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Strategies for Medication Safety: An Organization-Based Approach Focusing on High-Alert Medications and Clinical Pharmacy Services in Helsinki University Hospital

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ACADEMIC DISSERTATION
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ABSTRACT

Medication errors are the single most important preventable factor jeopardizing patient safety. According to the ongoing World Health Organization's third Global Patient Safety Challenge on medication safety, the key risk areas are high-risk situations, polypharmacy, and transitions of care. Extending pharmacists' involvement in patient care and patient-safety work has been systematically addressed in patient safety initiatives since the early 2000s. Growing evidence on patient safety risks related to medications in the Finnish healthcare system has created a need to develop new strategies to manage these risks.

This study explores strategies for medication safety in Finland with a special focus on hospitals by using Helsinki University Hospital (HUS) as a case. The strategic development areas researched from an organizational approach were managing high-alert medications (Studies I-II) and evolving clinical pharmacy services to meet the needs of the organization in assuring medication safety (Studies III-IV). The study applied a systems approach to medication risk management based on the Theory of Human Error as a theoretical framework.

The study was conducted in two phases. In phase I (Studies I-II), HUS's high-alert medications were identified using the hospital's reports on medication errors (MEs) and adverse drug reactions (ADRs) which were compared with hospitals' drug consumption and the Institute for Safe Medication Practices' (ISMP) list of high-alert medications. This method was first developed and piloted with a strategic sample (n=249) of the MEs reported in 2007-2013 (Study I). The method was found to be applicable for identifying high-alert medications and was used with larger data in Study II when ADR (n=401) and ME (n=11,668) reports of HUS from 2015-2016 were analyzed. The top therapeutic groups and active substances in ADR and ME reports were not similar. Medicines such as antineoplastic agents, antithrombotics, opioids, and insulins, should be considered high-alert medications in HUS.

Phase II (Studies III-IV) assessed the clinical pharmacy services contributing to medication safety in Finnish hospitals. Study III explored pharmacist-led medication reconciliation and review procedures in two emergency departments (EDs) in HUS and Kuopio University Hospital (KUH). A sample of 150 patients, 75 from each hospital, aged ≥65 years, living at home and using ≥6 medicines were involved. Almost all patients, 100% in HUS and 99% in KUH, had discrepancies in their admission medication chart. Admission diagnosis was linked to drug-related problems (DRPs) of 16% of patients in HUS and 29% in KUH. Of these, high-alert medications were linked to 11% in HUS and 8% in KUH. Other acute DRPs were identified in 19 patients (25%) in HUS and 54 patients (72%) in KUH. Furthermore, the majority of

patients (89% in HUS and 100% in KUH) had non-acute DRPs, which needed actions in primary care.

Study IV explored the recent evolution of clinical pharmacy services in Finnish hospitals to promote medication safety within a timeframe of 2011-2016 by using an online survey targeted at all hospital pharmacies (n=24) and medicine dispensaries (n=131 in 2011; n=28 in 2016). The overall response rate was 60% in 2011 and 52% in 2016. Clinical pharmacy services were provided by 85% of the responding units in 2016, while only 51% of the units in 2011. Pharmacists had, in particular, extended their duties towards system-based medication safety work. Participation in long-term continuing education focusing on clinical pharmacy and medication safety had clearly become more common in 2016 compared to 2011.

This study provided a university hospital-specific approach to recent strategies and developments in medication risk management in Finland. Organizational high-alert medications can be identified using ADR and ME reports. More coordinated national collaboration is needed in order to combine the information gathered from ADR and ME incident data to better understand the risks of medication use. ED medication history-taking should be further developed with clinical pharmacists' involvement in medication reconciliation and reviews. Patient-centered work by clinical pharmacists contributing to medication safety has recently increased remarkably and extended to new tasks in Finnish hospitals. This is in line with international and national systems-based patient safety guidelines and policy initiatives and should be continued.

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CONTENTS

LIST OF ORIGINAL PUBLICATIONS (I-IV)

This thesis is based on the following original publications and a submitted manuscript, referred to in the text by their Roman numerals (I-IV).

I Tyynismaa L, Honkala A, Airaksinen M, Shermock K, Lehtonen L: Identifying high-alert medications in a university hospital by applying data from the medication error reporting system. J Patient Saf. 2017 Jun 1. doi: 10.1097/PTS.0000000000000388. [Epub ahead of print].

II Schepel L, Lehtonen L, Airaksinen M, Lapatto-Reiniluoto O: How to identify organizational high-alert medications. J Patient Saf. 2018 Jul 7. doi: 10.1097/PTS.0000000000000512. [Epub ahead of print].

III Schepel L, Lehtonen L, Airaksinen M, Ojala R, Ahonen J, Lapatto-Reiniluoto O: Medication reconciliation and review for older emergency patients' requires improvement in Finland. Int J Risk Saf Med. 2018 Oct 12. doi: 10.3233/JRS-180030. [Epub ahead of print]. 2019;30(1):19-31.

IV Schepel L, Aronpuro K, Kvarnström K, Holmström A-R, Lehtonen L, Lapatto-Reiniluoto O, Laaksonen R, Carlsson K, Airaksinen M: Strategies for improving medication safety in hospitals: evolution of clinical pharmacy services (submitted manuscript).

DEFINITIONS OF THE KEY CONCEPTS

Adverese drug event (ADE)
Any injury occurring during the patient's drug therapy resulting either from appropriate care or from unsuitable or suboptimal care (Council of Europe, CoE 2005). The definition includes adverse drug reactions and medication errors.

Adverse event (also patient safety incident or medical error)
An incident that results in harm to a patient (World Health Organization, WHO 2009). An adverse event is caused by medical management, in contrast to a process or complication of a disease (CoE 2006a).

Adverse drug reaction (ADR)
A response to a medicinal product that is noxious and unintended, resulting not only from the authorized use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse, off-label use, and abuse of the medicinal product (EU Directive 2010/84EU1).

Clinical pharmacy (see also pharmaceutical care)
An area of pharmacy concerned with the science and practice of rational and appropriate medication use (American College of Clinical Pharmacy, ACCP 2008, ACCP 2014, European Society of Clinical Pharmacy, ESCP 2017).

Comprehensive medication review (CMR)
A medication review procedure applied nationally in Finland and requiring accreditation training for pharmacists conducting it (Leikola 2012). The procedure is based on collaboration between pharmacists and other healthcare professionals, particularly physicians. CMR includes a patient interview and clinical medication review with structured, evidence-based forms and a case report format with documented action and follow-up plans from a multidisciplinary case conference.

Contributing factor
A circumstance, action or influence that is thought to have played a part in the origin or development of an incident or to increase the risk of an incident (Reason 2000, WHO 2009).

Drug-related problem (DRP)
An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes (Pharmaceutical Care Network, PCNE 2017).

Drug safety (see also pharmacovigilance)
Safety related to pharmaceutical products, usually concentrated on adverse drug reactions (Stakes and Rohto 2006, Turner 2009).

High-alert medication
Drugs that bear a heightened risk of causing significant patient harm when used in error (wrong drug, wrong dose, wrong route, etc.). Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients (Institute for Safe Medication Practices, ISMP, 2010, ISMP 2014).

Hospital pharmacy
Area of pharmacy which is located in hospitals and health centers. Includes purchasing, distribution and preparation of drugs and clinical pharmacy services such as drug information and medication safety services (Franklin and van Mil 2005, Bond and Raehl 2008).

Medication chart
Patient's list of medications which are in use. Should include prescription medication, over-the-counter medications, and herbal and nutritional products. Part of the patient's medical chart in the electronic health record system (also called medication administration chart, MAR).

Medication error (ME)
Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer (National Coordinating Council of Medication Errors Reporting, NCC MERP, 1998). Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing; order communication; product labeling, packaging and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

Medication error reporting system (MER)
An electronic or paper-based system that is used for systematically collecting information on medication errors, with the aim of identifying medication safety risks and thus enabling healthcare providers to improve quality of care (Hoffmann et al. 2008).

Medication reconciliation
A process of creating and maintaining the most accurate list possible of all medications a patient is taking, including drug name, dosage, frequency, and route, and using that list to guide therapy (Institute for Healthcare Improvement, IHI 2011).

Medication review
A structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimizing the impact of medicines, minimizing the number of drug-related problems, and reducing waste (Clyne et al. 2008).

Medication safety
A freedom from accidental injury during the course of medication use; activities to avoid, prevent, or correct adverse drug events which may result from the use of medications (CoE 2005, WHO 2009).

Near miss (also a close call or a potential adverse drug event)
A medication error that has the potential to cause an adverse drug event, but did not, either by luck or because it was intercepted and corrected (Reason 2000, CoE 2005).

Patient safety
Freedom from accidental injuries during the course of medical care, activities to avoid, prevent, or correct adverse outcomes which may result from the delivery of healthcare (Kohn et al. 2000, CoE 2005, WHO 2009).

Pharmaceutical care
According to the principles of pharmaceutical care, the role of pharmacists in patient care is to ensure the quality of medication therapies, with an emphasis on interprofessional collaborative care and patient interaction (Hepler and Strand 1990, American Society of Health-System Pharmacists ASHP 1993 Cipolle et al. 2004, PCNE 2013, ACCP 2014).

Pharmacovigilance
The science and activities relating to the detection, assessment, understanding and prevention of the adverse effects of pharmaceutical products (CoE 2005, EU Directive 2010/84EU1).

Risk management
Activities or measures taken by an individual or a healthcare organization to prevent, remedy or mitigate the occurrence or reoccurrence of a real or potential (patient) safety event (Dückers et al. 2009).

Safety culture
An integrated pattern of individual and organizational behavior, based upon shared beliefs and values, that continuously seeks to minimize patient harm which may result from the processes of care delivery (CoE 2006a).

Systems approach
An approach to safety stating that errors are generally consequences of systematic factors, e.g., weaknesses in organizational processes (Reason 2000). Building system defenses to reduce and prevent errors is the main method of safety improvement in a systems approach.

ABBREVIATIONS

ACCP	American College of Clinical Pharmacy
ADE	Adverse drug event
ADR	Adverse drug reaction
APhA	American Pharmacists Association
ASA	Acetylsalicylic acid
ASHP	American Society of Health-System Pharmacists
ATC	Anatomical Therapeutic Chemical
CMM	Comprehensive medication management (United States)
CDTM	Collaborative drug therapy management (United States)
CoE	Council of Europe
CPR	Cardiopulmonary resuscitation
CMR	Comprehensive medication review (Finland)
DDD	Defined daily doses
DRP	Drug-related problem
EAHP	European Association of Hospital Pharmacists
ED	Emergency department
EU	European Union
ESCP	European Society of Clinical Pharmacy
EUNetPaS	European Union Network for Patient Safety
EXPH	Expert Panel on effective ways of investing in Health (set by European Commission)
Fimea	Finnish Medicines Agency
FIP	International Pharmaceutical Federation
GTT	Global Trigger Tool
HaiPro	Reporting System for Safety Incidents in Health Care Organizations (Finland)
HUS	Helsinki University Hospital
ICU	Intensive care unit
IMM	Integrated medicines management (Northern Ireland)
ISMP	Institute for Safe Medication Practices (United States)
JCAHO	Joint Commission Accreditation of Healthcare Organizations
JCI	Joint Commission International
KUH	Kuopio University Hospital
LIMM	Lund Integrated Medicines Management (Sweden)
ME	Medication error
MSAH	Ministry of Social Affairs and Health (Finland)
MTM	Medication Therapy Management
NCC MERP	National Coordinating Council of Medication Errors Reporting (United States)
NHS	National Health Service (United Kingdom)
NICE	National Institute for Health and Care Excellence (United Kingdom)
OTC	Over-the-counter
PaSQ	European Union Network for Patient Safety and Quality of Care
THL	National Institute for Health and Welfare (Finland)
TPN	Total parenteral nutrition
WHO	World Health Organization

1 INTRODUCTION

Patient safety consists of the identification, analysis and management of patient-related risks and incidents, in order to make patient care safer and minimize harm to patients (Aspden et al. 2004, NPSA 2004, CoE 2005). Medication safety is a part of patient safety and is defined as "a freedom from accidental injury during the course of medication use; activities to avoid, prevent, or correct adverse drug events which may result from the use of medications" (CoE 2005, WHO 2009). Patient safety incidents are estimated to be the third leading cause of deaths in the US (Makary and Daniel 2016) and the fourteenth leading cause of the global disease burden (WHO 2018). Unsafe medication practices and medication errors (MEs) are the single most important preventable factor jeopardizing patient safety (WHO 2017). Approximately 6% of hospitalized patients experience an adverse drug event (ADE) during their hospital stay (Krähenbühl-Melcher et al. 2007), and around 25% of medication-related injuries are estimated to be preventable (Aspden et al. 2007). Globally, the estimated costs of MEs are 42 billion USD annually (WHO 2017).

Organizational actions have a crucial role in patient and medication safety development (Kohn et al. 2000). Recommended strategies to develop patient and medication safety are leadership and knowledge with a national focal point to set the goals, performance standards and expectations for safety, identifying and learning from error with error-reporting systems, creating a safety culture and implementing safety systems in healthcare organizations (Kohn et al. 2000, CoE 2006a+b). These should be based on the systems approach which is commonly illustrated by the Theory of Human Error (Reason 1990, Reason 2000).

Most recently, the World Health Organization (WHO) released the third Global Patient Safety Challenge, which focuses in medication safety (WHO 2017). The goal of the program "Medication Without Harm" is to reduce the level of severe avoidable harm related to medication by 50% over 5 years, globally. The key areas of the challenge are high-risk situations, polypharmacy and transitions of care. High-risk situations include high-risk settings, e.g. hospital settings with more serious clinical situations and the use of more complex medications, high-risk patients, e.g. young children, older adults, patients with concomitant kidney or liver disease and high-alert medications associated with a high risk of severe harm if used improperly. The WHO states that understanding these situations is crucial and suggests regular medication reviews to manage polypharmacy and medication reconciliations to prevent serious MEs in all transitions of care.

A multidisciplinary approach is the basis of developing medication safety (CoE 2006a+b, EXPH 2014). The European Directorate for the Quality of Medicines and Healthcare (EDQM) within the Council of Europe (CoE) has invited European governments and policymakers to implement the pharmaceutical care philosophy and working methods in their national healthcare systems (EDQM 2012). According to the principles of pharmaceutical care, the role of pharmacists in

patient care is to ensure the quality of medication therapies, with an emphasis on collaborative care and patient interaction (Hepler and Strand 1990, ASHP 1993 Cipolle et al. 2004). Even though pharmaceutical care and patient-centered clinical pharmacy services have been shown to improve quality, safety and efficiency of care and reduce its costs (Kaboli et al. 2006, Bond and Raehl 2008, Perez et al. 2008, Touchette et al. 2014), their diffusion to many health systems, for example in Europe, has been slow (Frontini et al. 2013).

Growing evidence on patient safety risks relating to medications in the Finnish healthcare system has created a need to develop new strategies to manage these risks (Juntti-Patinen et al. 2002, Mustajoki 2005, Lindén-Lahti et al. 2009, Pitkä 2009, Ruuhilehto et al. 2011, Koskinen 2013, Lapatto-Reiniluoto et al. 2015, Eronen 2015, Härkänen 2014, Holmström 2017). In Finland, the first medication safety initiative was established in 2005, when each healthcare unit was guided to set up a medication safety plan (MSAH 2005, Airaksinen et al. 2012). The first National Patient Safety Strategy was set for 2009-2013 (MSAH 2009), and the new HealthCare Act, enacted in 2011, obliged a medication safety plan as part of a patient safety plan in every healthcare organization. Learning from errors and the new safety culture were facilitated through a voluntary patient safety incident reporting system (HaiPro), which was launched in 2007 and is currently used by more than 60% of Finnish healthcare organizations (Ruuhilehto et al. 2011, Awanic 2018).

University hospitals have a crucial role in implementing national patient and medication safety initiatives. Helsinki University Hospital (HUS) started to report patient safety incidents with HaiPro in 2007. More systematic patient safety work began in 2011, when the Chief Patient Safety Officer and multiprofessional Patient Safety Steering group started their work and the first patient safety plan was developed (HUS 2011). Learning from medication error and adverse drug reaction reports and standardizing the medication use process were the main medication safety actions during 2011-2014 (HUS 2011-2014). Although clinical pharmacy services have been provided in HUS since the 1990s, their focus has been on drug logistics, dispensing per oral doses and preparing parenteral drugs (Huotari et al. 2008).

This study explored strategies for medication safety in HUS with a special focus on high-alert medications (Studies I-II) and clinical pharmacy services (Studies III-IV, Figure 13, see the Chapter 4.1). Both qualitative and quantitative research methods and various data sources were used (Figure 13). The study applied a systems approach to medication risk management based on the Theory of Human Error as a theoretical framework (Reason 2000). The study objectives cover the key areas of the WHO's Patient Safety Challenge "Medication Without Harm" (WHO 2017) and the EDQM's recommendations for implementing pharmaceutical care philosophy and working methods in healthcare (EDQM 2012). The objectives are also coherent to the medication safety objectives of the National Medicines Policy 2020 (MSAH 2011).

