Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization

Citation for published version:

Digital Object Identifier (DOI):
10.1002/cpt.682

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Clinical pharmacology and therapeutics

Publisher Rights Statement:
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Pharmacology and Therapeutics Education in the European Union Needs Harmonization and Modernization: A Cross-sectional Survey Among 185 Medical Schools in 27 Countries

DJ Brinkman\textsuperscript{1,2}, J Tichelaar\textsuperscript{1,2}, M Okorie\textsuperscript{3}, L Bissell\textsuperscript{3}, T Christiaens\textsuperscript{4}, R Likic\textsuperscript{5}, R Mačulaitis\textsuperscript{6}, J Costa\textsuperscript{7}, EJ Sanz\textsuperscript{8}, BI Tamba\textsuperscript{9}, SR Maxwell\textsuperscript{10}, MC Richir\textsuperscript{1,2}, MA van Agtmael\textsuperscript{1,2}; for the Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT)

Effective teaching in pharmacology and clinical pharmacology and therapeutics (CPT) is necessary to make medical students competent prescribers. However, the current structure, delivery, and assessment of CPT education in the European Union (EU) is unknown. We sent an online questionnaire to teachers with overall responsibility for CPT education in EU medical schools. Questions focused on undergraduate teaching and assessment of CPT, and students’ preparedness for prescribing. In all, 185 medical schools (64%) from 27 EU countries responded. Traditional learning methods were mainly used. The majority of respondents did not provide students with the opportunity to practice real-life prescribing and believed that their students were not well prepared for prescribing. There is a marked difference in the quality and quantity of CPT education within and between EU countries, suggesting that there is considerable scope for improvement. A collaborative approach should be adopted to harmonize and modernize the undergraduate CPT education across the EU.

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?
- A previous study showed that few teaching hours in European medical schools were devoted to clinical pharmacology and that there is a lack of trained individuals in this area. Additionally, a recent study showed that the prescribing competencies of final-year medical students in Europe were poor, resulting in many potentially harmful prescribing errors.

WHAT THIS STUDY ADDS TO OUR KNOWLEDGE?
- There is marked variation in the quality and quantity of CPT education within and between EU countries. CPT teaching and assessment throughout the EU is mainly based on traditional learning methods. Most medical schools do not provide students with the opportunity to practice real-life prescribing and do not consider their students to be well prepared for prescribing as a junior doctor.

WHAT QUESTION DID THIS STUDY ADDRESS?
- This international multicenter study investigated the current structure, delivery and assessment of pharmacology and clinical pharmacology and therapeutics (CPT) education in European Union (EU) medical schools.

HOW THIS MIGHT CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?
- A collaborative approach should be adopted to harmonize and modernize the undergraduate CPT education across the EU.

Prescribing drugs safely and effectively is a fundamental skill that medical graduates must acquire, because after graduation they will prescribe drugs on a daily basis, often with minimal supervision. Inappropriate prescribing may lead to prescribing errors, resulting in exacerbation or prolongation of illness, patient harm, and high healthcare costs.\textsuperscript{1,2} Since graduates from medical schools in the European Union (EU) are entitled to work in different EU countries, they should have uniform and adequate prescribing competencies (i.e., knowledge, skills, attitudes). However, concerns have been expressed that medical graduates across the EU are not adequately prepared for their prescribing duties.\textsuperscript{3} In the UK, recently graduated doctors were found to be responsible for a large number of prescribing errors and reported not feeling adequately prepared for their prescribing responsibilities.\textsuperscript{4,5} Furthermore, a recent multicenter study involving 17 European medical schools showed a general lack of essential prescribing

