5):815-822. doi:10.1002/cpt.682
6. Adeyeye E, New BJM, Chen F, Kulkarni S, Fisk M, Coleman JJ. Sustainable medicines use in clinical practice: A clinical pharmacological view on eco-pharmaco-stewardship. *Br J Clin Pharmacol*. Nov 15 2021;n/a(n/a)doi:10.1111/bcp.15140



NEDERLANDSE SAMENVATTING

LIST OF PUBLICATIONS

DANKWOORD

CURRICULUM VITAE / BIOGRAPHY

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NEDERLANDSE SAMENVATTING

Beste lezer, welkom bij dit proefschrift, want laten we eerlijk zijn: dit laatste hoofdstuk is waarschijnlijk het eerste dat je openslaat. Als het ook het enige hoofdstuk is dat je wilt lezen, dan is dat natuurlijk helemaal prima! Maar om je toch een beetje uit te nodigen om het hier niet bij te laten heb ik dit hoofdstuk bewust geschreven als een beknopte supersamenvatting. De *Introduction* en *Summary and discussion* in het kort. Voor meer diepgang verwijs ik je graag naar die hoofdstukken (hoofdstuk 1 en 11), of natuurlijk naar de losse studies (hoofdstuk 2 t/m 10).

Artsen uit heel Europa leren tijdens de opleiding onvoldoende om veilig medicatie voor te schrijven. Laatstejaars geneeskundestudenten voelen zich niet zeker en maken te veel fouten met (potentieel) ernstige gevolgen voor de gezondheid van patiënten. Veilig voorschrijven van medicatie is een praktische vaardigheid die je beperkt kunt leren uit theoretische leerboeken en colleges. De beste manier op veilig voor te leren schrijven is door het te doen – het liefst in het echt met supervisie, anders aan de hand van authentieke patiëntproblemen. Toch wordt er aan de Europese medische faculteiten nog veel traditioneel en weinig probleemgestuurd ("problem-based") lesgegeven.

In dit proefschrift onderzocht ik hoe digitaal onderwijs kan helpen om het klinische farmacologie onderwijs internationaal te verbeteren en te harmoniseren. Digitaal onderwijs heeft als voordeel dat het eenvoudig op meerdere plekken tegelijk kan worden gebruikt, en dat het na een enkele (vaak kostbare) ontwikkeling duurzaam en zonder hoge lasten hergebruikt kan blijven worden. Digitaal onderwijs heeft ook (potentiële) nadelen, zo is het engagement mogelijk lager en daarmee de leereffecten onzeker. Bovendien was het de vraag of digitaal onderwijs wel geschikt is om de complexe vaardigheid van het voorschijven te leren.

Daarom is het eerste deel van dit proefschrift gericht op de vraag: **Wat bestaat er aan digitaal onderwijs voor klinische farmacologie, en wat zijn de effecten daarvan?** In **hoofdstuk 2** toonden we middels een literatuurstudie aan dat er verschillende vormen van digitaal onderwijs worden gebruikt, variërend van e-learning modules tot podcastseries en serious games. De meeste studies beschreven de effecten slechts op het niveau van een voor- en nameting of een evaluatie door studenten. Deze waren allemaal positief. Over effecten op "hardere" uitkomstmaten, zoals het aantal voorschrijffouten of reductie van antibioticavoorschriften, konden we de door de heterogeniteit van de onderzoeken geen uitspraak doen. Bovendien werden de gebruikte digitale onderwijsmethoden vaak in weinig detail beschreven, en hadden we het vermoeden dat er veel onderwijsmethoden bestaan waar niet over gepubliceerd wordt (publicatiebias). Daarom hebben we in **hoofdstuk 3** aan onze internationale collega's uit (bijna) heel Europa gevraagd of zij hun digitale leermethoden aan ons wilden omschrijven en laten inzien. Twee derde van de respondenten gebruikte digitaal onderwijs voor klinische farmacologie, en in totaal werden 89 onderwijsmethoden omschreven. Naast e-learnings waren er ook innovatievere onderwijsmethoden zoals farmacokinetiek-simulatoren en elektronisch voorschrijfsystemen

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waar studenten vrij in kunnen oefenen ("sandbox"-omgevingen). Ongeveer 40% van de onderwijsmethoden was probleemgestuurd. Opvallend was echter dat het merendeel van de onderwijsmethoden alleen beschikbaar was gemaakt voor studenten van de eigen universiteit. Slechts twee van de 89 omschreven onderwijsmethoden hadden een zogenaamde open onderwijs licentie die (minimaal) aanpassing en hergebruik (voor niet-commerciële doeleinden) toestaat.