2 REVIEW OF THE LITERATURE

2.1 THEORETICAL CONTEXT OF PATIENT AND MEDICATION SAFETY

Reason´s Theory of Human Error (2000) has been widely used as a theoretical framework in system-based patient and medication safety work (Kohn et al. 2000, WHO 2011). To manage errors and risk in organizations and processes, psychologist James Reason (1990, 2000) has explained the challenge of human error with two approaches: the person and the system, which lead to different philosophies of error and risk management. The theory is based on observations and research on cultural characteristics of high-reliability organizations, i.e. systems operating in hazardous conditions but experiencing fewer adverse events and an almost complete absence of catastrophic failures, such as nuclear power plants and air traffic control centers (Weick 1987, Weick et al. 1999, Reason 2000). Although these industries are far from healthcare, they share operational characteristics that are also relevant in healthcare settings, such as high-tempo, time pressure or emergency situations where the control of patients shifts to the staff members on the spot. This means that "High-reliability organizations are not immune to adverse events, but they have learned the knack of converting these occasional setbacks into enhanced resilience of the system" (Reason 2000).

Traditionally, the person approach to human error has been a dominant approach in healthcare (Reason 2000). It focuses on unsafe acts, errors and procedural violations of people on the frontline. In this approach, individual healthcare practitioners (e.g. physicians, nurses, pharmacists) are blamed for errors primarily due to human behaviors such as forgetfulness, inattention, poor motivation and competence, carelessness, negligence and recklessness. Errors are explained as moral issues, assuming that bad things happen to bad people, who have consciously chosen unsafe behavior. However, the majority of the unsafe acts are not intentional (Marx 1997). The management of errors with a person approach relies on reducing unwanted variability in human behavior and usually leads to programs that appeal to people's fear, writing another procedure, disciplinary measurements, and blame culture (Reason 2000). This approach easily ignores the circumstances where people work and can lead to similar, repeating errors, despite the people involved.

The basis of a systems approach is the premise that humans are fallible and errors, caused by omissions or commissions, are to be expected even in the best organizations with the best people (Reason 2000). Instead of seeing errors as causes of actions, they are consequences of systemic factors such as complex processes with unclear responsibilities. Because we cannot expect endlessly perfect human performance, the conditions under which humans work must be changed. When an error occurs, the focus should be on how and

why the defenses failed, not investigating who blundered. An effective error and risk management strategy relies on a blameless reporting culture and learning with analysis of errors and near misses (Reason 1997). This study applies the systems approach in the Theory of Human Error (Reason 2000).

Learning allows the prospective error and risk management with the development of process defenses, barriers and safeguards to prevent errors and risks (Reason 2000). Defenses can, for instance, be engineered (e.g. alarms, physical barriers, automatic shutdowns, check and double-check), rely on people and their competences and routine care processes (e.g. surgeons, anesthetists, pilots) or depend on procedures and administrative controls. However, these defensive layers also have weaknesses. Reason (2000) described this with the "Swiss Cheese" Model of System Accidents. Defenses are illustrated as slices of Swiss cheese with multiple holes, but, unlike the cheese, these holes are continually opening, shutting and shifting their location. The errors and near misses occur when the holes in many layers momentary line up and permit the passing of an error through different steps of the process. Kettunen (2007) has described a fatal medication error due to methotrexate overdose in a Finnish central hospital with the Reason's Swiss Cheese Model (Figure 1, Holmström 2017).

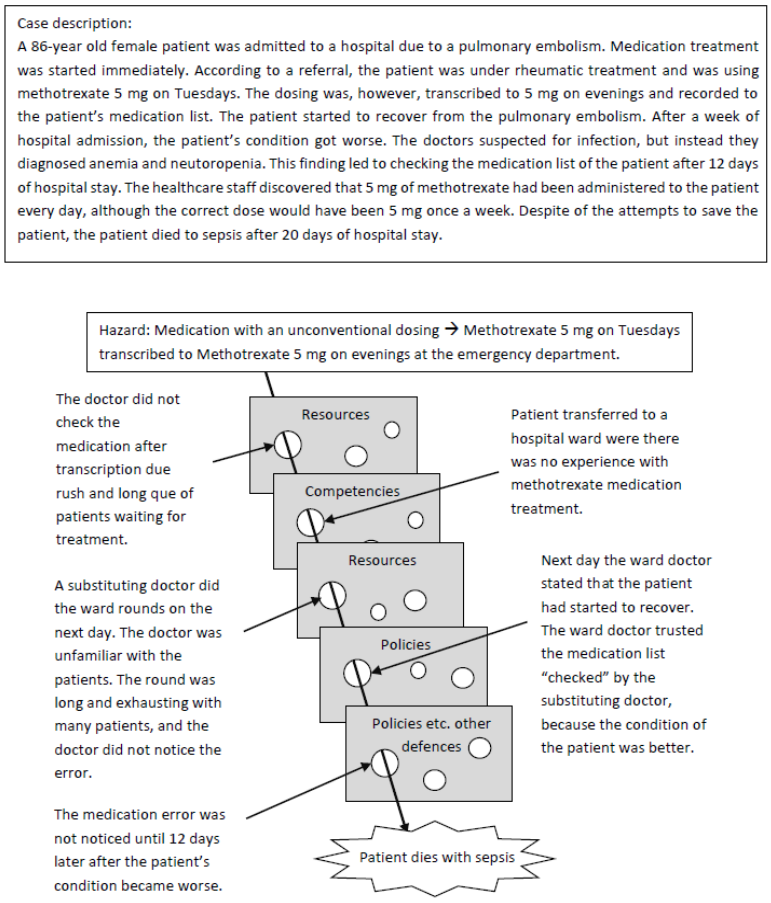

Figure 1. Application of Reason's Swiss cheese model (2000) to illustrate a fatal system error related to medication use in a Finnish central hospital (Holmström 2017, original case description Kettunen 2007).

2.2 MEDICATION SAFETY AS A PART OF PATIENT SAFETY

Patient safety incidents (also called adverse events or medical errors) are estimated to be the third leading cause of deaths after heart diseases and cancer in the United States (Makary and Daniel 2016) and the fourteenth leading cause of global disease burden comparable to tuberculosis and malaria (WHO 2018). Patient safety is defined as "a freedom from accidental injuries during the course of medical care, activities to avoid, prevent, or correct adverse outcomes which may result from the delivery of healthcare" (Kohn et al. 2000, CoE 2005, WHO 2009). Patient safety consists of the identification, analysis and management of patient-related risks and incidents, in order to make patient care safer and minimize harm to patients (Aspden et al. 2004, National Patient Safety Agency, NPSA 2004, CoE 2005). When the Institute of Medicine (IOM) published the report "To Err Is Human: Building a Safer Health System", it started an open discussion about safety concerns in healthcare and designing processes of care where patients are safe from accidental injury (Kohn et al. 2000). It is based on the systems approach of the Theory of Human Error (Reason 1990, Reason 2000). This started system-based patient and medication safety work and created a new research area. Kohn et al. (2000) stated that the complex problem required multifaceted responses and recommended:

1) **Leadership and knowledge:** a national focal point to set the national goals for patient safety and develop knowledge and understanding of errors with patient safety research.

2) **Identifying and learning from errors:** to create an environment that encourages organizations to identify errors, evaluate causes and take actions to improve performance; and design and implement nationwide, mandatory and voluntary incident reporting systems.

3) **Setting performance standards and expectations for safety** for healthcare organizations through regulatory and related mechanism, such as licensing, certification and accreditation. Professional societies should establish a permanent committee dedicated to safety improvement. The Food and Drug Administration should increase attention towards, in particular, the safe use of lookalike and soundalike drug names, packaging and labelling.

4) **Implementing safety systems in healthcare organizations.** Patient safety programs with defined executive responsibility and proven medication safety practices.

Medication safety is part of patient safety and is defined as "a freedom from accidental injury during the course of medication use; activities to avoid, prevent, or correct adverse drug events which may result from the use of medications" (CoE 2005, WHO 2009). Unsafe medication practices and medication errors are the single most important preventable factor jeopardizing patient safety (WHO 2017). Approximately 6% of hospitalized patients experience an ADE during their hospital stay (Krähenbühl-Melcher et al. 2007). About 25% of medication-related injuries are estimated to be preventable (Aspden et al. 2007). Globally, the costs associated with medication errors are 42 billion USD annually (WHO 2017).

Following the IOM report (Koht et al. 2000), the Council of Europe (CoE) established expert groups in order to assess the situation in Europe and to set recommendations for improving patient and medication safety (CoE 2006a). Moreover, the CoE stated that medication errors are poorly managed in Europe and suggested European healthcare organizations to (CoE 2006a):

1) Take steps to establish medication error reporting systems;
2) Establish and use a common terminology concerning harm to patients caused by medications;
3) Create a culture of safety; and
4) Set up a national recognized focal point for safe medication practices.

A multidisciplinary approach to developing medication safety, pharmacists conducting medication reviews to detect drug-related problems, electronic prescribing systems with clinical decision support and up-to-date medicine information and therapeutic guidelines were emphasized (CoE 2006b). In addition, the European legislative framework related to safe labelling and packaging was addressed.

Some years later, in 2008, the European Union (EU) launched the EUNetPaS (European Union Network for Patient Safety) project to promote patient safety culture, develop a core program for patient safety for higher education across Europe, implement reporting systems and improve medication safety in hospitals by identifying good practices, translating them into tools and testing these tools in selected hospitals (EUNetPaS 2008). In 2012, this was followed by the European Union Network for Patient Safety and Quality of Care (PaSQ) Joint Action, which was co-founded and supported by the European Commission within the Public Health Programme, in order to support the implementation of the Council Recommendation on Patient Safety especially as related to medication reconciliation procedures (PaSQ 2012).

Healthcare quality and patient safety issues became a key priority at an EU level, when the Directive on Cross Border HealthCare (Directive 2011/24/EU) entitling patients to seek treatment abroad, was enacted in 2011. For this purpose, the European Commission set an Expert Panel on effective ways of investing in Health (EXPH), in order to provide an opinion on a possible future EU agenda on quality of healthcare (EXPH 2014). The EXPH identified

indicators and proposed actions for healthcare quality and patient safety for EU Member States (EXPH 2014). The establishment of the coordination of all EU initiatives in healthcare quality, comparison across health policies and implementation of the Health Technology Assessment (HTA) network were proposed (EXPH 2014). Additionally, EXPH recognized the importance of information technology development (e.g. blame-free reporting and learning systems, implementation of telecare and coordinated use of big data), need for allocating more funding to health system research and promoting a Europe-wide health education program in new roles of patients and healthcare professionals (EXPH 2014).

At a global level, the WHO has taken a coordinating role in patient safety development, for instance with global patient safety challenges to gain commitment to reduce healthcare infections through improved hand hygiene ("Clean Care is Safer Care" in 2004) and risks associated with surgery ("Safe Surgery Saves Lives" in 2008) and more recently with the third Challenge on medication safety "Medication without harm" (WHO 2017). The aim of the third challenge is to reduce the global level of severe avoidable harm related to medication by 50% over 5 years. The key areas and suggested actions of the challenge are presented in detailed in Figure 2.

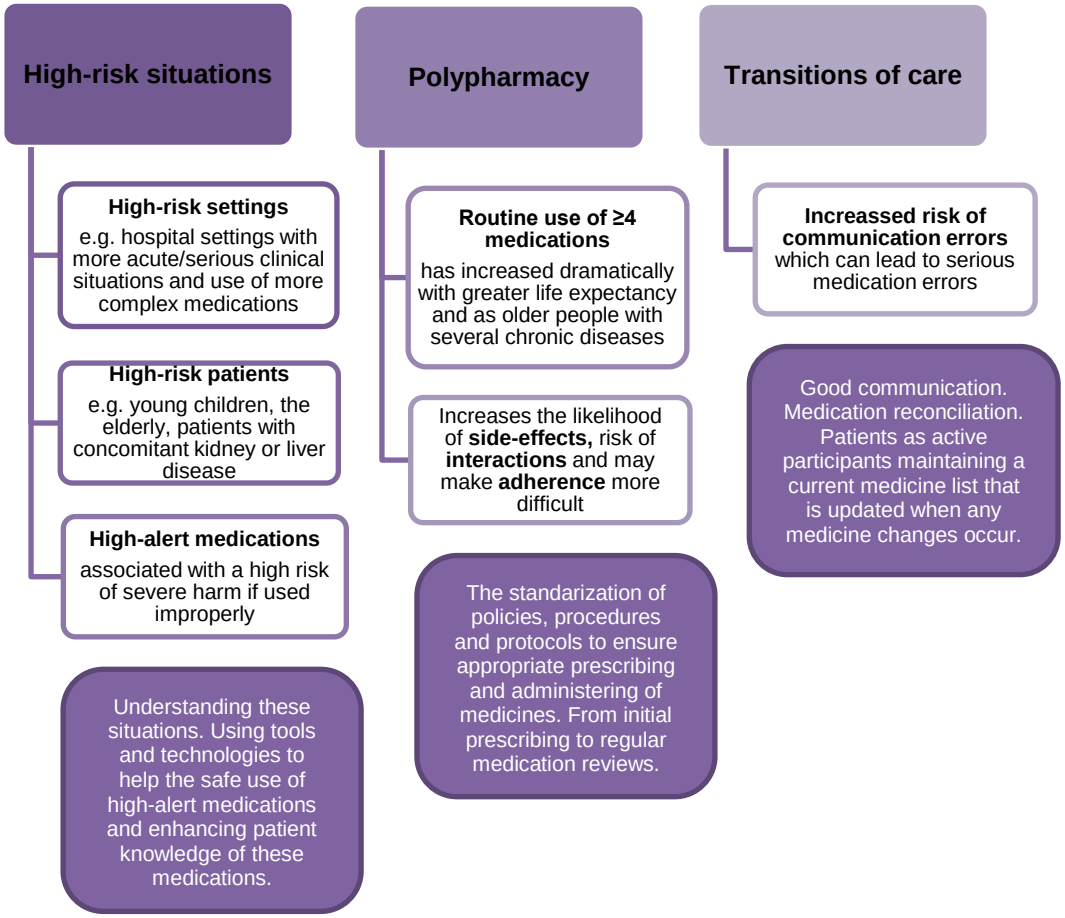

Figure 2. Key areas in WHO Global Patient Safety Challenge on Medication Safety (WHO 2017).

2.2.1 ASSOCIATION BETWEEN MEDICATION ERRORS, ADVERSE DRUG EVENTS AND ADVERSE DRUG REACTIONS

Safe pharmacotherapy can be divided into drug safety and medication safety (Figure 3, Stakes and ROHTO 2006, Turner 2009). Drug safety is related to pharmaceutical products, and is usually concentrated on adverse drug reactions (ADRs) (ROHTO 2006, Turner 2009). An ADR means a response to a medicinal product which is noxious and unintended and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease or the restoration, correction or modification of physiological function (CoE 2005). Medication safety refers to managing medication errors (MEs), which are unintended mistakes in the medication-use process caused by omissions or commissions (Figure 3, Stakes and ROHTO 2006, Turner 2009). An ME is "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer" (NCC MERP 1998, CoE 2005). Such events may be related to professional practice, healthcare products, procedure and systems, including prescribing, order communication, product labelling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use. A near miss (called also a close call or a potential adverse drug event), is a serious medication error that has the potential to cause an ADE, but did not, either by luck or because it was intercepted and corrected (CoE 2005).

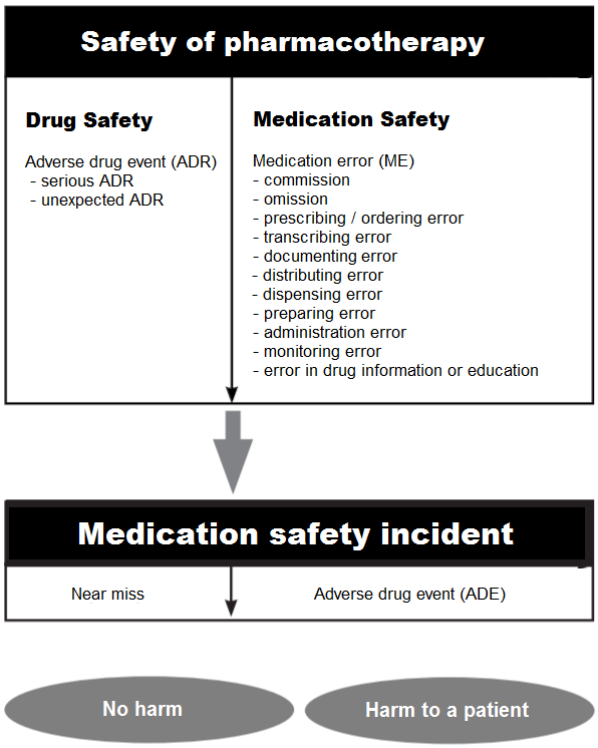

Figure 3. Terms related to the safe pharmacotherapy (adapted from Stakes and Rohto 2006).