\textsuperscript{1}\textsuperscript{1}\textsuperscript{Department of Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands; 2\textsuperscript{Research and Expertise Center in Pharmacotherapy Education (RECIPE), Amsterdam, The Netherlands; 3\textsuperscript{Medical Education Unit, Brighton and Sussex Medical School, Brighton, UK; 4\textsuperscript{Department of Clinical Pharmacology, Ghent University, Ghent, Belgium; 5\textsuperscript{Unit of Clinical Pharmacology, University of Zagreb School of Medicine, Zagreb, Croatia; 6\textsuperscript{Faculty of Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; 7\textsuperscript{Department of Pharmacology and Clinical Pharmacology, University of Lisbon, Lisbon, Portugal; 8\textsuperscript{Faculty of Medicine, University of La Laguna, Tenerife, Spain; 9\textsuperscript{Department of Pharmacology and Algesiology, Gr. T. Popa University of Medicine and Pharmacy, Iasi, Romania; 10\textsuperscript{Unit of Clinical Pharmacology, University of Edinburgh, Edinburgh, UK. Correspondence: DJ Brinkman (d.brinkman@vumc.nl)

Received 23 January 2017; accepted 6 March 2017; advance online publication 15 March 2017. doi:10.1002/cpt.682
competencies among 895 final-year students, which has potential consequences for patient safety. Poor undergraduate teaching in pharmacology and clinical pharmacology and therapeutics (CPT) may underlie this lack of prescribing competencies. Indeed, a survey conducted under the auspices of the World Health Organization (WHO) in 1988 showed that European medical schools devoted relatively little time to teaching clinical pharmacology and that there was a lack of trained individuals in this area. However, it is not known whether the situation has improved in the meantime, although recent studies showed marked differences in the quality and quantity of CPT teaching and training between medical schools in the same country. Although these findings are worrying, a new baseline evaluation is needed to serve as a starting point for a harmonized CPT curriculum throughout the EU, as suggested by the British Pharmacological Society (BPS) and European Association of Clinical Pharmacology and Therapeutics (EACPT) in 2007. Therefore, on behalf of the Education Working Group of the EACPT, we conducted this multinational study to gain insight into the current structure, delivery, and assessment of CPT education in EU medical schools. Based on the available literature, we hypothesized that there is marked difference in the quality and quantity of CPT education between EU medical schools.

RESULTS
From 9 May to 9 November 2016, 290 (95%) out of 304 EU medical schools were eligible to participate in this study. Luxembourg had only one medical school with a preclinical curriculum and thus was excluded. Additionally, four schools with a preclinical curriculum (three Belgium, four UK) and nine private medical schools (one Austria, eight Spain) were excluded. Of all eligible medical schools, 185 (64%) schools from 27 EU countries completed the online questionnaire. The mean response rate per country was 67%, ranging from 14% in Belgium to 100% in the Czech Republic, Estonia, Lithuania, Malta, the Netherlands, and Slovenia (see Supplementary Material Table 1).
The duration of the undergraduate medical curriculum (pre-clinical and clinical years) ranged from 5 to 6 years. In total, 145 of the medical schools (78%) offered a compulsory course in CPT, 21 (12%) an elective course, and 19 (10%) offered no course. Of those schools with a CPT course, 73 (44%) identified their course as vertically, 70 (42%) as spirally, and 23 (14%) as horizontally integrated (see definitions in Supplementary Material Figure 1). In all, 176 schools (95%) had a teacher responsible for CPT. The median number of estimated contact hours devoted to CPT teaching during the undergraduate curriculum was 68 (interquartile range 35–100). Countries in the eastern and southern region of the EU used more traditional learning methods, whereas countries in the western and northern region used more problem-based learning methods (Figure 1). Basic pharmacology was primarily taught and assessed in the early years of the medical curriculum, whereas clinical pharmacology and therapeutics was taught in the later years (Supplementary Material Figure 2).

Teaching methods and study materials
A variety of teaching methods were used (Figure 2). Lectures (75% (basic pharmacology) to 91% (therapeutics)) and self-study (57–59%) were the most common teaching methods for CPT, whereas patient simulation (4–24%) and one-on-one teaching with a supervisor (2–10%) were the least common methods. Some medical schools used bedside teaching (43%) and prescribing in clinics (37%) to teach therapeutics. Lectures (89%) and clinical cases (81%) were the most common study materials for CPT education, whereas eBooks (19%) and mobile applications (13%) were the least common materials (Figure 3).

Teachers involved in teaching development and delivery
In most medical schools, clinical pharmacologists (90%), senior clinicians who were not clinical pharmacologists (77%), and basic pharmacologists (74%) developed and delivered CPT education (Supplementary Material Figure 3). Some schools involved pharmacists (42%) and junior doctors (36%), and few involved educational experts (21%) or medical/pharmacy students (8%) in the development and delivery of their teaching program.