Op basis van dit eerste deel concludeerden we dat er voldoende en interessante mogelijkheden zijn voor digitale onderwijsmethoden om het internationale klinische farmacologieonderwijs te verrijken en te harmoniseren. Wel was opgevallen dat een relatief klein deel probleemgestuurd was, en dat de mogelijkheden om de bestaande onderwijsmethoden te delen ernstig beperkt werden door auteursrechtenlicenties. De overwegingen achter deze beperkingen waren nog niet duidelijk. Daarom stelden we in deel twee van dit proefschrift de vraag: **Hoe kunnen we de internationale samenwerking verbeteren?** In **hoofdstuk 4** hebben we, voor het eerste deel van dit onderzoek, middels een vragenlijst de meningen over delen en hergebruiken van onderwijsmaterialen onderzocht onder docenten klinische farmacologie uit bijna heel Europa. Deelnemende docenten hadden over het algemeen geen principiële bezwaren tegen het delen van hun onderwijsmethoden, maar op dat moment deelden zij hun materiaal nog nauwelijks. Vooral omdat ze hier (nog) geen netwerk voor hadden. Zij zagen belangrijke voordelen in het delen van lesmaterieel, zoals het (copy/paste) kunnen aanbieden van meer onderwijsmethoden zonder veel tijd of hoge kosten, of het onderwijsmateriaal van anderen gebruiken als inspiratiebron voor eigen werk. De belangrijkste drempels die zij ervaarden om onderwijsmateriaal te delen en her te gebruiken waren: verschillen in taal tussen de Europese landen en verschillen in richtlijnen, voorschrijfcultuur en beschikbaarheid van geneesmiddelen. Voor het tweede deel van deze studie hebben we de resultaten van de vragenlijst verwerkt tot een conceptraamwerk voor een online platform voor internationale docenten farmacotherapie, waarin we de genoemde voordelen van delen zoveel mogelijk benutten en de drempels om te delen zo klein mogelijk probeerde te maken. Bijvoorbeeld door alle onderwijsmethoden in het Engels aan te bieden, en altijd te voorzien van bronbestanden met open onderwijslicenties voor eventuele aanpassing aan de lokale situatie. Dit conceptraamwerk hebben we getoetst in een consensusbijeenkomst met internationale docenten tijdens het EACPT-congres (Stockholm, 2019). Met enkele kleine aanpassingen werd het raamwerk voor the European Open Platform for Prescribing Education (EurOP^{2}E) geaccepteerd (hoofdstuk 4, figure 3). Na deze studie, een beetje geholpen door de COVID-pandemie die de interesse voor het platform in een stroomversnelling bracht en de weg opende voor subsidie via Erasmus+, konden we gaan beginnen met de ontwikkeling van het platform en onderwijsmethoden voor op het platform. Hoewel we zelf meer dan voldoende ideeën hadden voor onderwijsontwikkelingen, vonden we het belangrijk om aan te sluiten bij de behoefte van de internationale collega's. Deze onderzochten we in **hoofdstuk 5,** middels een nominale groepstechniek interviewstudie onder 20 collega's uit 15 Europese landen. Uit deze studie

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bleek dat er naast (de verwachte) behoefte aan onderwerpen zoals probleemgestuurde casus, basale kennismodules en onderwijs over actuele thema's zoals inclusiviteit en diversiteit, planetary health en farmacogenetica ook behoefte was aan de ontwikkeling van innovatieve onderwijsmethoden zoals internationale online groepsdiscussies, serious games en "sandbox"-omgevingen van voorschrijfsystemen. Tenslotte, bleek uit de interviews dat de docenten niet alleen harmonisatie van het onderwijs wilden bereiken door een internationaal formularium en een standaard(set) examen(vragen), maar ook door zichzelf te ontwikkelen middels "teach-the-teacher" modules. Dit heeft de mogelijkheden van EurOP²E verder verbreed, en vormde aanleiding voor het nieuwe CP4T project - Clinical Pharmacology and Therapeutics Teach the Teacher.