An ADE is defined as “any injury occurring during the patient’s drug therapy resulting from either appropriate care, or from unsuitable or suboptimal care” (CoE 2005). The definition includes ADRs and MEs. The relationship between ADEs, MEs and ADRs is described in Figure 4 (Nebeker et al. 2004). Even though this relationship was described in 2004, it is still valid.

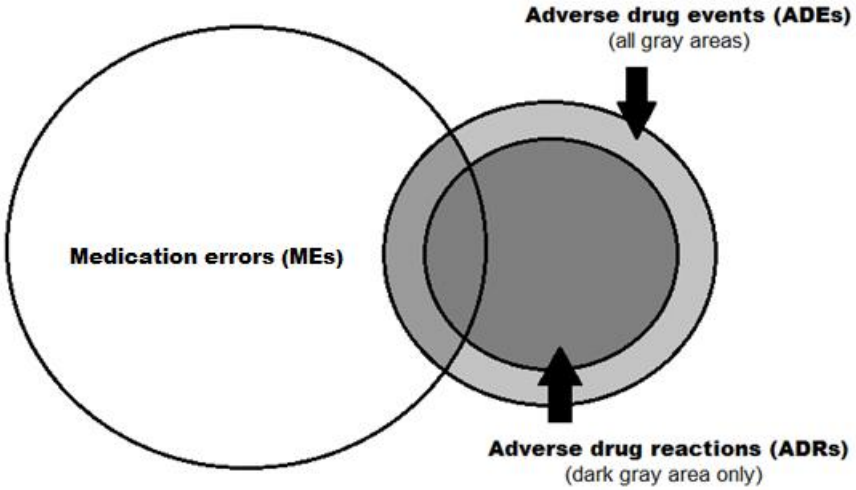

Figure 4. Relationship of MEs, ADEs and adverse drug reactions as presented in 2004 (Nebeker et al. 2004). The gray areas represent injuries caused by drug use (ADEs). The dark gray area represents harm caused by a drug (adverse drug reactions). Medication errors are significantly more common than ADEs, but they result in harm less than 1% of the time (Bates et al. 1995a). Conversely, about one quarter of ADEs are due to medication errors (Bates et al. 1995b).

ADR reporting and drug safety monitoring (pharmacovigilance) have evolved internationally during the past 80 years (Olsson 1998, Scurti et al. 2012). However, advancements have typically been drug- and molecule-oriented. The real-life medication-use process, including human error, has not received any great degree of attention (Reason 2000, Scurti et al. 2012). The first national medication error reporting (MER) system was established in the United States in 1987 (Cheng et al. 2011, Holmström 2017). During the early 2000s, the IOM strongly suggested reporting systems as a part of a comprehensive strategy to understand errors and improve patient safety with preventive actions (Kohn et al. 2000). MER systems were also launched in many other countries at that time (Cheng et al. 2011).

In the EU Directive 2010/84EU1, which came into force in July 2012, the term ‘adverse drug reaction’ was redefined as ‘a response to a medicinal product that is noxious and unintended, resulting not only from the authorized use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse, off-label use, and abuse of the medicinal product’. International efforts have been made to expand the role and scope of national pharmacovigilance centers to also include MEs (The Erice Manifesto 2007, Bencheikh and Benabdallah 2009, Pal et al. 2015, Cousins et al. 2015).

2.2.2 HIGH-ALERT MEDICATIONS AND OTHER PERSPECTIVES ON HIGH-RISK MEDICATIONS

The identification and management of high-alert medications is one of the key areas in the WHO Global Patient Safety Challenge on medication safety (WHO 2017). Moreover, Joint Commission International (JCI) requires hospitals to develop and implement a process to improve the safety of high-alert medications in their accreditation standards (JCI 2016). Improving the safety of high-alert medications is one of the six international patient safety goals which JCI has determined to be the most challenging areas of patient safety (JCI 2016).

The Institute for Safe Medication Practices (ISMP) defines high-alert medications as "Drugs that bear a heightened risk of causing significant patient harm when used in error (wrong drug, wrong dose, wrong route, etc.). Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients." The ISMP is a non-profit organization devoted to medication error prevention located in Philadelphia, the United States (ISMP 2018). The ISMP has published lists of high-alert medications to acute care, community and ambulatory care and long-term care settings (Tables 1-3, ISMP 2011, ISMP 2014, ISMP 2016). These lists are based on medication error reports submitted to the ISMP national Medication Error Reporting Program, reports of harmful errors in the literature, studies that identify the drugs most often involved harmful errors, and input from practitioners and safety experts.

Defining high-alert medications in different settings and organizations is important, because the patient profiles and medications used in different settings are not similar. Furthermore, pharmacotherapy education and skills of healthcare practitioners usually differ between, for instance, tertiary care hospitals and nursing home settings. In a university hospital, the list for acute care settings is the most crucial, but staff should also be familiar with the high-alert medications for ambulatory and long-term care settings. The ISMP suggests the use of these lists to determine which medications require special safeguards to reduce the risk of errors (ISMP 2014). These might include improving access to information about these drugs, limiting access to high-alert medications, using auxiliary labels and automated alerts, standardizing the ordering, storage, preparation, and administration of these products, and employing redundancies such as automated or independent double-checks when necessary. In addition, the ISMP notes that independent double-checks are not always the optimal error-reduction strategy and may not be practical for all of the medications on the list (ISMP 2014).

Table 1. High-alert medications for acute care settings (ISMP 2014).

Classes/categories of medications	Specific medications
adrenergic agonists, IV (e.g., adrenaline (am. epinephrine), phenylephrine, noradrenalin (am. norepinephrine)	adrenaline (am. epinephrine), subcutaneous
adrenergic antagonists, IV (e.g., propranolol, metoprolol, labetalol)	epoprostenol (Flolan), IV
anesthetic agents, general, inhaled and IV (e.g., propofol, ketamine)	insulin U-500 (special emphasis)
antiarrhythmics, IV (e.g., lidocaine, amiodarone)	magnesium sulfate injection
antithrombotic agents, including: • anticoagulants (e.g., warfarin, LMWH and unfractionated heparin) • Factor Xa inhibitors (e.g., fondaparinux, apixaban, rivaroxaban) • direct thrombin inhibitors (e.g., argatroban, bivalirudin, dabigatran etexilate) • thrombolytics (e.g., alteplase, reteplase, tenecteplase) • glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)	methotrexate, oral, nononcologic use
	opium tincture
	oxytocin, IV
	nitroprusside sodium for injection
cardioplegic solutions	
chemotherapeutic agents, parenteral and oral	
glucose (am. dextrose), hypertonic, 20% or greater	
dialysis solutions, peritoneal and hemodialysis	
epidural or intrathecal medications	
hypoglycemics, oral	
inotropic medications, IV (e.g., digoxin, milrinone)	
insulin, subcutaneous and IV	
liposomal forms of drugs (e.g., liposomal amphotericin B) and conventional counterparts (e.g., amphotericin B desoxycholate)	
moderate sedation agents, IV (e.g., dexmedetomidine, midazolam)	
moderate sedation agents, oral, for children (e.g., chloral hydrate)	
narcotics/opioids, IV, transdermal, oral (including liquid concentrates, immediate and sustained release formulations	
neuromuscular blocking agents (e.g., succinylcholine, rocuronium, vecuronium)	
parenteral nutrition preparations	
radiocontrast agents, IV	
sterile water for injection, inhalation, and irrigation (excluding pour bottles) in containers of 100 mL or more	
sodium chloride for injection, hypertonic, > 0.9% concentration	

Table 2. High-alert medications for community and ambulatory care settings (ISMP 2011).

Classes/categories of medications	Specific medications
antiretroviral agents (e.g., efavirenz, lamivuine, raltegravir, ritonavir, combination antiretroviral products)	carbamazepine
chemotherapeutic agents, oral (excluding hormonal agents) (e.g., cyclophosphamide, mercaptopurine, temozolomide)	chloral hydrate liquid, for sedation of children
hypoglycemic agents, oral	heparin, including unfractionated and low molecular weight heparin
immunosuppressant agents (e.g., azathioprine, cyclosporine, tacrolimus)	metformin
insulin, all formulations	methotrexate, non-oncologic use
opioids, all formulations	midazolam liquid, for sedation of children
pediatric liquid medications that require measurement	propylthiouracil
	warfarin

Table 3. High-alert medications for long-term care settings (ISMP 2016).

Classes/categories of medications	Specific medications
anticoagulants, parenteral and oral (including warfarin and newer agents)	digoxin, parenteral and oral
chemotherapeutic agents, parenteral and oral (excluding hormonal agents)	adrenaline (am. epinephrine), parenteral
hypoglycemics, oral (including combination products with another drug)	iron dextran, parenteral
insulins, all formulations and strengths (e.g., U-100, U-200, U-300, U-500)	methotrexate, oral, non-oncology use*
parenteral nutrition preparations	concentrated morphine solution, oral
opioids - parenteral, transdermal, and oral (including liquid concentrates, immediate- and sustained-release formulations, and combination products with another drug)	

Other countries than the US, such as the UK, Australia and Denmark have also published lists of high-risk medications (Table 4, Danish Medicines Agency, DMA, 2011, National Patient Safety Agency, NPSA, 2011, Clinical Excellence Commission, CEC 2012). The list of the NPSA's high-risk medications is principally based on Patient Safety Alerts and Rapid Response Alerts and the Reports of National Patient Safety Agency, which have arisen through analysis of patient safety incident reports and other safety information (NPSA 2011). The aim of these is to develop advice for the National Health Service that can help ensure the safety of patients. The Clinical Excellence Commission in Australia defines high-risk medications similar to ISMP and requires organizations to set the high-risk medicines register (a list) and to set standards/policies to specific high-risk medicines (CEC 2015). The Danish Medicines Agency's working group has determined high-risk medications as the "medicines most frequently involved in serious adverse drug events" either due the medicine's pharmacological property (e.g. narrow therapeutic index), errors in the medication process or inappropriate medication use by patients (DMA 2011). The Danish list is based on a literature review covering both the primary and the secondary sectors as well as by reviewing safety assessment score 3 adverse events from the Danish Patient Safety Database and published cases from the Danish National Agency for Patients' Rights and Complaints.

According to another systematic literature review, the TOP10 drugs causing fatal MEs were methotrexate, warfarin, opioids, digoxin, theophylline, anticoagulants other than warfarin, asetylsalicylic acid, NSAID, beta-blockers and antibiotics (Table 4, Saedder et al. 2014). The TOP10 drugs causing hospitalizations, prolonged hospitalizations, life-threatening conditions or disability due to MEs were methotrexate, theophylline, NSAID, opioids, digoxin, acetylsalicylic acid, diuretics, antiepileptics, beta-blockers and warfarin.

Table 4. Listed high-risk medications in the United Kingdom (NPSA 2011), Australia (CEC 2015), Denmark (DMA 2011) and in a systematic literature review (Saedder et al. 2014). ADEs = adverse drug events, MEs = medication errors.

United Kingdom (NPSA 2011)	**Denmark (DMA 2011)**	**Australia (CEC 2015)**	**Literature review (Saedder et al. 2014)**
• anticoagulants • insulin • diamorphine and morphine injections • lithium • methotrexate • midazolam injection • opioids (dosing) • injectable medicines • measurement and administration of liquid medicines • vaccine gold storage • omitted and delayed medications	<u>Medicine groups</u> most frequently involved in serious ADEs: • antibiotics (amoxicillin, ceftriaxone, ciprofloxacine, gentamicin, nevirapine, penicillin) • antidepressants (SSRI) • antipsychotics (haloperidol, quetiapine, zuclopenthixol) • antithrombotics and coagulation inhibitors (asetylisalicylic acid, clopidogrel, enoxaparin, phenprocoumon, tinzaparin, warfarin) • benzodiazepines (midazolam, triazolam) • cytostatics (carboplatin, daunorubicin, etoposide, 5-fluorouracil, methotrexate) • diuretics (furosemide, thiazide diuretics) • insulin • NSAIDs • opioids, strong (morphine, oxycodone)	<u>Policies:</u> • anticoagulants • hydromorphone • methotrexate (oral) • neuromuscular blocking agents • paracetamol • potassium (IV) • vincristine <u>A PINCH:</u> <u>High-risk medicine groups:</u> A: anti-infectives P: potassium and other electrolytes I: insulin N: narcotics (opioids and other sedatives C: chemotherapeutic agents H: heparin and other anticoagulants O: other unit level specific medications not mentioned above	<u>TOP10 drugs causing fatal MEs:</u> • methotrexate • warfarin • opioids • digoxin • theophylline • anticoagulants other than warfarin • asetylsalicylic acid • NSAIDs • beta-blockers • antibiotics <u>Top10 drugs causing severe MEs with severe harm (requiring hospitalizations):</u> • methotrexate • theophylline • NSAID • opioids • digoxin • acetylsalicylic acid • diuretics • antiepileptics • beta-blockers • warfarin

In addition to these approaches (medications causing severe harm when used in error, or medications related to ADEs and MEs, Tables 1-4), lookalike/soundalike (LASA) medication names and packages, drugs with narrow therapeutic index requiring monitoring (therapeutic monitoring or monitoring other laboratory results), new drugs and drugs that are seldom used, drugs to which patients are commonly allergic (e.g. penicillin) to or cause infection infusion reactions (e.g. biological drugs). Risk medications can also be categorized based on patient vulnerability: risk medications for newborn or pediatric patients (Table 5), older patients, patients with polypharmacy and/or multiple comorbidities e.g. renal or hepar impairment and pregnant or breast-feeding patients (Kaushal et al. 2001, Hoffman and Proulx 2003, Krähenbühl-Melcher et al. 2007, Poole and Carleton 2008, ISMP 2010, Maaskant et al. 2013, WHO 2017). Other perspectives are hazardous drugs which need special handling and commonly abused drugs; however, the first mentioned is related to worker safety instead of patient safety and the latter is not related to human errors.

Table 5. High-alert medications for inpatient pediatric patients based on literature search and compiled with an international Delphi expert panel (Maaskant et al 2013).

Classes/categories of medications	**Specific medications**
chemotherapeutic agents	amiodarone
	digoxin
immunosupressive medications	dopamine
	adrenaline (am. epinephrine)
lipid/total parenteral nutrition solutions	fentanyl
	gentamycin
opioids	heparine
	insulin
	morphine
	noradrenalin (am. norepinephrine)
	phenytoin
	potassium
	propofol
	tacrolimus

2.2.3 POLYPHARMACY AND INAPPROPRIATE PRESCRIBING IN OLDER ADULTS

Older patients face ADEs and medication errors more often than younger adults (Krähenbühl-Melcher et al. 2007, Bourgeous et al. 2010). This is considered a serious and growing public health problem (Scott et al 2010, Hamilton et al. 2011, WHO 2017). Age-related physiological, pharmacokinetic and pharmacodynamic changes make older patients more vulnerable to the effects of the drugs (ElDesoky 2007). Older patients usually have multimorbidities (co-existence of two or more chronic health conditions) which often leads to polypharmacy (Salive 2013), even when the treatment is appropriate and in line with the care guidelines.

Haijjar et al. (2005) found out that 41% of hospitalized older patients in US were using at least five to eight and 37% were using nine or more medications at discharge. In an Italian study, polypharmacy was even more common: 52% of patients were on five or more medications on admission and at discharge this rate increased to 67% (Nobili et al. 2011). Increasingly problematic polypharmacy has also been identified in Finnish studies (Jyrkkä et al. 2006, Hosia-Randell et al. 2008, Jyrkkä et al. 2009, Leikola et al. 2009, Ahonen 2011). Hanlon et al. (2005) found out that 59% of hospitalized older patients took one or more unnecessary prescribed drugs at admission. In addition, underuse of beneficial treatment and problems with adherence are common with the older patients (Ruths et al. 2003, van Dulmen et al. 2007).

A significant number of ADEs and ADRs leading to hospitalization among older patients are considered preventable (Beijer and de Blaey 2002, Winterstein et al. 2002). The WHO's Challenge on Medication Safety identifies older patients with polypharmacy as a high-risk group (Figure 2, WHO 2017). Instead of only focusing on a high number of used drugs, the focus should be on harmful, ineffective and inappropriate drugs. To manage adverse drug reactions ADEs and inappropriate polypharmacy in older patients, regular mediation reviews (WHO 2017) and other tools such as explicit and implicit criteria of potentially inappropriate medications have been established (Dimitrow et al. 2011). Of the potentially inappropriate medications criteria, the Beers Criteria by the American Geriatrics Society (2015) and STOPP/START criteria (O'Mahony et al. 2015) are widely used. These should be used to identify medications that should be avoided or assessed with older patients (ISMP 2016).

2.3 PATIENT AND MEDICATION SAFETY WORK IN FINLAND

2.3.1 EVOLUTION OF THE SYSTEM-BASED PATIENT SAFETY WORK

Establishing the National Patient Safety Network (2005) and the Patient Safety Steering Group (2006) by the Ministry of Social Affairs and Health have been important for initiating patient safety work in Finland (Figure 5, MSAH 2009, Airaksinen et al. 2012, Holmström 2017). The key actions of the Patient Safety Steering Group were to establish the first national patient safety strategy and guidelines for reporting adverse events in healthcare (Holmström 2017). The aims of the Finnish Patient Safety Strategy 2009-2013 were to embed the systemic patient safety culture and work (leadership and responsibilities) in the structures of the healthcare system (MSAH 2009).