Real-life prescribing in clinics
In most medical schools, students did not get the opportunity to practice real-life prescribing for patients under the supervision of a senior clinician during clinics. (Color figure can be viewed at wileyonlinelibrary.com)

Assessment methods
A variety of summative assessment methods were used (Figure 4). Written (73% (basic pharmacology) to 83% (therapeutics)) and oral examinations (31–40%) were the most common assessment methods for CPT, whereas student formulary (2–4%) and peer assessment (1–2%) were the least common methods. Few medical schools (≤30%) used practical assessments, such as objective structured clinical examinations (OSCEs) or workplace assessments in

Figure 2  Traditional learning methods are on the left and context-based learning methods on the right. WHO GGP, World Health Organization Guide to Good Prescribing. Real-life prescribing: the opportunity to prescribe drugs for real patients under the supervision of a senior clinician during clinics. [Color figure can be viewed at wileyonlinelibrary.com]

Figure 3  Written materials are on the left and online learning resources on the right. Student formulary: specified list of commonly prescribed drugs that students develop during their medical education. [Color figure can be viewed at wileyonlinelibrary.com]
Most schools did not explicitly assess students’ dosing knowledge (65%) or drug calculating skills (62%). In contrast to basic pharmacology (33%), most schools integrated the assessment of clinical pharmacology (58%) and therapeutics (64%) into a broader course assessment.

**Final prescribing assessment**

Eighty-six medical schools (47%) had no final prescribing assessment to evaluate final-year students’ competencies before graduation, 42 (23%) participated in a national assessment, 34 (18%) had a local assessment ranging from written, oral to online examinations, and 23 (12%) had both.

In the UK, a 2-h national online examination (60 multiple-choice questions (MCQ), extended matching questions (EMQs), prescribing requests) is used to assess prescribing knowledge and skills, such as writing prescriptions, reviewing medication, and calculating drug doses.10 In the Netherlands, a 2-h national online examination (60 MCQs) focused on ready knowledge required for safe prescribing is used.11 In both countries, individual medical schools can decide whether this examination is summative or formative. In France, prescribing knowledge is assessed as part of a 2.5-day summative final state examination. This computer-based examination uses narrative patient scenarios (24 cases) combined with MCQs, EMQs, and short answer questions, some of which relate to CPT.12 In Germany, there is a final state examination involving oral and practical examinations during which CPT can be assessed but is not obligatory. In Slovakia, there is a similar examination but CPT assessment is obligatory. The remaining countries have no final prescribing assessment before graduation, although in Cyprus, Poland, and Italy therapeutic decision-making is evaluated during a compulsory preregistration period after graduation.

**Quality, alignment, and structure of learning objectives**

In all, 153 medical schools (83%) defined specific learning objectives for CPT during the undergraduate curriculum, and 63 (41%) submitted their objectives for further evaluation. The mean overall quality of the objectives was 1.94 (standard deviation (SD) 0.57), with a score of 1.71 (0.73) for “Specific,” 1.89 (0.75) for “Measurable,” 1.98 (0.67) for “Achievable,” 1.94 (0.72) for “Relevant,” and 2.18 (0.90) for “Time-bound.” The objectives of 34 schools (54%) were not or little aligned with the learning and assessment activities, 19 (30%) were partly aligned, and 10 (16%) were adequately aligned. Most of the objectives for basic and clinical pharmacology (93%) and therapeutics (63%) were defined at the “knows” and “knows how” level of Miller’s pyramid; 36% of the objectives for therapeutics were defined at the “shows how” level (Figure 5). The most important themes identified in the learning objectives are summarized in Supplementary Material Table 2.

**Being prepared for prescribing**

Fourteen (8%) respondents described their final-year medical students as being “not prepared,” 113 (61%) as “fairly well,” 54 (29%) as “well prepared,” and four (2%) as “extremely well prepared” for prescribing as a junior doctor. A common reason for the lack of preparedness was that the CPT education was too theoretical, with too little emphasis on training real-life prescribing in clinical practice (22 free text comments). The probability of being “well prepared” or “extremely well prepared” rather than the other qualifications of preparedness was significantly associated with the presence rather than the absence of a final prescribing assessment (45% vs. 17%, P < 0.0001) and the presence rather than the absence of a competence assessment of dosing knowledge (41% vs. 27%, P = 0.048).