Een groot deel van de uit hoofdstuk 5 afkomstige ideeën hebben we gerealiseerd, veelal samen met Europese partners, en beschikbaar gemaakt op EurOP²E. **In deel drie van dit proefschrift demonstreren we de functie van het platform aan de hand van vijf publicaties over de open onderwijsmaterialen**. In **hoofdstuk 6** omschrijven we de haalbaarheid en evaluatie van een door studenten zelf ontworpen "educational escape room", in dit geval over de veiligheid en risico's van opioïde geneesmiddelen. Het toevoegen van spelelementen, zoals competitie, teamwerk en/of tijdsdruk aan onderwijs kan de motivatie onder studenten verhogen. Dit komt goed samen in een escape room met leerzame puzzels, echter omschrijft de literatuur een beperkte leeropbrengst van dit soort escape rooms. Dit is te verklaren door een wisselwerking tussen serieuze en leerzame opdrachten en leukere, maar vaak minder leerzame opdrachten. Door de studenten zelf de puzzels voor de escape room te laten ontwikkelen (voor elkaar), hoopten wij de positieve aspecten van een educational escape room te combineren met een behoud van leereffect. De studentenevaluatie toonde dat studenten het een redelijk leuke opdracht vonden en dat zij inderdaad (voor hun gevoel) meer leerden van het creëren van de opdrachten dan van het oplossen ervan. Ook toonden wij hiermee aan dat het een haalbare opdracht is, onze werkwijze staat uitgelegd in het artikel en op het platform om door docenten elders gerepliceerd te worden. In **hoofdstuk 7** adresseren we één van de actuele thema's (uit hoofdstuk 5). De geneeskunde kent vele richtlijnadviezen om patiënten anders te behandelen op basis van "race" of etniciteit. Zo adviseert de huisartsenrichtlijn bijvoorbeeld andere bloeddrukverlagers voor zwarte dan voor niet-zwarte patiënten. Belangrijk hierin is dat "race" in de Verenigde Staten en de medische literatuur gebruikt wordt als een sociale maat, die gebaseerd is op iemands zelfidentificatie met bepaalde bevolkingsgroepen. Dit heeft dus nadrukkelijk geen directe biologische of genetische betekenis. Mensen kunnen niet op biologische gronden worden ingedeeld in rassen en de rassenleer is een historisch sterk beladen concept. Het Nederlands kent, net als veel andere Europese talen, echter wel biologische betekenis toe aan de directe vertaling van "race" (ras). De biologische connotatie wordt in het geval van richtlijnadviezen verder versterkt doordat de sociale maat "race" wordt gebruikt om biologie (kans op ziekte, reactie op bloeddrukverlagers etc.) te voorspellen. Docenten zijn over het algemeen onvoldoende op de hoogte van de achtergronden van de race-based richtlijnadviezen

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en onderwijzen ze vaak onbedoeld, maar onterecht als gebaseerd op een biologische associatie. In dit hoofdstuk proberen we middels een literatuurstudie en opiniërend artikel de docenten hierover te informeren, te laten reflecteren en hun onderwijs te laten aanpassen. **Hoofdstuk 8** gaat ook over een actueel thema, het is een reactie op een review artikel met de oproep om meer aandacht te hebben voor de milieu-impact van medicatie, gericht aan de National Health Service in het Verenigd Koninkrijk en in mindere mate aan individuele voorschrijvers. In onze reactie betogen we dat de toekomst ligt bij de studenten, en dat zij ook bij de initiatieven moeten worden betrokken. Om dat te bereiken is het belangrijk om docenten farmacotherapie op te leiden meer aandacht te hebben voor de milieu impact van medicatie, we zien hierin een belangrijke rol voor EurOP^{2}E. Dit hoofdstuk vormde aanleiding voor een nieuw project, PlanED Prescribing waarvan de eerste resultaten inmiddels op het platform te vinden zijn. In **hoofdstuk 9** omschrijven en evalueren we een nieuwe onderwijsmethode, online discussies tussen interprofessionele (geneeskunde en farmacie) studenten uit verschillende landen over de beste medicatie-optimalisatie van patiënten met polyfarmacie. Volgens het "omdenken" principe, hebben we een van de belangrijkste bezwaren om online lesmateriaal te kunnen delen, namelijk de internationale verschillen, gebruikt om juist veel van te leren. Door te ontdekken hoe richtlijnen, beschikbaarheid, maar ook onderwijsstijlen internationaal gezien verschillen, leren studenten over de relativiteit van "evidence" in de geneeskunde. Dit evalueerden zij als zeer waardevol. De werkwijze is open gepubliceerd om te worden overgenomen, en er worden nog maandelijks groepen georganiseerd via EurOP^{2}E. Waarschijnlijk de meest omvangrijke van de suggesties uit hoofdstuk 5 is een database van herbruikbare casuïstiek. Handmatig maken van goede casus is veel werk en er zijn er veel nodig, bijvoorbeeld om fraude tegen te gaan bij toetssituaties. Uit de literatuur blijkt dat gefingeerde casus vaak geen goede afspiegeling zijn van de werkelijke diversiteit in de samenleving en dat er vaak vooroordelen insluipen (casus over HIV gaan bijvoorbeeld buitenproportioneel vaak over homoseksuele mannen). In **hoofdstuk 10** omschrijven we hoe kunstmatige intelligentie (OpenAI, chatGPT) dit proces kan versnellen en verbeteren. Het lukte om dertig kwalitatief goede casus te maken in een uur tijd, maar het proces is ingewikkeld en kan zonder kennis beperkt worden gerepliceerd. Ter bevordering van de diversiteit kan redelijk eenvoudig een door kunstmatige intelligentie gemaakte foto van een (niet-bestaande) patiënt worden gegenereerd. Doordat de mogelijke variabelen voor de patiëntkenmerken worden gerandomiseerd, zijn de casus zeer divers en inclusief, maar dit gaat in sommige gevallen ten kosten van de realiteit. Zo maakte chatGPT bijvoorbeeld casus over zwangere patiëntes van 65 jaar en ouder. Met handmatige controles zijn dit soort problemen goed te ondervangen. Naast een procesbeschrijving, hopen we de casuscreatie zo te stroomlijnen dat we binnenkort een grote collectie aan casus online kunnen publiceren.