The Finnish Patient Safety Strategy was used as a base for the Patient Safety Act and Decree, enacted in 2011 to support implementation of the new Health Care Act (1326/2010, 8 §, Figure 5, Airaksinen et al. 2012). The Patient Safety Act required all Finnish healthcare organizations (hospitals and primary healthcare centers) to develop a patient safety plan, including the system, processes, resources and persons in charge for patient safety within the organization (Airaksinen et al. 2012). The influences of this Act have been powerful and have led to nominating patient safety coordinators and steering groups and the implementation of voluntary, electronic patient safety incident reporting system (HaiPro) in many healthcare organizations (Figure 5, Ruuhilehto et al. 2011, Airaksinen et al. 2012). Establishing a patient safety incident reporting system and culture can be seen as a crucial milestone in the early phase of patient safety work in Finland.

The Ministry of Social Affairs and Health mandated the National Institute for Health and Welfare (THL) to coordinated the implementation of the patient safety strategy and initiatives in Finland and, for that purpose, a 4-year patient safety program was launched in 2011 (Figure 5, THL 2011, Airaksinen et al. 2012). Moreover, the Finnish Society for Patient Safety was established in 2010 (Figure 5, Finnish Society for Patient Safety 2011, Holmström et al. 2015). The society has been actively involved in national patient and medication safety promotion: the latest key action was the involvement in updating the Finnish Patient Safety Strategy for 2017-2021 in collaboration with the Ministry of Social Affairs and Health (Holmström 2017, STM 2017). The strategy, Patient and Customer Safety Program (2017-2021), was launched in 2017 and it also covers social care settings, for instance elderly care homes (Figure 5, MSAH 2017a). Its key strategic areas are largely the same as in the previous patient safety strategy (the work is to be continued).

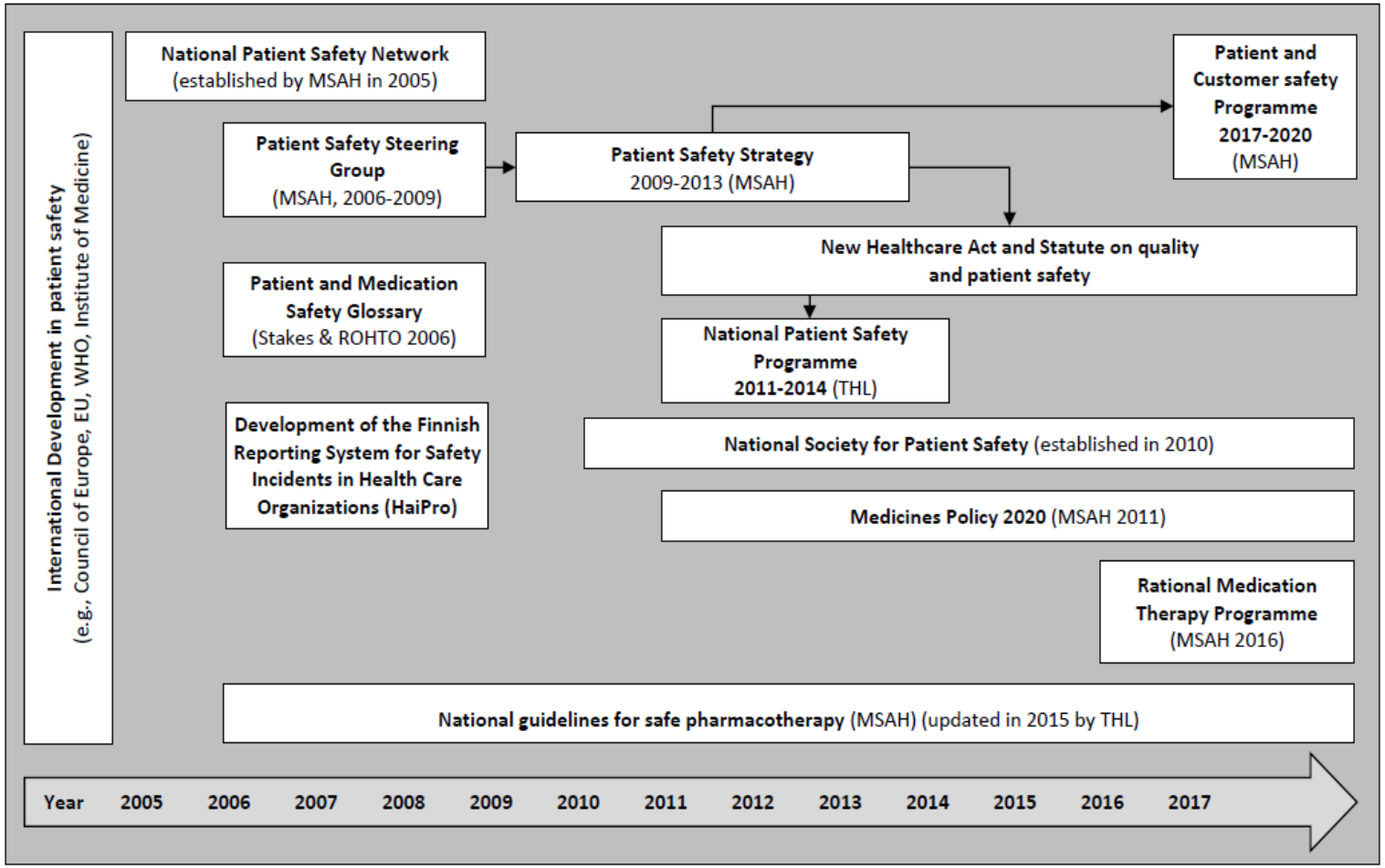

Figure 5. Governmental and other national actions to initiate system-based patient and medication safety work in Finland (Holmström 2017). MSAH = Ministry of Social Affairs and Health; THL= National Institute for Health and Welfare; ROHTO = (former) National Centre for Pharmacotherapy Development; Stakes = (former) National Research and Development Centre for Welfare and Health

2.3.2 MEDICATION SAFETY INITIATIVES

Early initiatives

Finland was actively involved in the CoE's expert groups on patient and medication safety in 2003-2006 (see Chapter 2.2., CoE 2006a+b, Airaksinen et al. 2012). The recommendations of the medication safety expert group inspired the National Centre for Pharmacotherapy Development (ROHTO) to establish a multidisciplinary working group on medication safety in 2004, aiming to create a Finnish glossary of terms related to patient and medication safety with systems approach (Figure 5, STAKES and ROHTO 2006).

In 2005, the Ministry of Social Affairs and Health had a working group developing a guide of safe medication practices (Safe Pharmacotherapy) in healthcare units (Figure 5, MSAH 2005). A key element was instructions to create unit-based medication safety plans, where the used medications, medication management process, competence and responsibilities of healthcare providers were described. Safe Pharmacotherapy Guide emphasized learning from MEs with a systems approach and root cause analysis (MSAH 2005, Airaksinen et al. 2012). One of the most noticeable impacts on the practice of this guide was the development of tools to ensure nurses' competence in pharmacotherapy, e.g. LOVe – eLearning material (Saano et al. 2014, Awanic 2017). The Safe Pharmacotherapy Guide was updated in 2015 (Inkinen et al. 2016). The main aim was still to guide the development of the medication safety plans, but the identification of high-alert medications was now also recommended. Furthermore, the importance of medication safety audits, updated medication charts and the need for medication reconciliation and reviews were highlighted (Inkinen et al. 2016). Medication safety audits were launched by adopting the US ISMP's Medication Safety Self-Assessment tool for hospitals (Celikkayalar 2008, Celikkayalar et al. 2016). The ISMP tool was validated by Finnish healthcare for assessing and auditing medication-use processes. The content of the tool was structured to support the development of medication safety plans (Celikkayalar 2008, Celikkayalar et al. 2016).

The current national Medicines Policy by 2020 was developed and published in 2011 (Figure 5, MSAH 2011). Medication safety was one future objective and the other aims set for medication safety by 2020 are to:

1) Develop the collaboration of surveillance, monitoring and steering of drug and medication safety;
2) Exploit register-based data to identify high-alert medications;
3) Enhance the quality of medicines management with clinical pharmacology services, hospital clinical pharmacy services, medicines information and unit-based medication safety plans; and
4) Create guidelines of the content, need and roles for each healthcare professional for comprehensive medication reviews.

Most recent initiatives

The Finnish government is currently preparing a major healthcare reform, which is planned to take place in 2020 (Finnish Government 2018, Kangas and Kalliomaa-Puha 2018). For this purpose, the Ministry of Social Affairs and Health appointed a steering group in 2016-2017 to draw up a Rational Pharmacotherapy Action Plan (Figure 5, MSAH 2018a). From medication safety perspective, the aim is to enhance medication management by the year 2022 (MSAH 2018a) with the following actions:

1) Establish a patient-specific electronic medication chart to the national patient data repository (Kanta);
2) Document patient-specific pharmacotherapy plans as a part of their care treatment plans;
3) Ensure accurate medication charts by medication reconciliations in multiprofessional collaboration in all transitions of care;
4) Regularly review patient medications multiprofessionally and identify the high-risk patient groups needing medication reviews most;
5) Ensure the knowledge and skills of the healthcare professionals to provide interactive medicine information to encourage patients to be active partners in their medication use process; and
6) Ensure continuous (closed-loop) care pathways that involve medicine use in the transitions of care between different health and social care organizations by coordinating and instructing the medication use process nationally and regionally.

To complement the Rational Pharmacotherapy Action Plan, the Foundation for Municipal Development published a research-based review on major medication safety concerns in Finland and suggestions for managing them in the ongoing healthcare reform (Hakoinen et al. 2017). The suggested solutions are:

1) Leadership, management, and coordination of medication safety;
2) Establishment of a national focal point for promoting and coordinating rational medication therapy and medication safety;
3) Operation culture, healthcare facilities and information technology systems should be supporting safe and rational medication therapy (suggested methods: learning from errors, proactive risk management, plan-do-check-act cycle);
4) Ensuring the comprehensive management of patients' medication therapy with clear responsibilities, multiprofessional collaboration and patient involvement;
5) Ensuring competence related to medication therapies and systems approach in medication safety; and
6) Systematic increasing and utilization of medication safety research.

2.3.3 MEDICATION SAFETY RESEARCH IN FINLAND

Patient and medication safety form a new research area that started to evolve as a response to the first reports raising concerns regarding the safety of health systems (Kohn et al. 2000, Aspden et al. 2004). During the last few decades, this research area has been rapidly growing. Research has been urgently needed to provide a more detailed picture of patient and medication safety risks in health systems to assess effectiveness of interventions intended to prevent risks and errors.

Concerning drug therapies, drug safety and pharmacovigilance research have a long history, both internationally as well as in Finland (Palonen et al. 2008, Kalliokoski 2012, Neuvonen 2013, Karonen 2013, Palva 2013, Karonen 2014, Karonen and Sommarberg 2016, Inacio 2018). Reporting and monitoring of adverse drug reactions started in Finland in 1966, i.e., around the same time as in many other European countries and in the US after the thalidomide disaster (Palva 2013, Inacio 2018). Signal detection of adverse drug reactions and related research has succeeded in identifying many medicines with severe ADRs, e.g. in Finland, approximately 20 drugs have been withdrawn from the Finnish market during the 2000s (Nurminen 2011). These ADRs were typically related to cardiovascular system (e.g. prolonged QT-time) or liver function. Additionally, pharmaceutical injury insurance came into force in Finland in 1994 (Ikkala 1996). Between the years 1990-2003, the most common drugs which caused compensated patient injuries were antimicrobiologicals for systemic use (Gylling et al. 2002, Palonen et al. 2008). Furthermore, the Finnish research related to clinical pharmacology (e.g. drug interactions and pharmacogenomics) has been remarkable (Neuvonen 2012, Neuvonen 2017).

Other early research in Finland on drug-related risks studied drug-related deaths in Helsinki University Central Hospital in 2000 (Juntti-Patinen et al. 2002). At that time, 5% of all deaths (n=75/1,511) were found to be certainly or probably drug-related. The most common adverse reactions leading to death were neutropenia caused by antineoplastic agents and gastrointestinal or intracranial hemorrhage due to anticoagulants or nonsteroidal anti-inflammatory drugs (NSAIDs). A follow-up study in 2012, showed that the incidence of fatal ADRs was lower: 3% of all deaths (n=52/1,708, Lapatto-Reiniluoto et al. 2015). Cytostatics and antithrombotics were still the leading causes of fatal ADRs, but NSAIDs and glucocorticoids caused fatal ADRs less often than in 2000.

Among the first systems-based patient and medication safety studies in Finland was by Mustajoki (2005). He piloted paper-based patient safety incident reporting in Peijas HUS. The majority (61%, n=129/210) of the reported incidents were related to medications. Results from the first larger-scale study on Finnish HaiPro data were similar: majority (51%,

n=32,706/64,405) of the reported patient safety incidents over 2007-2009 were related to medications (Ruuhilehto et al. 2011).

The first study focusing on medication errors reported to the electronic Reporting System for Safety Incident in HealthCare Organizations (HaiPro), was conducted in 2012 (Erkkilä 2012, Holmström 2017). The data consisted of patient safety incidents related to medication errors and near misses reported to the HaiPro system in Finland during 2007-2009 (n=32,592). Almost half of the reported MEs reached patients (51%) and the remainder (49%) were near misses. The most reported ME types were dispensing errors (33%), administration errors (25%) and documenting errors (17%). The following year Koskinen (2013) studied medication errors in cancer therapy in a university hospital. In total, 176 incident reports were analyzed relating to the use of anticancer drugs and supportive therapies. The most common medication errors were administration (27%), prescribing (11%), and ordering (10%). These medication errors were typically omission errors. Safety barriers e.g. double-checking prior to administration were in use, but they were not always fully effective and the electronic health record system lacked safety features. Holmström (2017) also assessed quality of HaiPro data for research purposes in terms of inter-rater reliability of categorization of information from ME reports. Erkkilä (2012), Koskinen (2013) and Holmström (2017) found out that the classification of medication errors was not always correct, which affected the quality of ME data.

In addition, Härkänen et al. have studied medication administration errors in another university hospital using HaiPro's medication safety incident reports, chart reviews and a global trigger tool (GTT) method and an observational method (Härkänen 2014, Härkänen et al. 2016). The observational method revealed fewer, but more severe, medication errors than medication safety incident reports (HaiPro) and GTT method. Observed errors were most likely related to an incorrect administration technique, whereas patient safety incident reports and GTT primarily revealed wrong doses

In addition to medication error reports in the HaiPro system, the documentation gathered by the Finnish authorities has been used to investigate medication errors (Lindén-Lahti et al. 2009, Pitkä 2009, Eronen 2016). Lindén-Lahti et al. (2009) studied serious medication errors (n=67) judged by the National Supervisory Authority for Welfare and Health (Valvira) between years 2000-2004. That study found out that patients with older age and polypharmacy were more often suffering the effects of medication errors. The most common error types were wrong procedure or course of action (in 40% of cases), wrong dose (31%) and wrong drug (28%). Errors were related to commonly used medications, and the most commonly involved high-alert medications were opioids, oral hypoglycemic agents, methotrexate, warfarin and heparin. Most of these errors (87%) were considered preventable.

Pitkä (2009) studied compensated medication errors in the data of the Patient Insurance Centre in 2005-2007. The data consisted of 227 cases which included 79 different drugs. Most of the medication errors were related to antithrombotic agents (20%), antibacterials for systemic use (15%) and cardiovascular drugs (11%). High-alert medications were related to 31% of the errors. The most common error types were omission of medication (21%), wrong dose (20%), wrong medicine (10%) and omission of contra-indication (9%). All of the errors were considered preventable. Eronen (2016) conducted a follow-up study from the compensated medication errors in 2013-2014 and the data consisted of 205 cases with 250 different drugs. Again, antithrombotic agents (19%) and antibacterials for systemic use (11%) were the most common medication groups involved. High-alert medications were involved in 37% of the cases.

HaiPro data and analysis of authority documentation of medication errors in Valvira and Patient Insurance Center have laid the foundation for other medication safety research in Finland. Medication safety research has grown to a large research area in Finland that has, remarkably, contributed to the recent development of medication management processes, prospective medication risk management, competence development and policy making (Hakoinen et al. 2017, MSAH 2018a, MSAH 2018d). Within medication safety research, the safety of pharmacotherapy of older adults has become a major topic as the safety risks are cumulating to this growing population segment (see Chapter 2.6.1. Jyrkkä et al. 2006, Kivelä and Räihä 2007, Hosia-Randell et al. 2008, Jyrkkä et al. 2009, Leikola et al. 2009, Ahonen 2011, Leikola 2012, Dimitrow 2016).

