CHAPTER

1

GENERAL INTRODUCTION
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Prescribing errors are common in hospitals – on average, a medication error occurs for every second patient admitted [1]. Although not all errors cause serious patient harm, it is essential to study the cause of these errors. Most in-hospital prescriptions are written out by the least experienced doctors, namely, junior doctors [2]. In the first years after graduation, many graduates work on hospital wards as the primary contact for patients and nurses and write out many prescriptions [2], which makes it essential that they can prescribe rationally and safely. Unfortunately, junior doctors make over 50% more prescribing errors than consultants (9.1% (7758 errors in 84797 orders) vs 5.9% (188 errors in 3177 orders) [2]. An explanation for these errors is the gap between the passive role of medical students and their active role as junior doctors [3]. Already in 1994, the WHO took steps to prevent patient harm and to improve rational prescribing, by publishing the “WHO guide to good prescribing” [4]. The guide provides a normative model to guide the process of rational prescribing in six-steps (the original six-step model is displayed in table 1).

<table>
<thead>
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<th>Step</th>
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<td>Define the patient’s problem</td>
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<td>Step 5</td>
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The guide has had a pivotal role in pharmacotherapy teaching, by identifying the need for active training in pharmacotherapy during the undergraduate medical training programme in order to promote good prescribing [4]. However, the guide itself is not appropriate as teaching method. To help pharmacotherapy teachers to teach prescribing, the WHO published the “Teacher’s guide to good prescribing”, based on the original guide to good prescribing [4, 5]. The teacher’s guide provides clear and relevant learning objectives and tools, with an underlying message that medical students should have the opportunity to treat real patients with appropriate supervision, to prepare them for their prescribing responsibilities as junior doctors [5]. The need for this has been recognized by medical students themselves. In a focus group study, they expressed the need to be actively involved in therapeutic decision-making during their medical education, in order to make the student–junior doctor transition less abrupt [6].
Since the publication of the two WHO guides, many European medical schools have incorporated therapeutic decision-making guided by the WHO six-step model into their curricula. All Dutch medical schools use the six-step model in their pharmacotherapy teaching [7]. A number of studies have investigated the effectiveness of the six-step model [8-10], and it has been found that use of the WHO six-step model not only improves students’ pharmacotherapy skills, but also their knowledge of basic and applied pharmacology, and increases satisfaction with education and self-confidence in prescribing [8]. To date, it is the only model that has been widely used and shown to improve prescribing [11]. However, despite the broad use of the six-step model and its apparent effectiveness, pharmacotherapy teaching (and its outcomes) still varies greatly within and between European countries [12]. A recent study of essential prescribing competencies among European medical students demonstrated yet again that undergraduate teaching in pharmacotherapy is inadequate and that European medical students lack necessary prescribing competencies [13]. This possibly reflects how pharmacotherapy is taught. Most curricula teach pharmacotherapy by means of traditional methods, including (passive) lectures [12]. Only a minority of medical schools provide clinical prescribing opportunities in the undergraduate medical curriculum [12]. Such prescribing opportunities, either by means of problem-based cases or clinical experience, are important and valuable learning moments. Students who have followed problem-based curricula and students who have prescribed before (under supervision) make (far) fewer errors than other students (-29.4% and -83%, respectively) [13]. An earlier study highlighted the importance of problem-based and context-based pharmacotherapy teaching and learning for improving the training of rational prescribing skills of medical students during their clinical clerkship in internal medicine [14].

Context
But what is context? As shown in the classical experiment of Godden and Baddeley, context can be conceptualized as the physical surroundings [15]. These authors found that divers recalled words better if recall took place in the same situation as when they studied these words (i.e., either underwater or on dry land), which was described as the “Same context advantage” [15]. Coles applied this to learning in general, and defined context learning as learning in a setting (context) similar to that of the future profession [16]. The study of Godden and Baddeley was replicated with medical students by Koen’s [17]. She studied the effect of physical context alone on the recall of certain words, but did not find the “same-context advantage” and thus concluded that the physical surrounding alone is unlikely to evoke the “same-context advantage” in medical education [17]. In the definition of context, Coles mentions ‘similar to,’ which seems to imply a close resemblance to, but different from, the actual workplace [16]. This difference in context seems to be binary (in context or out of context), whereas in reality context is continuous and can be modulated. In a follow-up study, Koen’s et al. identified three dimensions of context, namely, physical, semantic, and commitment [18]. They proposed a theoretical model for these dimensions, which they called an “enriched” context. When studied closely, this enriched context seems to be similar to learning in the real workplace [18].