Het platform is online sinds 1 juli 2023 en heeft inmiddels meer 3500 geregistreerde gebruikers onder wie meer dan 70 actieve docenten, er staan zeven uitgebreide teach-the-teacher cursussen op het platform en zeven andere open onderwijsmodules die vrij kunnen worden hergebruikt. We voegen nog regelmatig inhoud toe. De wetenschappelijke output van de eerder genoemde nieuwe projecten (CP4T voor docentprofessionalisering en PlanED prescribing voor planetary health onderwijs) zal eveneens op het platform beschikbaar komen. Om die reden is het te vroeg voor een evaluatiestudie naar de effecten van het platform en valt die buiten het bestek van dit proefschrift. Tot op heden is al het onderwijsmateriaal op het platform afkomstig van ons internationale team. Hoewel dit materiaal met veel enthousiasme wordt ontvangen en (her)gebruikt en dit "zendingswerk" uiteindelijk effectief kan zijn in het verbeteren en harmoniseren van het internationale farmacotherapieonderwijs, is het (nog) niet het doel dat wij met het platform voor ogen hadden. Het raamwerk uit hoofdstuk 4 heeft een fundament van gemeenschap en verbondenheid, waarin docenten samenwerken en zelf ook materiaal delen. Het is mogelijk dat het gevoel van verbinding meegroeit met de inhoud en populariteit van het platform, maar het blijft de Achilleshiel van dit project. Toekomstig werk moet actief proberen het groepsgevoel te versterken.

LIST OF PUBLICATIONS

2024

Bakkum MJ, Hartjes MG, Piët JD, Donker EM, Likic R, Sanz E, de Ponti F, Verdonk P, Richir MC, van Agtmael MA, Tichelaar J. **Using artificial intelligence to create diverse and inclusive medical case vignettes for education.** Br J Clin Pharmacol. 2024 Mar;90(3):640-648. doi: 10.1111/bcp.15977.

Donker EM, **Bakkum MJ,** Richir MC, Tichelaar J; EuroPE+, EuroP2E, CP4T and the EACPT Education working group. **Bridging the gap between clinical pharmacology and rational drug prescribing 2.0: An update after 30 years**. Br J Clin Pharmacol. 2024 Mar 14. doi: 10.1111/bcp.16051.

2023

Bakkum MJ, Donker EM, Spitaleri Timpone P, Hagen CAM, Richir MC, van Agtmael MA, De Ponti F, Tichelaar J; Erasmus+ consortia European Prescribing Exam, European Open Platform of Prescribing Education and Clinical Pharmacology and Therapeutics Teach the Teacher program, and the EACPT Education Working Group. **Educational value of international and intercultural differences in prescribing: the international and interprofessional student-run clinic project.** Eur J Clin Pharmacol. 2023 Apr;79(4):571-574. doi: 10.1007/s00228-023-03465-9.

Michiel J. Bakkum, Petra Verdonk, Elias G. Thomas, Floor van Rosse, Michael Okorie, Paraskevi Papaioannidou, Robert Likic, Emilio J. Sanz, Thierry Christiaens, João N. Costa, Lorena Dima, Fabrizio de Ponti, Jeroen van Smeden, Michiel A. van Agtmael, Milan C. Richir, Jelle Tichelaar. **A Clinical Pharmacology and Therapeutics Teacher's Guide to Race-Based Medicine, Inclusivity, and Diversity.** Clin Pharmacol Ther. 2023 Mar;113(3):600-606. doi: 10.1002/cpt.2786.

