Summary and General Discussion
Prescribing has been an essential competence for medical doctors since the time of the ancient Egyptians. To date, it is still one of the key clinical activities in the working life of most doctors and is probably the intervention that has the greatest influence on the health of patients. Besides being a core competence, prescribing is also one of the most complex and challenging tasks of doctors. Prescribers have to select the most suitable drug, dosage, route and frequency of administration, sometimes in the face of diagnostic uncertainty, while taking individual patient characteristics, such as age, gender, comorbidity and co-medication, into account. This prescribing process is getting more complicated because of the increasing age, frailty, multimorbidity and polypharmacy of patients. Furthermore, prescribing takes place in the complex social context of the clinical...
workplace with frequent interruptions and distractions, and the involvement of different healthcare professionals. With these complexities, it is perhaps not surprising that poor prescribing is common, especially among junior doctors who have the least experience. Indeed, one in ten of their prescriptions may contain errors, potentially leading to serious adverse drug events, such as prolonged hospital stays, unplanned hospital readmissions, significant morbidity and mortality, and high financial costs for healthcare authorities. To prepare medical students for their future role as prescriber, it is important that they receive high-quality and effective undergraduate education in clinical pharmacology and therapeutics (CPT) during their medical training. However, recent studies in Europe have shown that medical students and recent graduates believe that CPT education is inadequate and that they feel underprepared for and anxious about prescribing, a concern echoed by their supervisors. These issues formed the motivation for the studies described in this thesis, the main objective of which was ‘to improve clinical pharmacology and therapeutics education in the undergraduate medical curricula of European medical schools and ultimately contribute to improvements in the quality and safety of patient care’. The following research questions were derived from this main objective:

1. What is the current level of prescribing knowledge, skills and attitudes of medical students in European medical schools, assessed in different context settings?
2. What is the current quantity and quality of clinical pharmacology and therapeutics education in the undergraduate medical curriculum of European medical schools?
3. What learning outcomes should medical students have acquired in order to prescribe rationally by the time they graduate, and how should these be taught and assessed during undergraduate medical education in European medical schools?

This chapter summarizes and discusses the answers to these questions, placing them in a broader perspective. The main conclusions and recommendations are shown in Figure 1.

WHAT IS THE CURRENT LEVEL OF PRESCRIBING KNOWLEDGE, SKILLS AND ATTITUDES OF MEDICAL STUDENTS IN EUROPEAN MEDICAL SCHOOLS, ASSESSED IN DIFFERENT CONTEXT SETTINGS?

Chapter 2.1

In this chapter, we provided a systematic literature overview evaluating whether final-year medical students have attained the necessary competencies for rational prescribing. Additionally, we attempted to identify which prescribing competencies medical graduates should have acquired in order to prescribe rationally. The literature demonstrated a general lack of final-year medical students’ preparedness, self-confidence, and self-reported knowledge and skills, specifically regarding general prescribing, antimicrobial prescribing and pharmacovigilance. However, we found no clear consensus among CPT teachers on which prescribing competencies medical students should have been acquired before graduation. These findings suggest that changes in
undergraduate CPT education are urgently required and that there is a need for greater consensus among CPT teachers on which competencies are essential to ensure that medical students prescribe rationally.

**Chapter 2.2**

In order to evaluate the essential prescribing competencies, we performed an international cross-sectional study among 895 final-year medical students from 17 European medical schools. Participants were asked to complete a standardized computer-based assessment and questionnaire. The content of the assessment focused on knowledge and skills that every medical graduate in Europe should have attained before graduation. Although there were differences between medical schools, these final-year medical students generally lacked essential prescribing competencies. In particular, the students had a poor knowledge of drug interactions and contraindications, chose inappropriate therapies for common diseases and made prescribing errors. Students taught mainly with problem-based learning CPT curricula had significantly better prescribing competencies than students taught mainly with traditional learning curricula. Additionally, students lacked confidence about essential prescribing skills, and most were not satisfied about the quantity and quality of undergraduate CPT education. A vast majority felt that they were not adequately prepared for their future prescribing task as doctors. These findings suggest that undergraduate CPT education in many European schools is inadequate, which has potential consequences for the safety of patient care.