![Figure 4](https://wileyonlinelibrary.com)  
*Figure 4* The teacher-centered methods are on the left and student-centered methods on the right. OSCE, objective structured clinical examination. Workplace assessment: assessing rational prescribing for real patients during clinics. [Color figure can be viewed at wileyonlinelibrary.com]

![Figure 5](https://www.cpt-journal.com)  
*Figure 5* Guide to good prescribing. Miller’s pyramid for evaluating the structure of learning objectives.
The main findings of this study are that in the EU 1) CPT education varies greatly within and between countries; 2) CPT teaching and assessment are mainly based on traditional learning methods; 3) more than two-thirds of the schools do not provide students with the opportunity to practice real-life prescribing; 4) the assessment of CPT is often integrated into a broader course assessment, and almost half of the schools do not have a final prescribing assessment; 5) most (69%) medical schools do not consider their students to be well prepared for prescribing as a junior doctor; and 6) the overall quality of CPT learning objectives is poor, and objectives are often not consistent with the learning environment and assessment activities. While there was some variation between schools, these results suggest that there is considerable room to improve CPT education in many EU medical schools.

“Improving and harmonizing the teaching of the rational use of drugs at both undergraduate and postgraduate levels” in Europe is a main goal of the EACPT.13 It is important to ensure a uniform standard of prescribing among medical graduates, so as to facilitate their mobility across countries. However, we found a marked variation in the quality and quantity of CPT education within and between EU countries. Since the last analysis in 1988 showed similar results,7 it is surprising that the situation has not improved significantly. However, despite these large differences, some progress has been made in the past three decades. First, several schools have introduced a distinct or integrated prescribing assessment before graduation, and having such an assessment was significantly associated with a better perceived preparedness for prescribing as a junior doctor. A separate and robust prescribing assessment is necessary to ensure that new doctors are able to prescribe safely and effectively,10 particularly since most schools

Table 1 Scoring rubric for pharmacology and clinical pharmacology and therapeutics learning objectives according to the SMART criteria

<table>
<thead>
<tr>
<th>Score</th>
<th>Specific</th>
<th>Measurable</th>
<th>Achievable</th>
<th>Relevant</th>
<th>Time-bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Poor</td>
<td>• Broad, vague and unclear objectives • Not specific to drug groups, themes or core drugs and diseases that students should be familiar with</td>
<td>• Objectives are not clearly measurable and documentable</td>
<td>• Objectives are not or hardly feasible given student’s abilities and will likely not be achieved within the designated time frame</td>
<td>• Objectives cover no or little relevant knowledge, skills, and attitudes for CPT</td>
<td>• No or unclear time frame by which the objectives should be accomplished</td>
</tr>
<tr>
<td>2 = Suboptimal</td>
<td>• Specific objectives, but does not specify knowledge, skills and attitudes in detail • Specified list of themes/drug groups (e.g. cardiovascular drugs) that students should be familiar with but no list of core drugs and diseases • Uses verbs like understand, know, learn, list, describe and explain</td>
<td>• Objectives are only partly measurable and documentable</td>
<td>• Objectives are partly feasible given the student’s abilities and can only partially be achieved within the designated time frame</td>
<td>• Objectives cover some relevant knowledge, skills, and attitudes for CPT</td>
<td>• A clear time frame of what should be accomplished within the bachelor’s or master’s degree or undergraduate curriculum</td>
</tr>
<tr>
<td>3 = Adequate</td>
<td>• Specific objectives with a detailed description of the required knowledge, skills and attitudes for CPT • Specified list of core drugs and diseases that students should know about • Describes what the student should be able to do in clinical practice • Uses action verbs like prescribe, choose, show, select, review (NOT understand, learn, know)</td>
<td>• Objectives are clearly measurable and documentable</td>
<td>• Objectives are feasible given the student’s abilities and can be achieved within the designated time frame</td>
<td>• Objectives cover most of the relevant knowledge, skills, and attitudes for CPT</td>
<td>• A clear time frame of what should be accomplished within a course, module, semester or academic year</td>
</tr>
</tbody>
</table>

Based on the SMART mnemonic.27 Adapted from Lockspeiser et al.28 CPT, pharmacology and clinical pharmacology and therapeutics.