2022

Bakkum MJ, Richir MC, van Agtmael MA, Tichelaar J; EurOP2E consortium. **Sustainable medicines use in clinical practice-It is time to help the teacher**. Br J Clin Pharmacol. 2022 Jul;88(7):3030-3031. doi: 10.1111/bcp.15340.

Bakkum MJ, Loobeek BJ, Richir MC, Papaioannidou P, Likic R, Sanz EJ, Christiaens T, Costa JN, Dima L, de Ponti F, Kramers C, van Smeden J, van Agtmael MA, Tichelaar J; EurOP²E consortium. **Teaching resources for the European Open Platform for Prescribing Education (EurOP²E)-a nominal group technique study.** NPJ Sci Learn. 2022 Sep 30;7(1):23. doi: 10.1038/s41539-022-00141-y.

&

2021

Bakkum MJ, Tichelaar J, Papaioannidou P, Likic R, Sanz Alvarez EJ, Christiaens T, Costa JN, Mačiulaitis R, Dima L, Coleman J, Richir MC, van Agtmael MA; Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT) and its affiliated Network of Teachers in Pharmacotherapy (NOTIP). **Harmonizing and improving European education in prescribing: An overview of digital educational resources used in clinical pharmacology and therapeutics.** Br J Clin Pharmacol. 2021 Mar;87(3):1001-1011. doi: 10.1111/bcp.14453.

Bakkum MJ, Muntinga ME, Verdonk P, Tichelaar J. **Onderscheid maken op basis van huidskleur? [Treating black hypertensive patients: limited applicability of the guideline recommendations]**. Ned Tijdschr Geneeskd. 2021 Apr 15;165:D5835.

Bakkum MJ, Schouten VL, Smulders YM, Nossent EJ, van Agtmael MA, Tuinman PR. **Accelerated treatment with rtPA for pulmonary embolism induced circulatory arrest.** Thromb Res. 2021 Jul;203:74-80. doi: 10.1016/j.thromres.2021.04.023.

Bakkum MJ, Richir MC, Papaioannidou P, Likic R, Sanz EJ, Christiaens T, Costa JN, Mačiulaitis R, Dima L, Coleman J, Tichelaar J, van Agtmael MA; Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT) and its affiliated Network of Teachers in Pharmacotherapy (NOTIP). **EurOP^{2}E - the European Open Platform for Prescribing Education, a consensus study among clinical pharmacology and therapeutics teachers**. Eur J Clin Pharmacol. 2021 Aug;77(8):1209-1218. doi: 10.1007/s00228-021-03101-4.

Bakkum MJ, Richir MC, Sultan R, de la Court JR, Lambooij AC, van Agtmael MA, Tichelaar J. **Can Students Create Their Own Educational Escape Room? Lessons Learned from the Opioid Crisis Escape Room.** Med Sci Educ. 2021 Oct 15;31(6):1739-1745. doi: 10.1007/s40670-021-01425-5.

2019

Bakkum MJ, Tichelaar J, Wellink A, Richir MC, van Agtmael MA. **Digital Learning to Improve Safe and Effective Prescribing: A Systematic Review.** Clin Pharmacol Ther. 2019 Dec;106(6):1236-1245. doi: 10.1002/cpt.1549.

2017

Bakkum MJ, Overtoom HA, Loffeld RJ. **Een vrouw met een ileusbeeld [A woman with symptoms of an ileus].** Ned Tijdschr Geneeskd. 2017;161:D915.

&

Bakkum MJ, Loffeld RJLF. **Ascending Cholangitis due to Heavy Lifting.** Case Rep Gastroenterol. 2017 Aug 23;11(2):500-503. doi: 10.1159/000479550..

2016

Bakkum M, van Cruijsen H, Kooter AJ. **A 39-year-old woman with a mushroom intoxication. Amanita phalloides**. Neth J Med. 2016 Mar;74(3):136-7.

2015

Bakkum MJ, Danad I, Romijn MA, Stuijfzand WJ, Leonora RM, Tulevski II, Somsen GA, Lammertsma AA, van Kuijk C, van Rossum AC, Raijmakers PG, Knaapen P. **The impact of obesity on the relationship between epicardial adipose tissue, left ventricular mass and coronary microvascular function**. Eur J Nucl Med Mol Imaging. 2015 Sep;42(10):1562-73. doi: 10.1007/s00259-015-3087-5.

Romijn MA, Danad I, **Bakkum MJ**, Stuijfzand WJ, Tulevski II, Somsen GA, Lammertsma AA, van Kuijk C, van de Ven PM, Min JK, Leipsic J, van Rossum AC, Raijmakers PG, Knaapen P. **Incremental diagnostic value of epicardial adipose tissue for the detection of functionally relevant coronary artery disease. Atherosclerosis.** 2015 Sep;242(1):161-6. doi: 10.1016/j.atherosclerosis.2015.07.005.