**Chapter 2.3**

In this letter, we re-analysed data from the study described in the Chapter 2.2 and investigated the relationship between factual drug knowledge and treatment appropriateness. CPT education is traditionally focused on the acquisition of knowledge rather than on the acquisition of prescribing skills. We found a weak positive correlation between drug knowledge and the quality of treatment choices among final-year medical students. Although some drug knowledge is required in order to choose an appropriate drug treatment, it may play a less important role than previously assumed. More emphasis should be given to the training and assessment of prescribing skills (e.g., real-world prescribing) rather than the acquisition of knowledge (e.g., lectures) in the undergraduate medical curriculum.

**Chapter 2.4**

In this chapter, we investigated the prescribing skills and self-reported confidence of 403 medical students from one medical school during the fourth year of a context-learning pharmacotherapy curriculum. Additionally, we determined whether their self-reported confidence was associated with prescribing skills assessed in an objective structured clinical examination (OSCE). This examination consisted of performing a therapeutic consultation with a simulated patient with a common therapeutic problem. Afterwards, students were asked to complete an online questionnaire about the prescribing skills that had been assessed in the examination. Although students’ prescribing
performance was adequate, they lacked confidence in essential prescribing skills, i.e., verifying the suitability of the treatment for the patient and choosing the correct treatment. Additionally, there was a weak positive correlation between self-reported confidence and the actual performance of students. These results suggest that self-reported confidence is not an accurate measure of prescribing competence, and that students lack insight into their own strengths and weaknesses in prescribing.

Chapter 2.5

In this chapter, we evaluated the prescribing skills and self-reported confidence of 602 medical students from one medical school during the final (6th) year of a context-learning pharmacotherapy curriculum. Students were asked to perform several therapeutic consultations with real patients during their final clinical attachment (general practice). Afterwards, they were asked to complete an online questionnaire about their confidence in prescribing skills. This study showed that final-year medical students were sufficiently competent to carry out therapeutic consultations at the end of an undergraduate context-learning pharmacotherapy curriculum. Students could not only apply skills to clinical conditions in which they had been trained but also to new conditions, a so-called transfer effect. This effect has been found in previous studies and indicates that students in a context-learning programme only need to be trained in a limited number of diseases in order to reach an adequate level of prescribing. Although students’ performance was adequate, the majority did not feel confident about their essential prescribing skills. This lack of prescribing confidence should be addressed in educational programmes.

Considerations and limitations

Before we can answer the research question, some limitations have to be addressed. First, it may be difficult to define whether European students have sufficient or insufficient prescribing competencies because there is no internationally accepted norm. However, we evaluated knowledge, skills and attitudes that are absolutely necessary for rational prescribing, based on the opinion of a group of European CPT experts. We focused on competencies that are relevant to clinical practice, such as knowledge of common drugs and skills for common therapeutic problems. If students fail to acquire these competencies before graduation, we believe that this can be regarded as insufficient. Second, two studies were carried out in a single medical school, which potentially limits the generalizability of the findings. Third, the way in which prescribing skills were measured in simulated and real patient settings could be a problem. Although we based our scoring model on the World Health Organisation (WHO) 6-step model, which is the most widely used method for training rational prescribing, the validity and reliability of this instrument has not yet been established. Moreover, since the two studies measured prescribing competencies in a controlled environment, it can be questioned whether similar results would be found in clinical practice. However, it is unlikely that results would be better in real life, given the high workload, stress and distractions in the clinical workplace. Fourth, there are several competencies required for rational prescribing that we did not measure in our studies, such as drug history taking and therapeutic drug monitoring. As a final note,
Conclusions and recommendations
Taking the above limitations into account, we conclude that there is considerable evidence that European medical students lack the knowledge, skills and attitudes required for rational prescribing in different context settings. This lack of prescribing competencies might be because of inadequate CPT education in the undergraduate medical curriculum. Although students taught mainly with problem-based learning curricula had better prescribing competencies than students taught mainly with traditional learning curricula, their performance was still not satisfactory. Context-based learning CPT programmes might be useful to improve education, since we showed that medical students who participated in these programmes had adequate prescribing skills. Our results add to those of previous studies showing that context-based learning programmes improve the prescribing competencies of preclinical medical students.\textsuperscript{13,19} In order to improve the prescribing competencies of future European doctors, we suggest that a European core curriculum should be developed that incorporates elements of context-based learning, such as early experience in prescribing and real responsibility for patient care. A detailed blueprint for such a core curriculum will be discussed later. Future research should evaluate the efficacy of a context-learning CPT programme in a randomized controlled study, preferably in an international setting, with a large number of students and with postgraduate follow-up. Also, we recommend that CPT education should be continued during postgraduate training, in order to maintain this competence throughout the professional career.