*Score per criteria ranged from 1 to 3, with no half points. If objectives did not meet the requirement for a particular score, it received the next lower score.*
integrated the assessment of CPT into a broader course assessment, and hence students can compensate for a poor performance in this area by a good performance in other areas. Although the development of final prescribing assessments is promising, future studies should investigate whether these actually improve prescribing objectives after graduation.

Second, more medical schools had an identifiable CPT course (90% in 2016 vs. 77% in 1988), and, on average, more contact hours per school were devoted to CPT education during the undergraduate curriculum (95 h in 2016 vs. 35 h in 1988). Although these findings are encouraging, relatively few hours are devoted to CPT education (±2–3% of total study load) compared with other, mainly diagnostic, subjects. Curriculum designers tend to place more emphasis on diagnostic rather than therapeutic reasoning, with the former being perceived as more challenging and difficult. Consistent with the views of final-year students in Europe, CPT education was mainly based on traditional learning methods such as lectures and written examinations, rather than on context-based learning methods, such as patient simulation and workplace assessments. In fact, a large proportion (39%) of schools used solely traditional learning methods, which could in part explain why respondents indicated that students were not well prepared for rational prescribing. The predominance of traditional learning methods in pharmacology education has also been reported in the USA. Rational prescribing is a complex skill that requires various high-level cognitive processes, and thus attending lectures and passing written examinations probably do not prepare students sufficiently for this task. A recent study showed that students taught with mainly traditional learning curricula have significantly weaker prescribing competencies than students taught with mainly problem-based learning curricula. The WHO Guide to Good Prescribing model has been shown to be the only effective method to teach rational prescribing in a wide variety of international settings, yet fewer than 20% of the respondents used this model in their teaching program. This could be because these medical schools provide little practical teaching in the form of role-playing sessions and patient simulation, for which this model is best suited. Although a transition towards more practical teaching is necessary, the resource-intensive format of this teaching could be a challenge for medical schools with a small group of CPT teachers. The traditional aspect of CPT education is also reflected by the extensive use of written materials compared with online learning resources such as E-learning, eBooks, and mobile applications. More medical schools should use and share these resources because they increase accessibility to information, facilitate personalized training, standardization of content, and are suitable for assessing large cohorts of students simultaneously.

Third, more schools had a designated teacher responsible for CPT education (95% in 2016 vs. 79% in 1988), often a clinical pharmacologist or senior clinician. Such an individual is indispensable for ensuring that the principles of safe and effective use of medicines are emphasized throughout the curriculum. Only a minority of schools actively involved junior doctors and medical/pharmacy students in teaching and education. Yet “near-peer” education has proven to be beneficial and able to reduce the workload of the usually small group of teachers. Clinical pharmacists and nurse prescribers should be given a larger role as educators since they offer additional skills and attributes (e.g., reviewing medication charts) and could improve interdisciplinary collaboration for the prevention of prescribing errors.

The quality of CPT learning objectives was generally poor, with objectives often being broad, vague, and incomplete. Only...
13 schools used a specified list of core drugs and diseases that students should be familiar with before graduation. Clear objectives are important to verify whether learning outcomes are achieved.\(^{21}\)

Therapeutic objectives were often focused on skills acquisition (e.g., rational prescribing, see Supplementary Material Table 2) but did not dovetail with the learning environment (e.g., lectures) and assessment activities (e.g., written examinations). Better coordination between learning objectives and curriculum content is necessary to help students achieve high-level outcomes.\(^{25}\)

Our results should be interpreted in the light of some limitations. First, data were mainly derived from a single teacher at each school and may have been biased either because the respondents had vested interests or interpreted the questions differently. Second, although definitions were given, there may have been some overlap between CPT themes in the questionnaire. Third, since the questionnaire was not anonymous, respondents may have given socially desirable answers. Fourth, the low response rate in some countries (i.e., Austria, Belgium, Hungary, Italy) might have influenced the results. Fifth, the participating medical schools might have a high standard of CPT education, and thus the results might be optimistic. Sixth, we relied on medical schools to self-report their education, which may not reflect the actual content of the medical curriculum. Seventh, students might be offered other learning activities, which are outside the remit of the responsible teachers and thus not reported in the questionnaire.