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DANKWOORD

Hora est! Het is zo ver! Ik schrijf dit dankwoord ruim zes jaar na de start van mijn promotietraject in november 2017, en wat een reis is het geweest! Na een jaar werkervaring als ANIOS bij de Interne Geneeskunde in het Zaans Medisch Centrum sprak ik – op een bedrijfsuitje – de partner van één van de internisten. Dat was Michiel van Agtmael. Ik vertelde over mijn wens om een promotieonderzoek te doen en over mijn ervaring die ik tijdens de studie had opgedaan met het ontwikkelen van digitaal onderwijs. Nog geen week later kwam ik op gesprek bij hem en Jelle en korte tijd later kon ik beginnen. Onderwerp van mijn proefschrift? "Je hebt ervaring met digitaal onderwijs, toch? De details zien we later wel". Zo begon mijn carrière als arts-onderzoeker en arts-docent Farmacotherapie. De sectie was een warm bad met een heerlijk werkklimaat, de Google-achtige filosofie met veel vrijheid en autonomie zorgt nog altijd voor veel werkplezier. Het was vanaf dag één gezellig in kamer ZH4A50 waar we tussen het werk door ook veel konden lachen. De promotiefilmpjes voor collega's blijven legendarisch, ik kijk nu al uit naar de mijne. Lesgeven vond ik vanaf het begin erg leuk. De leercurve was steil, waar ik aan het begin soms het idee had nauwelijks meer te weten dan de studenten kwam de zekerheid met de ervaring en begon ik al snel meer mijn eigen stijl te ontwikkelen inclusief slechte grappen ("LAMA's (Long-acting Muscarine antagonisten), niet te verwarren met alpaca's"). Het onderzoek kende meer pieken en dalen. Het ontbreken van een vastgestelde onderzoeksvraag gaf mij veel vrijheid om dit proefschrift naar eigen inzicht in te delen. Tegelijkertijd zorgde het er ook voor dat ik lange tijd zoekende ben gebleven naar de rode draad die mijn onderzoeken verbindt. Na de gedachte om de effecten van digitaal onderwijs, in het bijzonder gamification, te onderzoeken en wellicht een serious game te ontwikkelen voor farmacotherapieonderwijs volgde nog een omzwerving naar het Farmacotherapieteam (F-team), waar ik klinische beslisapplicaties heb ontwikkeld (en mogelijk in onderzoek zou gaan valideren). Tijdens de EACPT focusmeeting in Birmingham met als onderwerp digitaal onderwijs – voor mij de eerste van vele onvergetelijke congresreizen – werd mij duidelijk dat er veel digitaal onderwijs beschikbaar is, maar dat de internationale collega's niet wisten van het bestaan hiervan en weinig actief delen. Terugkijkend, is dit het moment waarop het eerste zaadje voor EurOP^{2}E is geplant. Ondertussen had ik ook gamification als onderwerp nog niet helemaal laten varen (hoofdstuk 6) en was ik gegrepen door de achtergronden van "race-based medicine" en mede daardoor het bredere vraagstuk van diversiteit en inclusie (hoofdstuk 7 en 10). Door de vrijheid en het vertrouwen dat ik altijd heb gekregen, heb ik ook deze onderwerpen in dit proefschrift kunnen verwerken. Tijdens het proces was het soms overweldigend, maar achteraf ben ik ontzettend dankbaar dat ik hierdoor echt mijn eigen proefschrift heb kunnen samenstellen. Ik wil iedereen die mij daarbij heeft geholpen bedanken!

Te beginnen bij **Jelle.** Jouw rol in het ontstaan van dit proefschrift, maar ook in mijn persoonlijke ontwikkeling is niet in één woord uit te drukken. Allereerst ben je natuurlijk mijn (co)promotor, met co tussen haakjes want door al het harde werk van de afgelopen