History of medical education in the workplace (in the Netherlands)
In 2012, Dornan wrote “Workplace learning is as old as medicine itself”, which summarizes the history of workplace learning in a single sentence [19]. Although learning in the workplace might be as old as medicine itself, there have been and still are large differences in time and between countries. For centuries before the first European universities were founded, medical education occurred in the workplace in a master–apprentice context, based on the works of Hippocrates of Kos (460–377 BC) and Galen of Pergamon (Claudius Galenus 130–200) [20]. With the foundation of the first universities, students from the Netherlands studied medicine abroad, in Padua, Montpelier, and Bologna [20-23]. In addition to the limited number of university trained “doctores medicinae” (scholars in medicine), there were numerous “barber surgeons” who were trained in a completely different (guild) structure that was (almost) completely practice based [22].

Medical education in universities
With the founding of Leiden University, the first university in the Netherlands, in 1575, it was possible for students to study medicine in the Netherlands [23, 24]. The initial curriculum included predominantly lectures and no practice before graduation. This despite the efforts of Johannes van Heurne (1543–1601), one of the first professors, who proposed that bedside teaching should be introduced for students in 1593 [20, 24]. Van Heurne himself was trained as a physician in Padua, the cradle of bedside teaching, introduced by Giovanni Battista da Monte (1598–1552) [20, 23]. Unfortunately, the university rejected Van Heurne’s proposal that medical students should gain clinical experience [20].

When Utrecht University was founded in 1636, Willem van der Straaten (1593–1681), in his inaugural lecture, expressed his intention to introduce clinical teaching into the new medical curriculum [20]. He intended to combine his duties as practising physician with his position as professor. He wanted his students to be “not only theorists, but also practitioners when entering society as physician.” Soon thereafter, Leiden university introduced the “Collegium medico-practicum” [20, 23]. In the “Caecilia Gasthuis”, six beds for men and six beds for women and a room for the dissection of human cadavers were made available for clinical teaching, supervised by two professors [23]. Unfortunately, clinical teaching at Utrecht University ceased when Van der Straaten moved from Utrecht to Den Haag for his new job as the court physician of Frederik Hendrik, Prince of Orange (1584–1647) [20].

Herman Boerhaave
Leiden University medical school became very popular, and in the 17th century it attracted half of its medical students from abroad [24, 25]. Important contributors to this popularity were the freedom of religion and the ‘modern’ curriculum, which was more practical than theoretical [21, 26]. Many will have heard of Herman Boerhaave (1668–1738), a distinguished professor in this period. Boerhaave considered practice and clinical teaching important and enthusiastically...
re-introduced bedside teaching at the “Caecilia Gasthuis” [24]. Besides his progressive view on clinical teaching, Boerhaave also had very modern views on pharmacotherapy, as the historian Underwood amusingly wrote: “His prescriptions show little trace of polypharmacy, and the ingredients were used for their pharmacological action as known at that time.” [25]. Soon after Boerhaave’s death in 1738, the medical curriculum in Leiden changed again and undergraduate clinical training was reduced and became almost non-existent by the 18th and 19th centuries. In this era, the medical undergraduate curriculum consisted of a propaedeutic phase (only natural sciences), the candidate phase (during which students studied physiology, pathology, and anatomy, including dissecting animals/humans), a doctorate phase (theoretical ‘clinical’ lessons and passive patient demonstrations), and lastly a clerkship phase [21, 26].

Thorbecke & Flexner
In 1865, Thorbecke introduced a new law in the Netherlands that dictated that before a person could register as “a physician for medicine, surgery and obstetrics” he (and rarely, she) had to have followed a unified medical course, including both university education and 2 years of clinical experience [27, 28]. This law ended the confusion about the training of doctors and put a stop to training in the above-mentioned guild structure. Thorbecke’s law was quite unique in an international perspective: in the United States and the United Kingdom, the different standards for curricula and licensing persisted until about 1910 (Flexner report, USA) and 1944 (Goodenough Report, UK), respectively [25, 29-31]. In the early 1900s, most medical schools in the USA were small, for-profit schools with wide-ranging, non-standardized curricula, with large differences in quality and most were not affiliated with universities [29, 32]. This situation was reason for the Carnegie Foundation to ask Abraham Flexner to write a report and propose recommendations. In his reports, Flexner described the state of affairs of medical education in the USA/Canada, recommended how to improve medical education, and reviewed examples of medical education in Europe [29, 33, 34]. An important inspiration for his proposed reforms, including centralizing the responsibilities for medical education at universities, was his review of the situation in Germany (and the Netherlands) [29]. Besides the profound consequences of his reports on medical curricula in the 20th century, Flexner’s reports [33, 34] commented on the organization of medical education in the countries he reviewed. Thereby he offered an interesting perspective on Dutch medical education in the early 1900s. He mentioned the “total divorce of theoretical clinical instruction from practical experience of whatever kind” p.261 [34]. According to Flexner, the Dutch clerkships were deficient. Although students witnessed everything, clinical rotations were too rapid “responsible and experience of whatever kind” p.261 [34]. According to Flexner, the Dutch clerkships were deficient. Although students witnessed everything, clinical rotations were too rapid “responsible and experience of whatever kind” p.261 [34].