**CONCLUSIONS AND RECOMMENDATIONS**

Although some progress has been made in the past three decades, this study showed that there is still marked variation in the quality and quantity of CPT education within and between EU countries. This finding may underlie the general lack of prescribing competencies among European medical graduates. Since graduates from medical schools in the EU can move to different EU countries for their postgraduate training, they should have a uniform level of prescribing competencies. In order to achieve this, a collaborative effort is required to harmonize and modernize the teaching and assessment of the rational use of drugs at an undergraduate level. The EACPT Education Working Group has formulated a list of recommendations that can serve as starting point for a harmonized CPT curriculum for EU medical schools (Table 2).

**METHODS**

This cross-sectional survey involved medical schools in all 28 EU countries and was carried out in the academic year 2015–2016. Since we focused on CPT education during the entire medical curriculum, we excluded medical schools delivering only a preclinical curriculum (i.e., bachelor's degree). Additionally, we excluded private medical schools because their education is not accessible for all students. A 24-item web-based questionnaire (using surveymonkey.com) was developed, based on comparable studies,\(^{7-9,26}\) and validated by the Education Working Group of the EACPT during an online modification round (Supplementary Material Figure 1). The questionnaire asked specific questions about undergraduate teaching and assessment of basic pharmacology, clinical pharmacology and therapeutics, and the preparedness of students for their future task as prescribers. Basic pharmacology was defined as education about the basic principles of how drugs act in biological systems including pharmacodynamics (e.g., receptor and other drug targets), pharmacokinetics (e.g., absorption, distribution, metabolism, excretion), and pharmacogenetics; clinical pharmacology as education about the application of pharmacological principles and methods in clinical practice (e.g., rational drug selection, adverse drug reactions, drug interactions, errors, adherence); therapeutics as education about the process of rational prescribing for specific clinical conditions (i.e., how to choose a specific drug for an individual patient).

**Table 2**

| VOLUME 102 NUMBER 5 | NOVEMBER 2017 | 821 |

**ACKNOWLEDGMENTS**

This study was a project by the European Association of Clinical Pharmacology and Therapeutic (EACPT), initiated by the Working Group Research on Education. We thank all the respondents who participated in this study. We are additionally grateful to the following persons for their help in the data collection process: Prof. Viera Kristová (Comenius University, Slovakia), Prof. Petr Potmišli (Charles University Prague, Czech Republic), Dr Silvia Benemei (University of Florence, Italy), Prof. Jan Braszko (Medical University of Bialystok, Poland), Prof. Pierre
Bustany (University of Caen Lower Normandy, France), Dr Greta Wozniak (University of Cyprus, Cyprus), Prof. Ingolf Caspari (University of Kiel, Germany), Prof. Zdravko Kamenov (Medical University of Sofia, Bulgaria), Dr Dolors Capellà (University of Girona, Spain), Prof. Henrik Enghusen Poulsen (University of Copenhagen, Denmark), Prof. Markus Forsberg (University of Eastern Finland, Finland), Prof. Parakevi Papaioannidou (University of Thessaloniki, Greece), Dr Riba Pál (Semmelweis University, Hungary), Prof. John Waddington (Royal College of Surgeons, Ireland), Dr Baiba Jansone (University of Latvia, Latvia), Dr Toomas Marandi (University of Tartu, Estonia), Dr Lovro Ziberna (University of Ljubljana, Slovenia), Prof. Yvla Böttiger (Linköping University, Sweden).

CONFLICT OF INTEREST
The authors declared no conflict of interest.

AUTHOR CONTRIBUTIONS

© 2017 The Authors Clinical Pharmacology & Therapeutics published by Wiley Periodicals, Inc. on behalf of American Society for Clinical Pharmacology and Therapeutics

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.