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jaren heb je inmiddels zelf het *Ius Promovendi* aan de VU. In deze rol heb ik veel van je geleerd, niet alleen in het opzetten en uitvoeren van onderzoek maar ook jouw openheid over de achterliggende politiek was altijd heel leerzaam en waardevol. Daarnaast ben je als coördinator/manager een voorbeeld, ik hoop dat ik een toekomstige huisartsenpraktijk half zo goed kan runnen als jij de sectie farmacotherapie. OK – de roosters waren niet altijd even op tijd, maar de flexibiliteit en autonomie die je ons altijd hebt gegeven hebben mij in staat gesteld te groeien. Het belang dat je hecht aan teamuitjes, congressen en nascholingen is inspirerend. Ik kan me voorstellen dat ik met mijn kritische houding niet altijd even makkelijk was om op te leiden, ik waardeer hoe je me met de bijnaam "Ja, maar-meneer" op een luchtige wijze aan het denken hebt gezet. Bovenal was je voor mij een coach, als ik weer eens leek te verdrinken in zelfkritiek dan was jij de relativerende reddingsboei. Ook onze gesprekken over werk-privébalans en over mijn keuze voor de vervolgopleiding herinner ik me als heel waardevol. Jelle, zonder jou had ik hier niet gestaan, bedankt!

Milan, van jou heb ik ook heel veel geleerd. Jouw terugkerende feedback op onderzoeksvoorstellen en manuscripten "dit deel snap ik niet" heeft mij het belang van *keep it simple* in laten zien. Dat botste, zeker aan het begin, met mijn wens om alles tot in de puntjes goed te doen. Gaandeweg ben ik je pragmatisme gaan waarderen en omarmen. Het is een houding die ik ook in de huisartsenpraktijk probeer mee te nemen. Dank hiervoor!

Michiel, ik beschreef al kort het enthousiasme waarmee je mij in 2017 hebt aangenomen. In de jaren daarna heb ik geleerd dat dit enthousiasme jou typeert, en dat werkt aanstekelijk! Je enthousiasmeerde me om overal vol voor te gaan, zo betrok je me bij het F-team, is een vraag over de behandeling met fibrinolytica bij reanimatiesetting door longembolieën uitgemond in een nogal lijvig review-artikel en stond ik op jouw uitnodiging op afgelopen EACPT congres met een praatje over artificial intelligence in medical education. Tegelijkertijd stak je ook kritiek nooit onder stoelen of banken. Dat was soms confronterend, maar heeft menig congrespraatje, artikel en vooral titel (dit proefschrift) en acroniem (EurOP^{2}E) naar een hoger niveau getild. Bovendien gaf het betekenis aan je complimenten, die ik ook vaak genoeg heb mogen ontvangen. Bedankt voor de leerzame tijd!

Chair of the Thesis Committee, **prof.dr. Rashmi Kusurkar** and members of the Thesis Committee, **prof.dr. Ylva Böttiger, prof.dr. Michael Okorie, prof.dr. Olga Horvat, dr. Ellen van Leeuwen and dr. Jochen Bretschneider,** I would like to thank you for your time reading and assessing this PhD thesis.

The national and international academic partners who have participated in the different projects and coauthored the articles in this thesis, **Prof.Dr. Thierry Christiaens, Prof. Dr. Jamie Coleman, Prof.Dr. João Costa, Prof.Dr. Fabrizio de Ponti, Prof.Dr. Lorena Dima, Prof.Dr. Kees Kramers, Dr. Robert Likic, Prof.Dr. Romaldas Mačiulaitis, Prof. Dr. Michael Okorie, Prof.Dr. Paraskevi (Voula) Papaioannidou, Prof.Dr. Emilio Sanz, Dr. Floor van Rosse, Dr. Jeroen van Smeden and Dr. Petra Verdonk**, thank you for the wonderful collaboration, insightful feedback and good times during conferences and meetings. Studenten en directe collega's die hebben meegeschreven aan de artikelen in dit proefschrift, **Anne, Rowan, Jara, Pietro, Charlotte, Bryan, Elias, Erik, Joost en Mariëlle,** bedankt voor jullie hulp!

Vrienden van de sectie Farmacotherapie, **Annelot**, **Ayesha, David, Elias, Eline, Emma, Erik, Fleur, Iris, Joost, Julia, Mariëlle, Michael, Nella, Philippe, Rashudy, Rishi, Rowan en Siham**, bedankt voor de eeuwige gezelligheid in kamer ZH4A50, de heerlijke roti-avonden en legendarische congresreizen naar Rotterdam, Birmingham, Stockholm, Athene, La Laguna en Egmond aan Zee. Bedankt ook voor alle lessen die jullie van me over hebben genomen als ik mijn agenda weer eens niet op orde had. Bedankt voor jullie steun als het even tegenzat. Bedankt voor alles wat ik van jullie geleerd heb. En sorry voor mijn rommelige werkplek! **Lieke,** bedankt voor je altijd oprechte interesse en alle taken die je ons uit handen hebt genomen!

Erik en Mariëlle in het bijzonder bedankt dat jullie naast gezellige, flexibele en humoristische collega's ook paranimf willen zijn tijdens mijn verdediging!