Curricular reforms in the 20th and 21st century
The first major change in Dutch medical curricula, with a move away from conventional medical curricula (with the distinct separate theoretical and clinical part), occurred with the introduction of a problem-based curriculum at Maastricht University in 1976 [21]. This curriculum was similar to the problem-based curriculum of McMaster University’s Faculty of Medicine [21, 22]. Such curricula put emphasis on active learning focused on clinical problems [35, 36], with a view to preparing students more effectively for clinical practice [36], even though they did not work with real patients. In the following decades, other Dutch medical schools updated their curricula based on Maastricht’s experience and parts of Harden’s SPICES model (Student-centred, Problem-based, Integrated, Community oriented, with Electives and with Systematic clinical training) [22]. They also added workplace learning to the undergraduate curriculum [37]. Nowadays, workplace learning in undergraduate medical curricula exists in different guises: early clinical experience, practical placements, and clerkships [19].

Early clinical experience
A century after the first Flexner report, the Carnegie Foundation published a new call for the reform of medical education in 2010. In this report, they recommended immersing students in clinical practice in an early phase of their training, so that students can integrate skills and knowledge in a way that prepares them for future clinical practice [32, 38]. These early clinical experiences are meant to bridge the gap between preclinical and clinical undergraduate medical education that persisted in the revised (problem-based) curricula. The 2010 Carnegie Foundation recommendations are based on research into the value of early clinical experience. One study reported that early clinical experience could be used to orientate medical curricula towards the social context of practice, ease students’ transition into the clinical environment, motivate them, make them more confident in approaching patients, and make them more aware of themselves and others [39]. In addition, clinical experience might strengthen students’ theoretical knowledge, making it deeper and more contextualized, and increase their knowledge of behavioural and social sciences, and of the organization of health care and the role of professionals in it [39]. In 2006, Dorman et al. reviewed the literature on early clinical experience and concluded that it helped medical students socialize to medicine, to acquire knowledge and skills, and to make their learning more real and relevant [37]. In an update of this review in 2010, Yardley confirmed these findings, and additionally found opportunities regarding the consequences of early clinical experience to the health and disease of individuals and communities, as well as to students’ communication skills [40].
These promising innovations and recommendations to implement early exposure to clinical practice in medical curricula have led to the development of, for example, “tag-along” experiences such as observing doctors (“shadowing”), nursing attachments, and participating in care for real patients [37, 40]. It is remarkable that the context and nature of these early clinical experiences are so heterogeneous [37, 40]. An explanation for this heterogeneity might be the gap in the literature regarding the characteristics/factors contributing to effective early clinical experiences [40]. A clear factor determining effectiveness is student engagement, which is considered to be different from the context alone. For example, while listening to a consultation with a clinical supervisor may be a contextual experience, it hardly engages the student or affects learning [41]. In contrast, if a student can make a meaningful and valuable contribution, then he/she is engaged and likely to learn from the experience [19, 42]. Engagement is essential to workplace learning, as acknowledged in 450 BC by Confucius.

“Tell me, and I will forget
Show me, and I may remember
Involve me, and I will understand”
(Confucius, 450 BC)

Improving pharmacotherapy education
As part of the above-mentioned major curricular reforms in the 20th and 21st century, pharmacotherapy education has introduced problem-based learning using patient cases and role-playing of consultations [43, 44]. Although this problem-based learning approach appears to improve pharmacotherapy skills, there is still room for further improvement. Even with problem-based curricula, final-year medical students are insufficiently prepared for clinical practice [13]. New and effective innovations are needed – context learning, engagement, and early clinical experience are all aspects that can be introduced to further improve pharmacotherapy education. Taking these concepts together, the optimal and most realistic method to teach undergraduate medical students pharmacotherapy would be for them to prescribe, perform medication reviews, and solve actual pharmacotherapy problems involving real patients.

This hypothetical setting closely resembles the student-run clinic (SRC). An SRC is an outpatient clinic completely run and organized by undergraduate (para) medical students, from their first year onwards. In an SRC, medical students prepare and perform diagnostic and therapeutic consultations with real patients under the direct supervision of clinical specialists. These clinics have existed for many years, predominantly in the USA and Canada. In 2012, over 62% of US medical schools had at least one SRC, and in 2014 75% did [45, 46]. Despite consensus on the positive effects of participation on students, gaining early clinical experience is not the primary aim of SRGs [47]. These clinics were founded as free clinics in order to deliver care to patients who otherwise could not afford or attain regular (insured) health care [48]. Although these clinics are focused solely on the provision of care to the needy, they could provide a setting for context-based learning and early legitimate clinical experience. Pharmacotherapy education could benefit from such learning experiences, but research is needed to evaluate if and how this concept can be used.