The recent Rational Pharmacotherapy Action Plan by the Ministry of Social Affairs and Health (2018d) aims that, by 2020, research on and development of rational pharmacotherapy are a part of the health and social services system, research data is diversely utilized in steering the activities in the health and social services system and in making decisions on medicines policy and research and allocation of resources to the research areas presented in the research strategy are strong. The research strategy prioritizes the following areas of research: 1) Structures and operational preconditions promoting rational pharmacotherapy; 2) Processes in the implementation of pharmacotherapy to promote medication safety in different operational environments; and 3) Use of medicines and on the effectiveness and economy of medically assisted treatment (MSAH 2018d). These research priorities in the Rational Pharmacotherapy Action Plan also demonstrate the continuous need for medication safety research to guide development of structures and processes of medication management systems. It also demonstrates the multi-faceted nature of medication safety research with evolving methodologies.

2.4 MEDICATION MANAGEMENT AND MEDICATION SAFETY WORK IN HELSINKI UNIVERSITY HOSPITAL

In Finland, municipalities are responsible for organizing primary healthcare services, which are mainly provided by municipal health centers (Health Care Act 2011). The secondary special healthcare is organized by central hospitals, each of them located in their own hospital districts (n=21) owned by federations of municipalities (including Åland). For special tertiary healthcare, Finland is divided into five areas of responsibility, each with a university hospital. Private healthcare services complete the public health services. Helsinki University Hospital (HUS) provides tertiary and secondary care in 23 hospitals with approximately 3,000 hospital beds, serving a regional population of 1.6 million in Southern Finland.

According to Finnish legislation, medicines management of a hospital district should be provided by a hospital pharmacy (Medicines Act 395/1987, Rule of the Finnish Medical Agency, Fimea 6/2012). The medication management process in HUS is organized with central hospital pharmacy (HUS Pharmacy), which creates formularies, purchases, tenders, stores, compounds, prepares and delivers medicines and provides clinical pharmacy services to the HUS' health care units. Each hospital care unit has own medication storage (medication room), where medications are ordered and delivered from HUS Pharmacy. Medications are mainly stored in traditional medicine cabinets. First automated dispensing cabinets were taken into use in 2017, but integration to patient information system is not yet available. Orders (not regarded as prescriptions) from HUS Pharmacy to the care units' medication rooms are typically made by nurses and clinical pharmacists with electronic order system separate from patient information system. Phycisians must verify some orders e.g. opioids (Medicines Act 395/1987).

Prescribing is conducted by phycisians in an electronic patient information system, but there are several different patient information systems in use (e.g. different system in EDs, ICUs and hospitals wards). Paper-based prescribing systems are still in use in some limited units e.g. in operating and recovery rooms In the care units, medications are dispensed and prepared from multidose packages to patient-specific doses by nurses or clinical pharmacists. Patient-specific, ready-to-use or unit-doses prepared by HUS Pharmacy are only available for cytotoxic doses and pediatric total parenteral nutrition solutions. Administration is documented only for selected medicines and situations manually; bar-code scanning is not yet in use. HUS started to use new patient information system Apotti (provided by Epic) in November 2018 in one hospital and the rest of the organization is planned to follow in October 2019. Apotti will replace all different patient information systems within the hospital. It will be taken into use also in the primary and social care units in the Helsinki and Uusimaa area. HUS is also preparing for accreditation of Joint Commission International, which is planned to take place in 2020.

In HUS, one of the first medication safety actions was a policy that guided care units to develop medication safety plans according to the Safe Pharmacotherapy guide (MSAH 2005). More systematic patient safety work began in 2011, when the Chief Patient Safety Officer and multiprofessional Patient Safety Steering group started their work. The first patient safety plan was developed according to the new Health Care Act (1326/2010) and National Patient Safety Strategy (MSAH 2009). HaiPro was piloted in 2007 and extended to the entire organization in 2011. From a medication safety perspective, the first actions in 2011 were to analyze annual medication error adverse drug reaction reports (requested from the Finnish Medical Agency). HUS Pharmacy was responsible of these actions, which have been performed every year in addition to more specific, multiprofessionally worked, medication safety goals during 2012-2017 (HUS 2012-2018):

- **2012:** Implementing a national eLearning material (LOVe) to ensure nurses' competence in pharmacotherapy and standardization of drug administration procedure. HUS Pharmacy was guided to develop instructions related to safe medication practices.
- **2013:** Medication errors were identified as a major patient safety risk by using the patient safety reports, needing regular follow-up and actions.
- **2014:** A policy for describing and standardizing medication documentation, dispensing and double-checking prior to administration.
- **2015-2016:** A policy and a checklist for a medication reconciliation procedure and encouraging patients to maintain a home medication chart.
- **2016-2017:** Establishing a medication safety officer's post. Identifying University Hospital's high-alert medications and developing instructions for the safe use of high-alert medications.
- **2017-2018:** HUS Pharmacy and medication safety officer start medication safety audits. A medication safety strategy and development plan will be designed.

Since 2013, HUS has established a research group studying patient and medication safety. Studies have been employed in HUS's patient safety work.

In addition, drug safety activities have a significantly longer history in HUS: the National Poison Information Centre started in 1961 and the Teratology Information Service in 1994 (Hoppu 2011, Malm 2015). The clinical pharmacology unit was founded in 1968 in the University of Helsinki as the first in Nordic countries. From the beginning the pharmacologists have served as consultants for all clinics in HUS. During the last 5 years, patient safety activities have become more important, and HUS now has its own consulting clinical pharmacology specialist. Furthermore, HUS Pharmacy has provided clinical pharmacy services since the early 1990s (see Chapter 2.7).

2.5 MEDICATION SAFETY AS A CORE GOAL OF CLINICAL PHARMACY AND PHARMACEUTICAL CARE

Traditional pharmaceutical sciences embrace the knowledge on synthesis, chemistry and preparation of drugs, while clinical pharmacy is more oriented to the analysis of population needs with regards to medicines, ways of administration, patterns of use, and drugs effects on the patients. Clinical pharmacy is an area of pharmacy concerned with the science and practice of rational and appropriate medication use (ACCP 2008, ESCP 2017). Clinical pharmacy is one part, but is not synonymous with hospital pharmacy, which also includes several other activities such as procurement, distribution and compounding of drugs (Franklin and van Mil 2005).

Clinical pharmacy was first mentioned in international literature in the 1950s, but it is seen to have been started in the US and in the UK in the 1960s (Miller 1981, Calvert 1999). When Hepler and Strand launched the idea of pharmaceutical care in 1990s, the perspective of clinical pharmacy turned even more from a drug to a patient:

According to the principles of pharmaceutical care, role of pharmacists in patient care is to ensure the quality of medication therapies, with emphasis on interprofessional collaborative care and patient interaction. (Hepler and Strand 1990, ASHP 1993 Cipolle et al. 2004, PCNE 2013, ACCP 2014).

A need for a patient-centered role of clinical pharmacists originally arose from complex new drug therapies, ADEs and preventable, medication-caused deaths (Hepler and Strand 1990, Kohn et al. 2000). Hepler and Strand (1990) stated that it is not sufficient to simply dispense the correct drug, and, when the traditional role of pharmacists preparing pharmaceuticals has been taken over by the pharmaceutical industry, pharmacists should redirect their energies to greater social good in co-operation with other healthcare professionals.

The new patient-centered role of clinical pharmacists in the US required new skills and revising the pharmacy education with a new philosophy (Figure 6, Hepler and Strand 1990, Koda-Kimble 2008). Medical terminology, clinical use of drugs in diseases and patients, therapeutic problem solving, literature evaluation, and communication skills were needed. The strong science-base was maintained but the weight of specific subjects was changed: more biological and medical science and therapeutics courses, less chemistry and basic science laboratory practice. In addition, clinical training in patient care was required. The highest-level pharmacy practice is possible with soundly educated pharmacists with a Doctor of Pharmacy, residency and certification programs in the US (Knoer et al. 2016). To ensure the quality and uniformity of clinical pharmacists' work, standards of practice have been set (see Chapter 2.5.2, ACCP 2014, EAHP 2014).

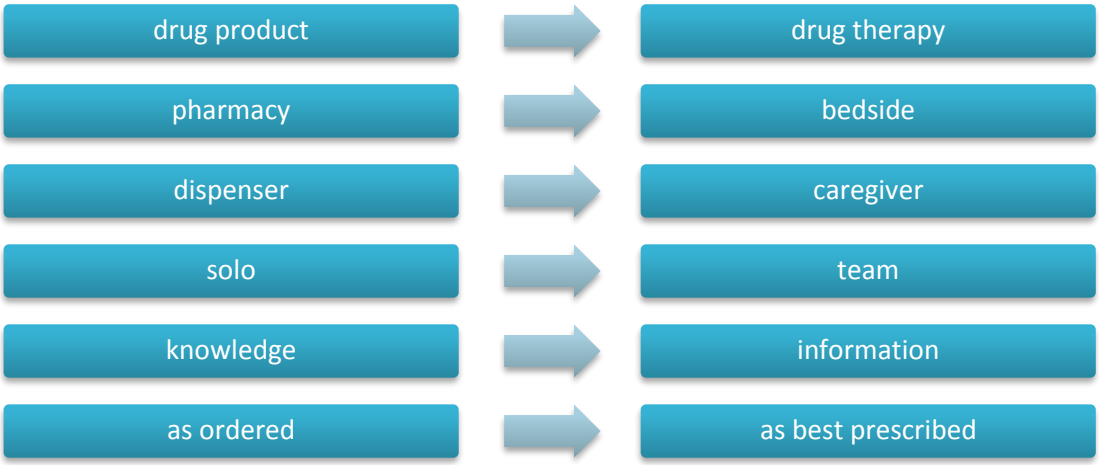

Figure 6. A shift in pharmacy practice philosophy of education after adopting the principles of pharmaceutical care (Hepler and Strand 1990, Koda-Kimble 2008, adapted).

2.5.1 DRUG-RELATED PROBLEMS

The aim of pharmaceutical care is to prevent drug-related morbidity, which is often preceded by a drug-related problem or medication-related problem (Strand et al. 1990, Hepler and Strand 1990). A drug-related problem (DRP) can be defined as a "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes." (PCNE 2017) and usually occurs due to inappropriate use of medicines (Figure 7).

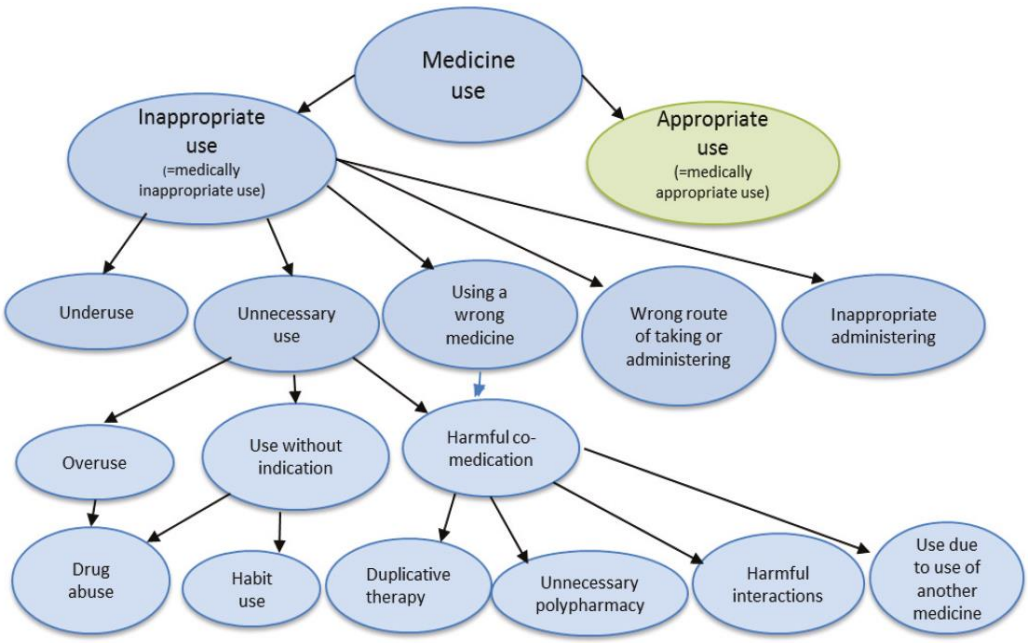

Figure 7. The concept "inappropriate use of medicines" comprises several different improper ways to use medicines, which potentially lead to DRPs (STAKES and ROHTO 2006, Dimitrow 2016)

Strand et al. (1990) created the first classification system for DRPs in the US with eight categories (Table 6). Later researchers in different countries have created several classification systems for DRPs and their causes (Basger et al. 2014). There has been no consensus on preference or structure of classification systems for different healthcare settings. Basger et al. (2015) chose seven DRP classification systems identified in a systematic literature review (Basger et al. 2014) and combined these into an aggregated system for classifying causes of drug-related problems (Basger et al. 2015). This hierarchical classification consists of nine cause-of-DRP categories (Table 6), 33 subcategories, and 58 sub-subcategories (Basger et al. 2015).

Table 6. Original DRP classification (Strand 1990) and aggregated system for classifying causes of DRPs (Basger et al. 2015)

Original DRP classification by Strand 1990 (United States)	Aggregated system for classifying causes of DRPs by Basger et al. 2015 (Australia)
1) untreated indication	1) drug selection
2) improper drug selection	2) drug form
3) subtherapeutic dosage	3) dose selection
4) overdosage	4) treatment duration
5) adverse drug reaction	5) drug use process
6) drug interactions	6) logistics
7) failure to receive drugs	7) monitoring
8) drug use without indication	8) unexpected or adverse drug reaction or no obvious cause of DRP
	9) other: a cause that cannot be classified into one of the eight categories

2.5.2 CLINICAL PHARMACY SERVICES

Especially in US and UK hospitals, clinical pharmacy services have evolved over the years and are integrated into interprofessional medical teams (Cobaugh et al. 2008, Child et al. 2011). Pharmacists optimize patient outcomes, for instance through providing recommendations for evidence-based medication selection on patient care rounds, offering drug information to other healthcare providers and patients, reviewing prescriptions and medications, monitoring therapeutic levels and drug responses, monitoring adverse drug reactions and medication errors, and reconciling medications at patients transition across the continuum of care (Cobaugh et al. 2008, Child et al. 2011). In addition, they provide anticoagulant services, compile formularies, conduct clinical outcomes research and take part in antimicrobiological stewardship programs. Pharmacy technicians have an assisting role in providing services.

Clinical pharmacy services can be divided into central services (Table 7) and decentralized, patient-specific services (Table 8, Bond and Raehl 2008). In particular, the patient-specific services are shown to improve quality, safety, efficiency and reduced costs of care (Kaboli et al. 2006, Bond and Raehl 2008, Perez et al. 2008, Touchette et al. 2014).

Table 7. Central clinical pharmacy services in the United States (Bond and Raehl 2008).

Central clinical pharmacy services	**Definition**
Drug-use evaluation	Check if, at minimum, drug-use patterns are analyzed and results are reported to hospital committee.
In-service education	Pharmacist presents scheduled continuing education to fellow employees (physicians, nurses, pharmacists) at least 4 times/year.
Drug information	Provided only if a formal drug information service with a specifically assigned pharmacist(s) is available for questions. Does not require a physical location called drug information center.
Poison information	Provided only if a pharmacist is available to answer toxicity and overdose questions on a routine basis with appropriate resources.
Clinical research	Performed by pharmacist either as a principal investigator or co-investigator. Pharmacist is likely to be (co)author of a published paper. Not when activity is limited to investigational drug distribution or record keeping.
Drug safety officer	Pharmacist(s) has specific time set aside each week to work on improving drug safety in the hospital.

Table 8. Patient–specific clinical pharmacy services (Bond and Raehl 2008).

Patient–specific clinical pharmacy services	**Definition**
Adverse drug reaction (ADR) management	Pharmacist evaluates potential ADR while the patient is hospitalized and appropriately follows through with physicians.
Pharmacokinetic consultation	Provided only if, at a minimum, the drug regimen, serum level, and patient's medical record are reviewed, and oral or written follow-up is provided.
Drug therapy monitoring	Provided only if a patient's medical record is reviewed, and oral or written follow-up is provided when needed. Monitoring is ongoing and repeated, often on a daily basis. Not if only drug orders are reviewed. Does not include pharmacokinetic consults, total parenteral nutrition (TPN) team, rounds, ADR management, or drug therapy protocol management.
Drug protocol management	Pharmacist, under the order of a prescriber, requests laboratory tests if needed and initiates or adjusts drug dosage to obtain the desired therapeutic outcome (e.g., aminoglycoside or heparin dosing).
Total parenteral nutrition (TPN) **team participation**	Pharmacist, at a minimum, reviews patient's medical records and/or provides written or oral follow up if needed.
Drug therapy counselling	Pharmacist provides counselling on drug therapy either during hospitalization or at time of discharge. Not if counselling involves solely review of label directions.
Cardiopulmonary resuscitation (CPR) team participation	Pharmacist is an active member of the CPR team attending most cardiac arrests when the pharmacist is present in the hospital.
Medical rounds participation	Pharmacist rounds with a medical team at least 3 days/week, actively providing specific input.
Admission drug histories	Pharmacist provides admission drug histories.