Liefste **Marcella,** dit avontuur hebben we samen beleefd. Een afwijzing voor publicatie, confronterende feedback of wekenlang thuiswerken tijdens de pandemie - het was niet altijd makkelijk, maar jouw liefde, steun en wijze woorden hebben mij er altijd weer bovenop geholpen. Bedankt voor al het tegengas dat je gaf tegen mijn innerlijke criticus. Bedankt dat je me overtuigde om op onze geweldige vakanties te gaan, ook als ik daar niet de ruimte voor voelde. Bedankt dat je me liet doorwerken ten kosten van schaarse uurtjes samen, en ook bedankt dat je het leven zo leuk maakt dat ik eigenlijk helemaal niet door wil werken. Ik hou van je!

Allerliefste **Flip,** op moment van schrijven ben je pas een jaar oud, maar toch heb je me erg geholpen om dit project tot een goed einde te brengen. Jouw geboorte heeft het belang van dit proefschrift enorm gerelativeerd en juist dat gaf me de energie om het af te maken. Ik kan niet wachten om je eruit voor te lezen…

Lieve **Pappa en Mamma,** zonder jullie had ik hier niet gestaan, en dat bedoel ik niet alleen letterlijk. Als dokter, maar nu ook als vader, merk ik hoe belangrijk een veilige, liefdevolle en stimulerende opvoeding is. En die heb ik van jullie gekregen! Of jullie me als dreumes al uitdaagde en als één van de eerste woordjes "consultatiebureau" leerden, of dat ik helemaal naar Zwitserland wilde voor mijn profielwerkstuk - niets was te gek. Dankzij jullie heb ik me optimaal intellectueel kunnen ontwikkelen en heb ik de emotionele skills om de minder leuke momenten van het promoveren te doorstaan en te groeien. Daarom kan ik binnenkort dit proefschrift verdedigen, en daar ben ik jullie heel dankbaar voor! Natuurlijk ook bedankt voor alle liefde, gezelligheid, (vaak veel te dure) cadeaus en alle hulp bij de oppas voor Flip.

Lieve schoonfamilie, **Karel, Margreet, Angelique, Robert en Pablo** bedankt voor jullie altijd oprechte interesse in de vordering van dit proefschrift. Bedankt voor de dagen oppas waarin ik het af kon maken en bedankt voor alle gezelligheid tussendoor!

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Lieve vrienden, **Edo & Marlies, Jim & Daphne, Bram & Kirsten, Victor & Miriam, Myron & Mirte, Steffie & Marco, Maria & Robin en Marina & Rik,** dank voor alle gezelligheid, spelletjes, etentjes, sport, drankjes, weekendjes weg en andere fantastische tijden. Sowieso bedankt daarvoor, maar vooral omdat ze met hielpen op te laden en verder te kunnen met dit proefschrift.

Opleiders, docenten en mede-AIOS van de huisartsenopleiding, dank voor jullie betrokkenheid, flexibiliteit en gezelligheid. Dankzij jullie heb ik dit proefschrift kunnen afronden naast de opleiding tot huisarts.

En tot slot dank aan de organisaties die een financiële bijdrage hebben geleverd aan de totstandkoming van dit proefschrift, **Research and Expertise Centre in Pharmacotherapy Education (RECIPE) en stichting SBOH.**

CURRICULUM VITAE / BIOGRAPHY

Chiel (M.J.) Bakkum was born on July 6, 1992 at the VU University Medical Center (VUmc) in Amsterdam, the Netherlands. In 2010, he graduated secondary school (St. Michael College, Zaandam), being awarded first-prize for his graduation thesis (profielwerkstuk). In that same year, he returned to VUmc to commence his medical training. During his studies, he graduated three summer schools, completed the Honours Programme with his research at the Cardiology department, helped digitize medical education for the Mobile Learning Initiative, and chaired the "internistische verdiepingsclub". In September 2016 he received his medical degree and started working as a junior doctor (ANIOS) at the Internal Medicine, Pulmonology and Cardiology departments of Zaans Medisch Centrum, Zaandam. In November 2017 he started working as a teacher and PhD-student at the pharmacotherapy department of VUmc. He combined this with training to become a clinical pharmacologist, received his basic teaching qualification (BKO) and completed a parttime chef-training (for fun). In september 2022 Chiel commenced his General Practitioner training at the Huisartensopleiding VUmc and he remained parttime at the pharmacotherapy department. He is scheduled to graduate his GP training in February 2026 – after which he hopes to combine a GP-practice with an academic career as a teacher (/ researcher).

Chiel lives in Zaandam with his fiancée Marcella and son Flip (October 30, '23).