Key points introduction
• Future prescribers need better training in order to prescribe safe and effectively.
• Learning in the workplace with responsibility could facilitate student learning.
• Workplace learning is as old as medicine itself.
• Engagement is essential to workplace learning.
• Student-run clinics could provide workplace learning with engagement and are a promising setting for pharmacotherapy education.
AIMS AND OUTLINE OF THIS THESIS

The central aim of the studies of this thesis was to determine if and how we can assess, adjust, and use the SRC concept to improve pharmacotherapy education. To this end, specific aims were formulated for the three parts of this thesis.

In the first part of this thesis, the concept, our goal was to systematically review the literature on the outcomes of student participation in SRCs. Moreover, we also investigated the feasibility of the learner-centred SRC concept in a European setting with insured patients.

In the second part, the learning experience, we evaluated the preliminary outcomes of participation by students and patients in an SRC. Secondly, we aimed to clarify which factors influence learning in an SRC.

In the third part, the concept applied to pharmacovigilance, we investigated whether future doctors are prepared for their role in pharmacovigilance. We also designed, developed, and evaluated the educational value of a student-run pharmacovigilance programme and adverse drug reaction reporting assignment.

OUTLINE OF THIS THESIS

Part 1: The concept
The first part focuses on the concept of SRCs from a medical education perspective. Chapter 2 describes a systematic literature review of learning in SRCs in which we reviewed the outcomes of student SRC participation, using the four levels of learning outcomes as described in Kirkpatrick’s hierarchy, namely, attitudes and motivation; skills and knowledge; behaviour, and patient/health care. Chapters 3 and 4 describe the adjusted concept, development, and feasibility of a learner-centred SRC (LC-SRC) in a European setting. Feasibility was assessed using questionnaires completed by all stakeholders (e.g., students, clinical supervisors, and patients). The LC-SRC was considered feasible provided that the quality of care is guaranteed, patients are satisfied, clinical supervisors and students consider the LC-SRC feasible, and sufficient attention is paid to pharmacotherapeutics.

Part 2: The learning experience
The second part of this thesis entails three studies evaluating the SRC project from the perspective of supervisors, patients, and students. In Chapter 5, we investigated different types of motivation and proficiency in CanMEDS competencies of participating students. Motivation was measured using validated questionnaires, such as the Academic Motivation Scale and the Intrinsic Motivation Inventory. The CanMEDS competencies were evaluated by faculty using mini-clinical examinations of competence. In Chapter 6, we evaluated a student-run cardiovascular risk management (CVRM) programme from the patient’s perspective. The student-run CVRM programme was set up to offer primary prevention for cardiovascular disease to patients with known risk factors. After each consultation, patients were asked to complete an evaluation questionnaire to provide students with feedback and to evaluate the consultation. In Chapter 7, we investigated how students learn in an SRC and which factors influence this learning. In this study, we used a qualitative design with semi-structured interviews of students who were currently participating or who had previously participated in these clinics, either as student or as coordinator. Using a grounded theory approach with three consecutive coding stages, we analysed the data to identify themes.

Part 3: The concept applied to pharmacovigilance
The third part of this thesis covers pharmacovigilance, a specific aspect of pharmacotherapy that focuses on drug safety and adverse drug reactions. We chose this specific subject in order to expose students to pharmacotherapeutic problems, such as the management of adverse drug
reactions. In this part, we investigated pharmacovigilance education and how to improve it using the factors underlying learning in SRCs.

In Chapter 8, we report on a nationwide pharmacovigilance study involving medical students (third to sixth year) from all eight medical schools in the Netherlands. This study explored the preparedness of future doctors for their role in pharmacovigilance. Using various questionnaires, we assessed pharmacovigilance awareness, skills, and knowledge. In Chapter 9, we describe and evaluate the student-run pharmacovigilance programme. In designing this programme, we applied the SRC concept to pharmacovigilance teaching and training. We evaluated the programme in terms of student learning outcomes and the value of the programme to the National Pharmacovigilance Centre, Lareb (additional value of reports). In Chapter 10, we evaluate the merits of an adverse drug reaction reporting assignment. In designing this assignment, we applied factors previously identified as underlying experience-based learning and learning in SRCs. We investigated how students experienced this assignment and assessed the value of their reports for pharmacovigilance.

Lastly, in Chapter 11, the general discussion, we summarize the findings of the different studies of this thesis, paying attention to their strengths and weaknesses. Practical implications are discussed as well as suggestions for future research.

As all the chapters of this thesis are based on articles published in or submitted for publication in peer-reviewed journals, some repetitiveness is inevitable.

REFERENCES