WHAT IS THE CURRENT QUANTITY AND QUALITY OF CLINICAL PHARMACOLOGY AND THERAPEUTICS EDUCATION IN THE UNDERGRADUATE MEDICAL CURRICULA OF EUROPEAN MEDICAL SCHOOLS?
Chapter 3.1
In this multicentre study, we investigated the current structure, delivery and assessment of CPT in 185 medical schools from 27 European Union (EU) countries. Teachers with overall responsibility for CPT education in each medical school were asked to complete an online questionnaire. The questionnaire asked specific questions about undergraduate teaching and assessment of CPT, and medical students’ preparedness for prescribing. Although the quantity and quality of CPT education differed within and between EU countries, teaching and assessment were mainly based on traditional learning methods (e.g., lectures, written examinations), especially in the southern and eastern regions. On average, a relatively small proportion of the total study load per medical school was devoted to CPT education (95 hours; ±2-3% of total study load). Most respondents did not provide students with the opportunity to practise real-life prescribing and considered their students not well prepared for prescribing. CPT was often integrated into a broader course assessment, and almost half of the schools did not have a final prescribing assessment. Medical
schools with a separate prescribing assessment at the end of the curriculum perceived their students to be better prepared for prescribing as doctors. Also, the overall quality of CPT learning objectives was poor, and objectives were often not consistent with the learning environment and assessment activities. These results suggest that there is considerable room for improvement of CPT education in many EU medical schools.

Chapter 3.2
In this letter, we evaluated the outcome measures used in intervention studies of CPT education. We found that the vast majority of studies used ‘soft’ endpoints to evaluate the effect of educational interventions, such as the modification of knowledge and skills in a controlled environment. These soft outcomes are difficult to interpret in terms of their value for CPT education, because an increase in knowledge and skills assessed in a controlled environment does not necessarily translate to improved performance in clinical practice. Therefore, hard outcomes studies are urgently needed because evidence-based CPT education can be designed only if there is enough supportive high-quality research available.

Considerations and limitations
Some issues need to be addressed before conclusions can be drawn. First, since we evaluated CPT education in EU medical schools, the current situation in European countries that are not part of the EU (e.g., Switzerland, Norway) is unknown. However, we have no reason to believe that the quantity and quality of CPT education in these countries will be very different. Second, although the majority of EU medical schools responded (64%), some EU countries had a low response rate (i.e., Austria, Belgium, Hungary and Italy). Third, our evaluation was based on self-report of individual teachers, which may not reflect the actual content of curricula. Fourth, we did not use a systematic approach to review the intervention studies of CPT education. However, two recent systematic reviews on this topic reported similar findings.17,18