Despite the experiences of the UK and Ireland, decentralized, patient-specific clinical pharmacy services, with a pharmacist working in the ward (or other care units) at least 50% of the time or visiting the ward daily, were not very common in Europe in 2010 (Frontini et al. 2013). The European Directorate for the Quality of Medicines and Healthcare (EDQM) and the CoE have invited European governments and policymakers to implement the pharmaceutical care philosophy and working methods in their national healthcare systems (EDQM 2012, EDQM 2017). Medication reconciliation, medication reviews and specific medication management models are examples of clinical pharmacists providing pharmaceutical care.

2.5.2.1 Medication reconciliation

Medication errors are common at the admission stage (Tam et al. 2005, Tully and Buchan 2009). Estimated medication error rates vary from 4% to 14% (Chin et al. 1999, Caterino et al. 2004). As much as one-third of prescribing errors that occur in hospitals are a consequence of an incorrect medication history taken at the time of admission (Dobrzanski et al 2002). Furthermore, exchange of the patient's electronic drug records and communication among care settings (between different organizations and even between different units in the same organization) is complicated.

Medication reconciliation is one of the key strategies to prevent ADEs and improve patient safety at all transitions in care (Institute for Healthcare Improvement, IHI 2011, WHO 2017). This was the 2005 Hospitals' National Patient Safety Goals established by the US Join Commission on Accreditation of Healthcare Organizations (Joint Commission 2005). "Medication reconciliation is the process of creating and maintaining the most accurate list possible of all medications a patient is taking – including drug name, dosage, frequency, and route – and using that list to guide therapy" (IHI 2011). The process involves three steps:

1) Verification (collection of the medication history)
2) Clarification (ensuring that the medications and doses are appropriate)
3) Reconciliation (documentation of changes in the orders)

The process can be considered to be complete when each drug the patient is taking has been actively continued, discontinued, held or modified at each transition point (IHI 2011).

Different approaches have been taken to complete medication reconciliation. In some hospitals, physicians are responsible for the entire process, but a multidisciplinary approach including nurses and pharmacists is also common. Clinical pharmacists seem to obtain more comprehensive medication histories than physicians (De Winter et al. 2010, Hatch et al. 2011, Mueller et al. 2012). The responsibilities of each professional conducting medication reconciliation should be clarified and the process should be standardized on the organizational level (IHI 2011, WHO 2013). Successful medication reconciliation procedures have reduced medication errors and overlapping work associated with the management of medication orders (Whittington and Cohen 2004, Rozich et al. 2004, Nassaralla et al. 2009, Murphy et al. 2009).

2.5.2.2 Collaborative medication reviews

Around 10-30% of hospital stays for older patients are drug-related (Hanlon et al. 1997, Beijer and Blaey 2002). Medication reviews reduce ED visits and an inpatient medication review conducted by pharmacists in close contact with physicians may lead to fewer admissions and lower morbidity (Gillespie et al. 2009, Christensen and Lundh 2016). It is recommended that regular medication reviews are performed in order to manage polypharmacy by identifying, resolving and preventing ADEs and drug-related problems (Hepler and Strand 1990, WHO 2017).

"Medication review is a structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimizing the impact of medicines, minimizing the number of medication-related problems and reducing waste" (Clyne et al. 2008). In the hospital setting, a comprehensive medication review is an activity distinct from the more routine review of medication charts that pharmacists make on each ward visit and should generally be undertaken when there is a concern about the potential interaction of medicines or if the patient has not been responding to their medication as expected (Healthcare Commission 2007). Different medication review procedures are internationally used in both outpatient and inpatient settings (Clyne et al. 2008, APhA 2008, Bulajeva et al. 2014, Australian Government 2015, NICE 2015). To meet the different situations and needs, medication reviews can be classified into three types (Table 9, Clyne et al. 2008).

Table 9. Characteristics of types of medication review (Clyne et al. 2008, adapted). Different types of review are not hierarchical but each has a distinct purpose.

	Purpose	**Patient involve-ment**	**Access to patient's clinical data**	**Includes all prescription medicines**	**Includes prescription, complementa-ry and OTC medicines**	**Review of medicine and/or condition**
Type 1: Prescription review	Address technical issues relating to the prescription e.g. anomalies, changed items, cost effectiveness	No*	Possibly**	Possibly***	No	Medicines
Type 2: Concordance and compliance review	Address issues relating to the patient's medicine-taking behavior	Usually*	Possibly**	Yes	Yes	Medicines use
Type 3: Clinical medication review	Address issues relating to the patient's use of medicines in the context of their clinical condition	Yes	Yes	Yes	Yes	Medicines and condition

*Any resulting changes to prescribed medicines must involve the patient/carer. **Medicines use review by community pharmacist may not include access to patient's clinical notes. ***A prescription review may relate to one therapeutic area only rather than all prescribed medicines. OTC = over-the-counter.

The prescription review (type 1) can be performed without the patient and is useful when patients are admitted to hospital, transferred between care settings or in emergency care situations (Clyne et al. 2008). It can be limited to one therapeutic area. This review can reveal the need for a face-to-face review with the patient. The concordance and compliance review (type 2) takes place in partnership with the patient and enables an exploration of the patient's medicine-taking, beliefs about medicines and ability and intent to take medicines (Clyne et al. 2008). The aim is to ensure the patient knows what to do if problems occur and to support their self-care. It is appropriate when patient is discharged from hospital, after the patient is prescribed new medicine, and for patients with polypharmacy. The clinical medication review (type 3) has a more holistic approach and takes place with patient and with access to the patient's clinical data (Clyne et al. 2008). The purpose of clinical review is to ensure that the medical conditions of the patient are optimally managed considering the pros and cons of treatment options and side-effects. The clinical review can be used to adjust medicines in light of clinical indicators and patient-reported symptoms. It should be conducted regularly for patients with long-term conditions and patients with ADEs. The clinical medication review will often be conducted by a prescriber or by a specialist practitioner, e.g. an accredited pharmacist (Clyne et al. 2008). Medication reviews can be targeted with patient-related, condition-related, medication-related and environmental triggers (Figure 8, Clyne et al. 2008).

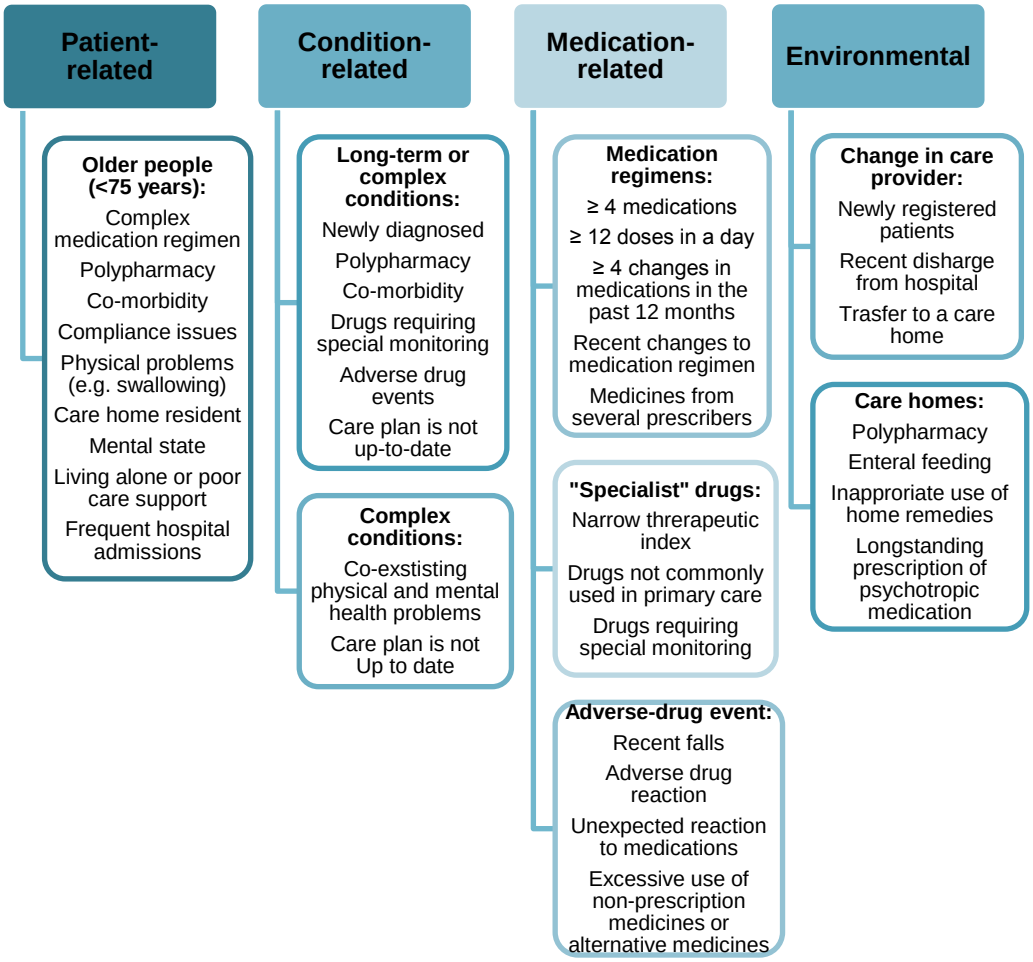

Figure 8. Targeting groups and triggers to medication reviews (Clyne et al. 2008, adapted).

2.5.2.3 Medication management models

A need for defining the essential elements of consistent pharmaceutical care process has been identified in the US (Harris et al. 2014). “The process should be easily understood, measurable, researchable, and readily documented and coded by the practice or other organization in which the clinical pharmacist works” (Harris et al. 2014). According to the American College of Clinical Pharmacy, the essential elements are (Harris et al. 2014):

1) Assess the patient and his/her medication therapy;
2) Develop a plan of care;
3) Implement the plan; and
4) Evaluate the outcomes of the plan.

In particular, the US and the UK have published medication management models of provided clinical pharmacy services and pharmaceutical care (Scullin et al. 2007, ACCP 2015, NICE 2015). Medication Therapy Management (MTM), Comprehensive Medication Management (CMM) and Collaborative Drug Therapy Management (CDTM) are medication management models provided in the US (ACCP 2015). Medicines optimization is a holistic, interprofessional medicine-management model in the National Health Service (NHS) in the UK (NICE 2015) and Integrated Medicines Management (IMM) is provided in Irish hospitals (Scullin et al. 2007).

MTM includes five core areas: medication therapy review, personal medication record, medication-related action plan, intervention and/or referral; documentation and follow-up. The Medicare Modernization Act of 2003 required Medicare Part D prescription drug plans to include MTM services to targeted beneficiaries. This provided pharmacists an opportunity to offer and be reimbursed for such services, but has its limitations: pharmacists do not always have access to patients’ clinical data and collaboration with other healthcare providers is not necessarily included (ACCP 2015). When the Affordable Health Care Act ("Obamacare") passed in 2010, new interprofessional, collaborative practice models that provide patient-centered care were needed.

CMM is a standard for direct patient care provided by clinical pharmacists in the United States (ACCP 2015, Table 10). CMM ensures that individual patients are assessed to determine whether the patient’s medications are appropriate, effective and safe. CMM always includes an assessment of the patient’s clinical status and requires collaboration among other members of the healthcare team.

Table 10. Comprehensive Medication Management (ACCP 2015).

Comprehensive Medication Management (CMM) Clinical pharmacists' process of care in team-based practices in the United States
1) Assessment of the patient - review medical record using a problem-oriented framework - obtain and document complete medication history - obtain, organize and interpret patient data - prioritize patient problems and medication-related needs **2) Evaluation of the medication therapy** - assess appropriateness of current medications → health conditions, indication and the therapeutic goals of each medication - evaluate effectiveness, safety, and affordability of therapies - assess medication use and adherence of therapies - identify medication-related problems and evaluate collaboratively the need for interventions **3) Development and initiation of plan** - review patient's active medical problem list for individualized assessment and plan for optimizing outcomes - formulate a comprehensive medication management assessment and plan to achieve patient-specific outcomes - educate patient/caregivers to ensure understanding of the plan, optimize adherence, and improve therapeutic outcomes - establish patient-specific measurable parameters and time frames for monitoring and follow-up **4) Follow-up & medication monitoring** - Coordinate with other providers to ensure that patient follow-up and future encounters are aligned with the patient's medical and medication-related needs - revisit medical record to obtain updates on the clinical status medication-related needs - conduct ongoing assessments and refine care plan to optimize therapy and ensure that individual goals are achieved - monitor, modify, document and manage the care plan

CDTM is a practice agreement between one or more physicians and qualified pharmacists who work within the context of a defined protocol (ACCP 2015). In addition to areas covered with CMM, it permits the clinical pharmacist to assume responsibility for performing patient assessments; ordering drug therapy-related laboratory tests; administering drugs; and selecting, initiating, monitoring, continuing and adjusting drug regimens. In 2015, 48 states (94%) had legislative provisions for CDTM and, in states without specific CDTM legislation, clinical pharmacists may collaborate with physicians to provide CMM (ACCP 2015).

Medicines optimization is a holistic, interprofessional medicine-management model in the NHS in the UK (NICE 2015). It is a person-centered approach to safe and effective medicine use emphasizing shared decision-making with the patient. The aim is to manage problematic polypharmacy and interactions, prevent ADEs and drug-related problems and promote medicines adherence. Topics of recommendations and key priorities for the implementation of the medicines optimization model are presented in Table 11. In particular, admission, transfer between different care providers and discharge are identified as being prone to adverse events and unintentional

changes in patients' medications (NICE 2015). The actions and collaboration of all healthcare and social care practitioners and greater patient engagement are in focus in medicines optimization. The role of pharmacists is particularly essential in PINCER intervention (a pharmacist-led information technology intervention for medication errors, Avery et al. 2012), discharge counselling, medicines reconciliation, medication review and when strategic decisions are made about medicines use or when care pathways that involve medicine use are developed (Table 11, NICE 2015).

Table 11. Medicines optimization in the National Health Service in England and role of pharmacists (NICE 2015, adapted). *PINCER is a pharmacist-led information technology intervention for medication errors (Avery et al. 2012).

<table>
<tr><td colspan="3">Medicines optimization in the National Health Service in England
Topics of recommendations (1-48), key priorities (4,14,16, 22) for implementation and role of pharmacists</td></tr>
<tr><td>Systems for identifying, reporting and learning from medication errors (1-11)</td><td><u>Key priority for implementation, recommendation 4</u>:
Organizations should consider using multiple methods to identify medication errors – for example, health record review, patient surveys and direct observation of medicines administration. They should agree the approach locally and review arrangements regularly to reflect local and national learning.</td><td><u>Role of pharmacists:</u>
A dedicated pharmacist support to applying the principles of the PINCER* intervention to reduce the number of medication errors</td></tr>
<tr><td>Medicines-related communication systems when patients move from one care setting to another (12-17)</td><td><u>Key priority for implementation, recommendations</u>
• <u>14:</u> Health and social care practitioners should share relevant information about the person and his/her medicines when a person transfers from one care setting to another.
• <u>16:</u> Consider sending a person's medicines discharge information to their nominated community pharmacy, when possible and in agreement with the person.</td><td><u>Role of pharmacists:</u>
Organizations should consider arranging additional support for some groups of people when they have been discharged from hospital, such as pharmacist counselling.</td></tr>
<tr><td>Medicines reconciliation (18-24)</td><td colspan="2"><u>Key priority for implementation, recommendation 22</u>:
Organizations should ensure that medicines reconciliation is carried out by a trained and competent health professional – ideally <u>a pharmacist, pharmacy technician,</u> nurse or doctor – with the necessary knowledge, skills and expertise including: 1) effective communication skills, 2) technical knowledge of processes for managing medicines and 3) therapeutic knowledge of medicines use.</td></tr>
<tr><td>Medication review (25-27)</td><td colspan="2"><u>Role of pharmacists:</u>
The medication review may be led, for example, by a pharmacist or by an appropriate health professional who is part of a multidisciplinary team.</td></tr>
<tr><td colspan="3">Self-management plans (28-30)</td></tr>
<tr><td colspan="3">Patient decision aids used in consultations involving medicines (31-42)</td></tr>
<tr><td colspan="3">Clinical decision support (43-46)</td></tr>
<tr><td>Medicines-related models of organizational and cross-sector working (47-48)</td><td colspan="2"><u>Role of pharmacists:</u>
Organizations should involve a pharmacist with relevant clinical knowledge and skills when making strategic decisions about medicines use or when developing care pathways that involve medicines use.</td></tr>
</table>

Integrated medicines management service (IMM) was created in Northern Ireland to support the implementation of comprehensive pharmaceutical care in Irish hospitals (Scullin et al. 2007). The idea is to provide clinical pharmacy services at each stage of the patient's hospital journey, from admission through discharge (Table 12). IMM is targeted to patients who are: 1) taking four or

more regular medications; 2) taking high-risk drug(s); 3) taking antidepressants and were 65 years or older; and/or 4) had a previous hospital admission within the last 6 months (Scullin et al. 2007). IMM service has reduced length of stay and increased time to readmission (Scullin et al. 2007, Scullin et al. 2012). The IMM model has been successfully adopted in Sweden (Lund Integrated Medicines Management Model, LIMM, Bergkvist et al. 2009, Bergkvist et al. 2011, Hellström et al. 2011, Bondesson et al. 2012).

Table 12. Integrated medicines management in the Northern Ireland (Scullin et al. 2007, adapted).

Integrated medicine management (IMM) Clinical pharmacy service in the Northern Ireland		
1) Admission	**2) Inpatient monitoring and counselling**	**3) Discharge from the hospital**
- constructing an accurate medication history, allergies, side-effects and adherence	- daily review of drug treatment taking into account therapeutic goals, relevant clinical chemistry and hematology results, and, where appropriate, therapeutic drug monitoring - graded significance of the interventions - tailored counselling to suit the needs of each individual patient, focusing on drugs which had been commenced or discontinued, high-risk drugs, and other situations where pharmaceutical advice was deemed necessary - technicians manage drug stock on the wards	- generation and authorization of a discharge prescription according to the protocols - preparing a medicines record sheet outlining all medications, dosage instructions and other relevant information such as changes to the patient's medications and laboratory findings while hospital - faxing medicines record sheet to the general practitioner in primary care - patient consultation and counselling

2.5.3 STANDARDS OF PRACTICE FOR CLINICAL PHARMACISTS

The American College of Clinical Pharmacy (ACCP) has set expectations for clinical pharmacists, both within the US and countries around the world (Table 13, ACCP 2014). These standards cover the pharmacists' process of care and documentation; involvement in collaborative; team-based practice and privileging; professional development and maintenance of competence; professionalism and ethics, research and scholarship and other responsibilities. The standards define for the public, healthcare professionals and policymakers, what they can and should expect of clinical pharmacists.

Table 13. Standards of practice for clinical pharmacists in the United States (ACCP 2014, adapted).

Qualifications: Clinical pharmacists are practitioners who provide comprehensive medication management and related care for patients in all settings. They are licensed pharmacists with advanced education and training including practice in team-based, direct patient care. Accredited residency training or equivalent post-licensure experience required to entry into direct patient care and board certification is also required.
Process of care: Delivering collaborative, comprehensive medication management to optimize patient outcomes. Assessment of the patient's medication-related needs e.g. reviewing medical records, obtaining medication history. Evaluation of medication therapy (appropriateness, effectiveness, safety, affordability, medication-related problems). Development and implementation of plan of care. Follow-up evaluation and medication monitoring
Documentation: Directly to patient's medical record in all settings. Medication-related assessment plan, medication history, allergies, adverse drug events, active problem list with assessment of each problems and plan of care to optimize medication therapy
Collaborative, team-based practice and privileging: Work with other health professionals as members of the health care team to provide high-quality, coordinated, patient-centered care. Collaborative drug therapy management
Professional development and maintenance of competence: Certification, licensure and their maintenance. Consistent participation in continuing professional development activities that enhance direct patient care.
Professionalism and ethics: Clinical pharmacists have a covenantal, fiduciary relationship with their patients and act in the best interest of individual patients within the context of legal and ethical parameters. Clinical pharmacists exhibit the traits of professionalism: responsibility, commitment to excellence, respect for others, honesty and integrity, and care and compassion.
Research and scholarship: Clinical pharmacists support and participate in clinical translational and health services research. Contributing the evolving literature in evidence-based pharmacotherapy. Disseminating and applying research findings that influence quality of patient care.
Other responsibilities: Educators, researchers, clinical preceptors/mentors, administrators, managers, policy developers and consultants.

The quality standards and goals for hospital and clinical pharmacy services have also been launched in Australia (Standards of practice for clinical pharmacy services, the Society of Hospital Pharmacists of Australia, SHPA, 2013) and Europe (the European Statements for Hospital Pharmacy, European Association of Hospital Pharmacist, EAHP, 2014). All of these statements emphasize a collaborative, patient-centered role for the clinical pharmacist where medication reviews, obtaining medication history, reconciling medications, educating and informing patients, caregivers and other healthcare professionals and developing and ensuring the safe medication-use process are key areas of clinical pharmacy services.

European statements are based on Basel's statements on the future of hospital pharmacy (International Pharmaceutical Federation, FIP 2009, EAHP, 2014). The statements express commonly agreed objectives which every European health system should aim for in the hospital pharmacy services (EAHP 2014). The statements are divided in six sections: 1): Introductory statements and governance; 2): Selection, procurement and distribution; 3): Production and compounding; 4): Clinical pharmacy services; 5): Patient safety and quality assurance; and 6): Education and research. Sections 4-5 (Table 14-15) are the most important for clinical pharmacists.

Table 14. The European Statements for Hospital Pharmacy, Section 4: Clinical pharmacy services (EAHP 2014).

4.1 Hospital pharmacists should be involved in all patient care settings to prospectively influence collaborative, multidisciplinary therapeutic decision making; they should play a full part in decision making including advising, implementing and monitoring medication changes in full partnership with patients, carers and other healthcare professionals.
4.2 All prescriptions should be reviewed and validated as soon as possible by a hospital pharmacist. Whenever the clinical situation allows, this review should take place prior to the supply and administration of medicines.
4.3 Hospital pharmacists should have access to the patient's health record. Their clinical interventions should be documented in the patients' health record and analyzed to inform quality improvement interventions.
4.4 All the medicines used by patients should be entered on the patient's medical record and reconciled by the hospital pharmacist on admission. Hospital pharmacists should assess the appropriateness of all patients' medicines including herbal and dietary supplements.
4.5 Hospital pharmacists should promote seamless care by contributing to the transfer of information about medicines whenever patients move between and within healthcare settings.
4.6 Hospital pharmacists, as an integral part of all patient care teams, should ensure that patients and carers are offered information about their clinical management options, and especially about the use of their medicines, in terms they can understand.
4.7 Hospital pharmacists should inform, educate and advise patients, carers, and other healthcare professionals when medicines are outside of their marketing authorization.
4.8 Clinical pharmacy services should continuously evolve to optimize patient outcomes.

Table 15. The European Statements for Hospital Pharmacy, Section 5: Patient safety and quality assurance (EAHP 2014).

5.1 The "seven rights" (the right patient, right medicine, right dose, right route, right time, right information and right documentation) should be fulfilled in all medicines-related activities in the hospital.
5.2 Hospital pharmacists should ensure the development of appropriate quality assurance strategies for medicine-use processes to detect errors and identify priorities for improvement.
5.3 Hospital pharmacists should ensure their hospitals seek review of their medicine-use processes by an external quality assessment accreditation program, and act on reports to improve the quality and safety of these programs.
5.4 Hospital pharmacists should ensure the reporting of adverse drug reactions and medication errors to regional or national pharmacovigilance programs or patient safety programs.
5.5 Hospital pharmacists should help to decrease the risk of medication errors by disseminating evidence-based approaches to error reduction including computerized decision support.
5.6 Hospital pharmacists should identify high-risk medicines and ensure appropriate procedures are implemented in procurement, prescribing, preparing, dispensing, administration and monitoring processes to minimize risk.
5.7 Hospital pharmacists should ensure that medicines administration is designed such that transcription steps between the original prescription and the medicines administration record are eliminated.
5.8 Hospital pharmacists should ensure accurate recording of all allergy and other relevant medicine-related information in the patient's health record. This information should be accessible and evaluated prior to prescription and administration of medicines.
5.9 Hospital pharmacists should ensure that the information needed for safe medicines use, including both preparation and administration, is accessible at the point of care.
5.10 Hospital pharmacists should ensure that medicines stored throughout the hospital are packaged and labelled so to assure identification, maintain integrity until immediately prior to use and permit correct administration.
5.11 Hospital pharmacists should support and implement systems that allow traceability of all medicines dispensed by the pharmacy.

2.6 CLINICAL PHARMACY SERVICES IN FINNISH HOSPITALS

Medicines management and clinical pharmacy services of hospitals and health centers can be provided by a hospital pharmacy or a smaller medicine dispensary (Medicines Act 395/1987, Rule of the Finnish Medical Agency, Fimea 6/2012). Hospital pharmacies are located in university hospitals, central hospitals and in some larger health centers with inpatient wards (Fimea 2017a-b). Medicine dispensaries supply medicines in smaller healthcare units in the public and private sector. Some of these are independent and others in the public sector are managed by hospital pharmacies.

There are approximately 9,500 pharmacists in Finland and about 7% of them are working in hospitals or health centers (Finnish Pharmacists' Association 2018). Hospital pharmacy is a somewhat new area in the Finnish healthcare system: community pharmacies supplied medicines to hospitals until 1928 when the first hospital medicine storages were founded. The first hospital pharmacy was established in the 1960s (Peldán 1967). The term ward pharmacy is used in Nordic countries and means pharmacy services provided on hospital wards. Because the tasks of pharmacists on wards have been somewhat logistical, the term 'clinical pharmacy services' has not totally been established. However, the disagreement around the term *clinical pharmacy* and its relationship to *pharmaceutical care* is common in European countries (Dreischulte et al. 2016). Furtehermore, the pharmacists working on wards usually have a Bachelor of Pharmacy degree, whereas pharmacists with Master's degrees are usually working on managing, leading or pharmacy specialist positions (Tyynismaa 2012).

The first clinical pharmacy posts were started in the 1980s (Laakkonen et al. 2005, Tyynismaa 2012). The number of hospital clinical pharmacists increased slowly during the 1990s, primarily due to the labor shortage of nurses (Tyynismaa 2012, Ryynänen et al. 2013). In the beginning, the duties of clinical pharmacists have been rather logistical and technical (e.g. ordering drugs from a hospital pharmacy to wards and ward's drug stock control, and preparing and diluting drugs, Tiiro et al. 2005), because they have often been formed based on wards' expectations and to ease the workload of nurses (Tyynismaa 2012).

"The third wave" in Finland was seen in the beginning of 2000s when new clinical pharmacy posts with more patient-centered tasks (e.g. medication reviews, patient information, educating and inducting ward's personnel, medication error reporting) were established in many hospitals due to different multiprofessional development projects often related to continuing education programs (Tyynismaa 2012, Ryynänen et al. 2013). Clinical pharmacy and system-based medication safety oriented hospital pharmacy specialization programs have been available since 2010 (Laaksonen et al. 2011) and a shorter accreditation program for ward pharmacy was available a few

years after 2009. Postgraduate accreditation training for comprehensive medication review (CRM) started in 2008 (Leikola et al. 2009) and later also a shorter, one-year training program for medication reviews has been available. In addition to the participation in continuing education programs, the Safe Pharmacotherapy: A National Guide for Pharmacotherapy in Social and Health Care of the Ministry of Social Affairs and Health (2006) was also a promoting factor with its suggestions to exploit more clinical pharmacy services in the healthcare settings (Tyynismaa 2012).

According to the national survey to hospital pharmacies and medicine dispensaries (n=71) in 2011, 51% of the respondents of the survey provided clinical pharmacy services and there were 157 clinical pharmacists who worked on 242 different wards (Tyynismaa 2012, Ryynänen et al. 2013). In 2011, the most common tasks of clinical pharmacists were drug information to ward personnel (100% of the respondents reported this task), dispensing per oral drugs to a patient-specific doses (83%) and logistic tasks (83%, Figure 9).
The next year (2012), another survey for clinical pharmacists revealed that the majority of the working time of clinical pharmacists was spent on logistical tasks, even though hospital and clinical pharmacists believed their expertise should be exploited in more clinical and patient-centered duties (Hartikainen et al. 2014). Prescription reviews, medication history taking and medication reconciliation at admission, informing and educating nurses and inducting ward's personnel were seen as the most important duties of clinical pharmacists (Hartikainen et al. 2014).

Lack of required skills and provision of clinical pharmacy education have been seen a hindering factor in the development of clinical pharmacy services (Tyynismaa 2012, Ryynänen et al. 2013). Also, when the benefits of clinical pharmacy services have been studied, the measurements and results have concentrated on the benefits of the logistic tasks e.g. savings in drug consumption and drug waste (Ojala et al. 2007, Toppinen et al. 2008, Tyynismaa 2012, Ryynänen et al. 2013, Pakarinen 2014). Recently, several pilot projects and studies of collaborative, pharmacist-led medication reviews and medication reconciliations have promoted a more patient-centered role for clinical pharmacists (see Chapter 2.4.3.1).

In 2012, Hartikainen et al. (2016) surveyed clinical pharmacists' thoughts about the most important risks in the medication-use process, what medication safety protections were in use and how medication safety could be promoted. The most commonly reported risks were rushing and working under pressure, deviation in working methods (e.g. preparing, dispensing and administering of drugs), specific medications (e.g. high-alert medications, lookalike/soundalike medications), oral orders, transferring and updating patient's medical history and electronic medical records (Hartikainen et al. 2016). Double-checking of dispensed medications prior to administration, prescription and medication reviews, education, induction and up-to-date instructions were the most common clinical pharmacists' reported areas to ensure medication safety.

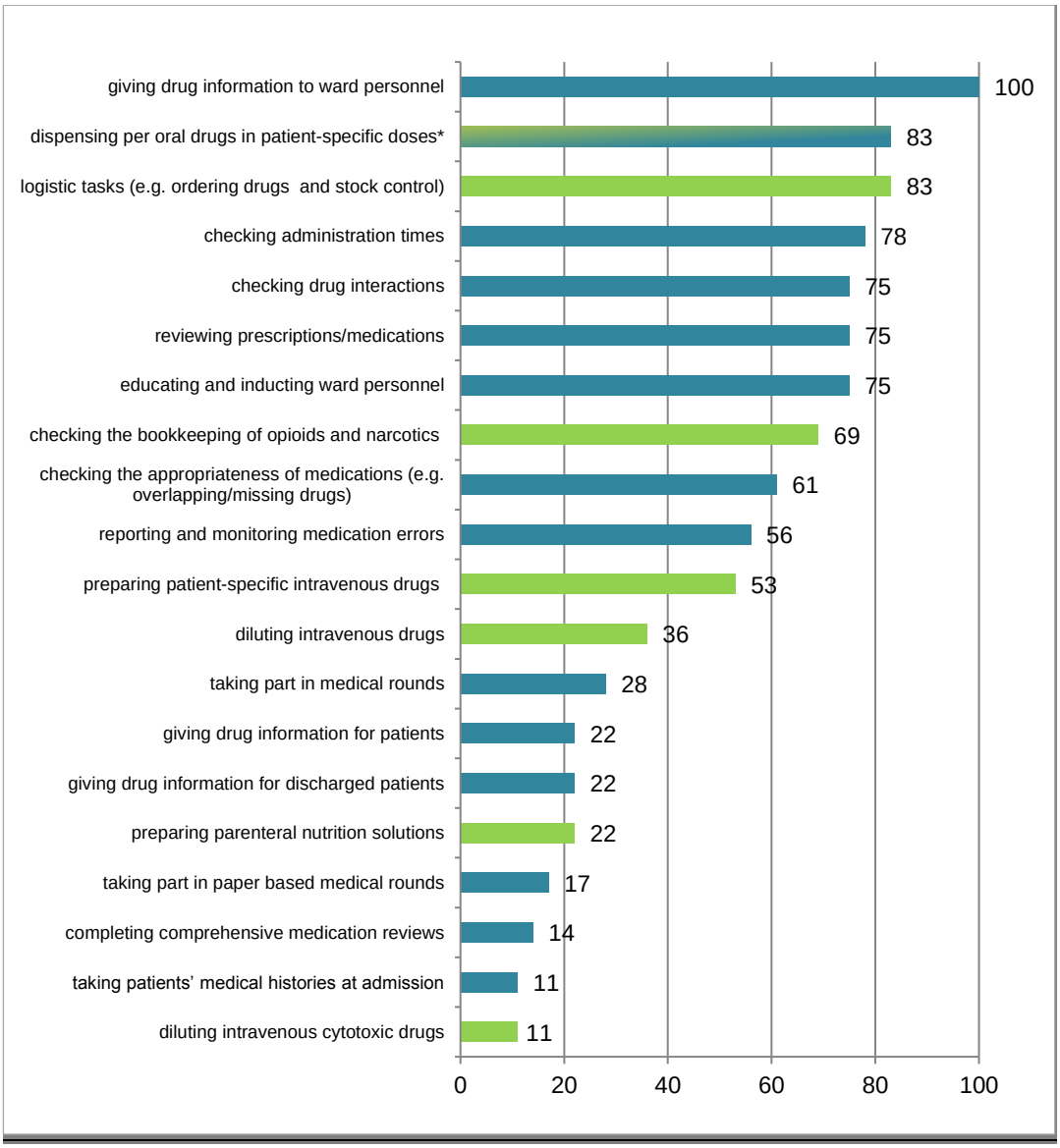

Figure 9. The most commonly reported tasks (%) of the Finnish clinical pharmacists in a national survey for hospital pharmacies and medicine dispensaries (n=71) in 2011 (Tyynismaa 2012). Blue Columns: patient-centered tasks and green Columns: logistical and technical tasks.*Dispensing can be seen as a clinical or as a logistical task whether or not a prescription review is included

2.6.1 COMPREHENSIVE MEDICATION REVIEW PROCEDURES

Increasing problematic polypharmacy with drug interactions and the use of potentially inappropriate medicines for the older patients were also identified in Finland during 2000-2010 (Jyrkkä et al. 2006, Kivelä and Räihä 2007, Hosia-Randell et al. 2008, Jyrkkä et al. 2009, Leikola et al. 2009, Ahonen 2011). The Ministry of Social Affairs and Health recommended multiprofessional collaboration and annual medication reviews to promote

safe medication use among the older patients (The Ministry of Social Affairs and Health 2007). For that purpose, the CMR procedure for community settings and related postgraduate accreditation training for pharmacists were developed (Leikola et al. 2009, Leikola 2012, Leikola et al. 2012). CMR includes a patient interview and medication review with structured, evidence-based forms and a case report format with documented action and follow-up plans from a multidisciplinary case conference (Figure 10, Leikola et al. 2012, Leikola 2012).