Conclusions and recommendations
Although some progress has been made in the past decades, there is still a marked variation in the quantity and quality of CPT education within and between European countries. Overall, the quantity of CPT education in most medical schools is low, and the quality is poor because education is mainly based on traditional learning methods. Furthermore, we conclude that there is little high-quality evidence available about which interventions are effective in CPT education. To improve research in CPT education, future studies should investigate the effect of educational interventions on hard outcomes, such as prescribing behaviour in clinical practice. Taken together, there is considerable room for improvement of CPT education in many countries. A collaborative approach should be adopted in order to harmonize and modernize CPT education across Europe.
Chapter 4.1
In this study, we aimed to identify the information about commonly prescribed drugs that junior doctors should know in order to prescribe rationally in daily practice. We conducted a two-round Delphi study involving 32 general practitioners and 28 registrars and consultants from academic and teaching hospitals in the Netherlands. The participants were asked to assess a preliminary list of knowledge items about three commonly prescribed drugs: amoxicillin, diclofenac and hydrochlorothiazide. We identified similarities between the three drugs and formed a list of general knowledge items applicable to other commonly prescribed drugs. This list consists of 10 knowledge items that junior doctor should know about the drugs they frequently prescribe. This list could be useful in the development of curricula and training programmes and for assessing the prescribing competence of future doctors.

Chapter 4.2
In this multicentre study, we aimed to reach consensus on key learning outcomes for teaching and assessing CPT during undergraduate medical training in European medical schools. Based on a systematic literature review, we developed a list of 307 learning outcomes. Subsequently, we carried out a modified Delphi procedure consisting of three questionnaire rounds and organized a face-to-face panel meeting. 92 experts from 25 European countries completed all three questionnaire rounds, and 33 experts attended the meeting. 232 learning outcomes from the original list, 15 newly suggested and 5 rephrased outcomes were included. These 252 learning outcomes should be included in undergraduate CPT curricula to ensure that European graduates are able to prescribe rationally. Additionally, we developed a blueprint for a European core curriculum in CPT describing when and how the outcomes could be taught and assessed in the medical curriculum. The blueprint can be adapted to suit the local preferences of medical schools, given differences in the culture and resources of different institutions.

Considerations and limitations
Curriculum developers in European medical schools may be overwhelmed by the large number of learning outcomes and may think it would be impossible to implement these in their already overcrowded curriculum. However, we think it is feasible to implement these learning outcomes in the curriculum if they are integrated into different modules over several study years. This requires clear leadership and good coordination, because the outcomes compete with many other outcomes in different modules. Moreover, it is important to note that one learning outcome is not equivalent to a single training or assessment. Many outcomes (usually 5-10) can be covered...
during one training or assessment. Furthermore, CPT teachers in each medical school should not
do all the teaching and assessment alone. Instead, other teachers across the curriculum should be
involved in the development and delivery of CPT, which will be discussed in more detail in the next
section. Although the proposed blueprint is resource intensive, we believe that this or a similar
curriculum design is required in order to prepare students adequately for the complex task of
rational prescribing.

The studies also had some limitations that need to be addressed. First, we only included Dutch
physicians in the study about essential drug knowledge, which potentially limits the generalizability
of the findings. In the European Delphi study, not all outcomes for which there was not full
agreement could be discussed during a face-to-face panel meeting because of the limited
time frame. Additionally, few junior doctors participated in the European expert panel, which is
unfortunate because they may have a good understanding of the prescribing requirements at
the time of graduation.

Conclusions and recommendations
To answer the research question, we conclude that 252 learning outcomes should be included
in undergraduate CPT curricula to ensure that European medical graduates are able to prescribe
rationally. Moreover, we identified 10 items that junior doctors should know about commonly
prescribed drugs in order to prescribe rationally in daily practice. To help medical schools to
implement the identified learning outcomes, we have developed a blueprint for a European core
curriculum in CPT that describes how and when the outcomes could be taught and assessed. This
blueprint is described in more detail in the next section.