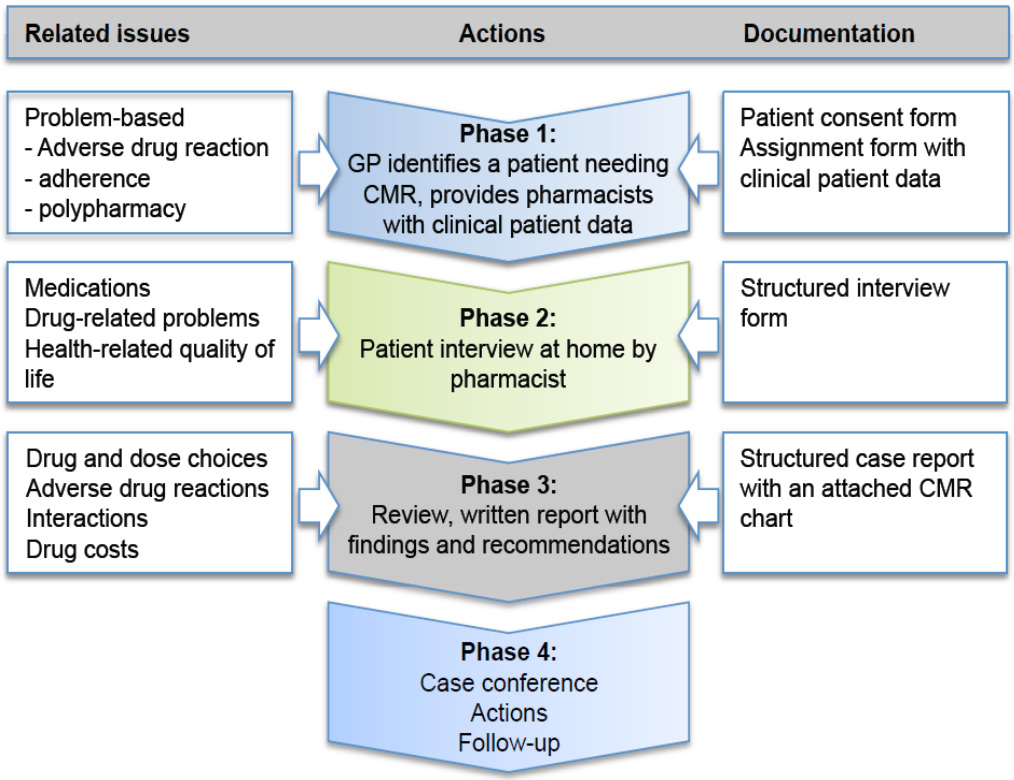

Figure 10. Phases of the CMR procedure and related documentation forms (Leikola 2012)

It is a clinical medication review (type 3) according to Clyne's (2008) typology. It has four operational phases (Figure 10) and covers four dimensions: 1) aging and safety, 2) co-morbidities, 3) polypharmacy and 4) adherence (Figure 11, Leikola et al. 2012).

Multiple electronic resources and tools are nowadays available to conduct the medication reviews, which have made medication reviews quicker and easier to conduct: e.g. national current care and geriatric pharmacotherapy guidelines, databases of medication use in the older patients, screening tools for interactions and burden of ADEs, drug choice and doses to patients with renal or hepar impairment and a database which includes information about genotypes that are associated with drug responsiveness or drug-induced adverse effects (Abomix 2018, Fimea 2018, The Finnish Medical Society Duodecim 2018, Medbase Ltd 2018, Toivo et al. 2018).

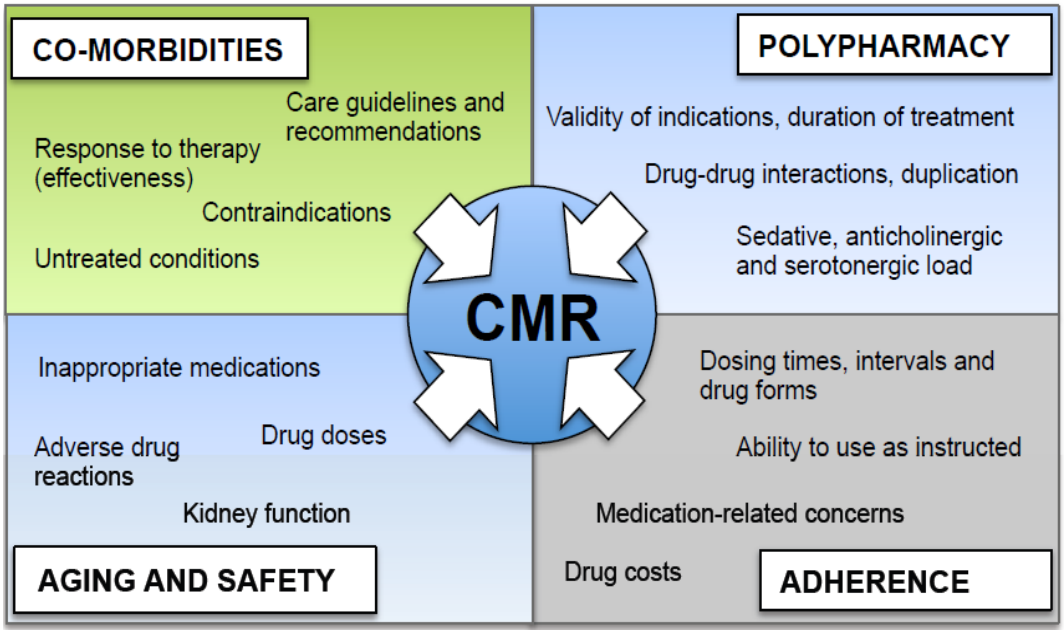

Figure 11. Four dimensions covered by the CMR procedure to ascertain safe and appropriate pharmacotherapy among older patients (Leikola 2012).

The original CRM procedure has evolved to various modifications especially to the Finnish care home and home care settings (Moberg et al. 2014, Kvarnström et al. 2014, Räisänen et al 2014, Kuitunen et al. 2014, Kumpusalo-Vauhkonen et al. 2016, MSAH 2017b, Toivo et al. 2018). Often the pharmacist-conducted patient interview has been replaced by a system where a nurse collects the background information and necessary clinical data of the patient. For those purposes, a tool for assessing risks for drug-related problems to be used by practical nurses caring for home-dwelling clients aged ≥65 years have been developed (Dimitrow et al. 2014, Dimitrow et al. 2015, Dimitrow 2016). To meet the needs of tertiary hospital care with short treatment periods, modern electronic health records and drug screening databases, the hospital pharmacy of Kuopio University Hospital has piloted a medication reconciliation and review procedure with shorter forms elaborated from the original CRM procedure (Valkonen et al. 2014). Pharmacists-led medication reconciliations and prescription reviews have also been successfully applied in the Kymenlaakso Central Hospital surgical ward (Ahlqvist et al. 2014).

Despite the multiple available electronic tools, integrated medicines management process is not common in Finland: healthcare professionals work independently and no one seems to have clear responsibility for identifying and solving individual patients' drug-related problems (Kallio et al. 2016). Clinical pharmacists' role in coordinating the identifying and solving drug-related problems would beneficial in Finland also (Toivo et al. 2018).

2.7 CLINICAL PHARMACY SERVICES IN HELSINKI UNIVERSITY HOSPITAL

The evolution of ward and clinical pharmacy services in HUS is somewhat similar to the rest of the Finland. Ward and clinical pharmacy services are provided by HUS Pharmacy, which is the hospital pharmacy of HUS, Hospital District of Helsinki and Uusimaa, in the capital area and Kymenlaakso in South-Eastern Finland. In addition to tertiary and secondary care, HUS Pharmacy provides services to also the primary care units and the Finnish Defense Forces.

The first ward pharmacist (with a Bachelor's degree) started to work in HUS's pediatric intensive care unit (ICU) in 1993 (Figure 12). The main duties were the ward's drug stock control and preparing infusion fluids. The number of clinical pharmacists increased slowly: in 2006, there were 10 ward pharmacists in HUS (e.g. in adult emergency department and ICU, adult and pediatric operating rooms, adult hematology ward and pediatric oncology ward). After 2006, the demand for ward pharmacy services clearly increased, particularly due to the labor shortage of nurses (Huotari et al. 2008). Expanding clinical pharmacy services was one of the goals in the first strategy of HUS Pharmacy in 2006. In 2007, one pharmacist (with Master of Pharmacy degree) was, for the first time, set up in a leadership position for all ward pharmacists (among other duties) and this position became full-time in 2011.

Benefits and outcomes of ward pharmacy services were, again for the first time, measured in the internal and surgical ward in the HUS Hyvinkää Hospital during 2007-2008 (Toppinen et al. 2008). At that time, the main tasks of ward pharmacist were wards' drug stock control and dispensing per oral doses, which saved the working time of nurses. Moreover, the wards' drug stock value and drug expenditures decreased. The HaiPro tool was not yet in use, but the wards documented medication errors with an electronic documentation sheet (VIIVI). The number of documented medication errors decreased by 37% in the internal ward and 50% in the surgical ward (Toppinen et al. 2008). Pharmacists also identified drug interactions, provided drug information and education to the wards' personnel.

In 2008, HUS Pharmacy set up a working group aiming to develop ward pharmacy services in order to be able to answer the increased demand (Huotari et al. 2008). At that time, there were 12 pharmacist posts and three pharmacy assistant posts covering 34 wards in HUS (Figure 12). Huotari et al. (2008) wrote in their final report, that ward pharmacy services provided by HUS Pharmacy are concentrated on drug logistics and technical tasks instead of patient-oriented pharmaceutical care, which was seen as crucial in the Safe Pharmacotherapy Guide (MSAH 2005). They identified that a lack of knowledge and skills related to clinical pharmacy required adopting a more patient-oriented role. There was an evident need for continuing education related to clinical pharmacy, which was not available at the time. In addition, information of medication orders or medication charts were not yet available

in the HUS's electronic patient information system in 2008, which was seen as a hindering aspect to, for instance, starting pharmacist-led prescription reviews.

After 2008, several continuing education programs became available (e.g. accreditation training in comprehensive medication reviews in 2008, accreditation training for ward pharmacy in 2009, and specialization training in hospital and health center in 2010). Some of the HUS's ward pharmacists participated in new continuing education programs. In addition, the basic education of pharmacists was developed to provide better clinical pharmacy skills. After 2010, electronic databases for assessing drug interactions became available in Finland and patient safety work started with patient safety incident reporting in HUS in 2011. These enabled more patient-centered tasks such as prescription reviews, patient information and reporting and analyzing medication errors for some pioneer clinical pharmacists.

As of 2018, HUS Pharmacy has over 100 clinical pharmacists and pharmacy assistants working on more than 100 wards and other healthcare units in tertiary (majority), secondary and primary care (Figure 12). In addition to pharmacists with a Bachelor's degree, there are two clinical pharmacists with a Master of Pharmacy degree working in oncologic and pediatric clinics and three pharmacists (M.Sc. Pharm) in developing, managing and leading clinical pharmacy services. However, some of the increase can be explained by the organizational changes: several hospital pharmacies and medicine dispensaries have been joined to HUS Pharmacy in recent years.

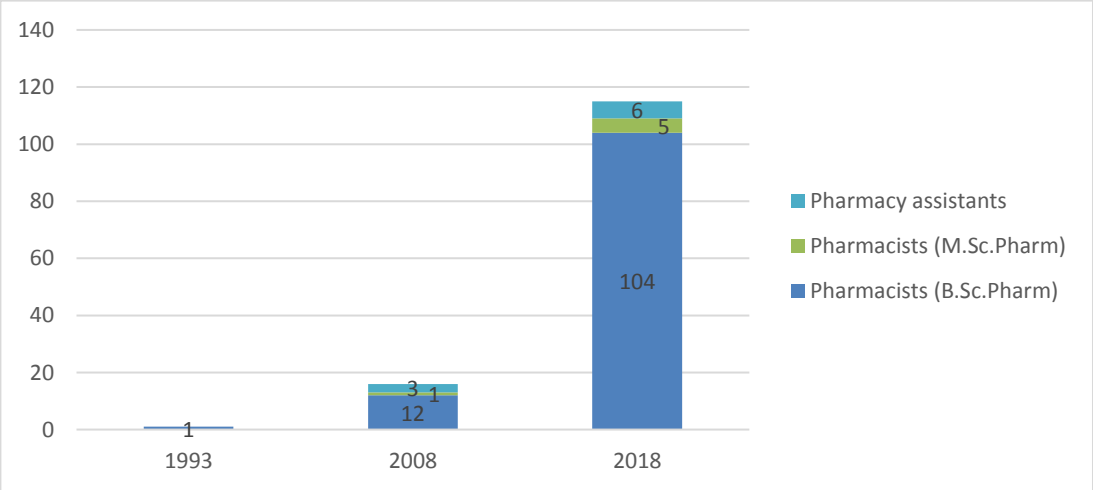

Figure 12. Number of pharmacists and pharmacy assistants working with clinical pharmacy services in HUS Pharmacy in 1993, 2008 and 2018.

Instead of only expanding clinical pharmacy services, currently the focus is on changing the role of clinical pharmacists. HUS Pharmacy's strategic goal is to provide clinical pharmacy services which promote medication safety. The aim is to standardize the tasks of clinical pharmacists and the key areas are: 1)

Medication reconciliation at admission, discharge and transitions of care; 2) Prescription reviews and clinical medication reviews during hospitalization; 3) Counselling patients on their medications before discharge; and 4) Auditing and developing medication use processes and analyzing medication error reports. Logistical and technical tasks of clinical pharmacists will be moved to pharmacy assistants with the help of drug automation technology (e.g. automated dispensing cabinets). To ensure the competence of clinical pharmacists to conduct these duties, in-house continuing education programs (e.g. clinical medication reviews) have been organized with the clinical teacher, who works 50% of time in HUS Pharmacy and 50% in the Clinical Pharmacy Group in HUS. However, the more patient-centered role of pharmacists is leading to a situation where clinical pharmacy services cover only working hours (8 am to 4 pm) on weekdays will not be sufficient for tertiary care units. HUS Pharmacy has an ambition to also provide clinical pharmacy services in the evenings and weekends in the future.

In 2017, the five university hospital pharmacies started a benchmarking collaboration and developed strategic indicators for clinical pharmacy services. These indicators came into use in February 2018, and are presented with HUS Pharmacy's information from 2-7, 2018 in Table 16. In the beginning the aim is simply to gather information and get used to measuring, not to compare university hospital pharmacies.

Table 16. Strategic indicators for clinical pharmacy services used in all five university hospitals with half-year data (2-7/2018) from HUS Pharmacy, Helsinki University Hospital.

Strategic indicator:	**n (*%)**
Percentage* of working time used in patient-centered tasks	33% (0-100%)
Clinical medication reviews	203
Medication reconciliations	3381
Patient counselling	199
Provided induction sessions to the healthcare staff	317
Provided education sessions to the healthcare staff	166
Taking part in medication error report analysis	155
Medication safety audits	5
Taking part in developing and updating medication safety plans	82

In addition to decentralized clinical pharmacy services, HUS Pharmacy provides centralized clinical pharmacy services: medicines information, clinical medication reviews, drug formula, services for clinical trials and coordination of medication safety and medication safety audits. These are especially targeted to the wards and care units which do not have clinical pharmacists and to support the clinical pharmacists.

2.8 SUMMARY OF THE KEY FINDINGS OF THE LITERATURE REVIEW

- Unsafe medication practices and medication errors are the most important preventable single factor jeopardizing patient safety. According to international studies, approximately 6% of hospitalized patients experience an ADE and about 25% of medication-related injuries are estimated to be preventable. Moreover, Finnish studies have revealed that medication errors are a major concern in patient safety.

- A systems approach is crucial to manage errors in healthcare. When an error occurs, the focus should be on how and why the defenses failed, not investigating who blundered. An effective error and risk management strategy relies on a blameless culture and learning from errors and near misses. Healthcare organizations should identify errors, evaluate causes and take prospective actions to improve performance with patient and medication safety programs. This work has been started in Finland and HUS from 2005. However, there is no national focal point for patient and medication safety.

- The WHO released the third Global Patient Safety Challenge on medication safety "Medication without harm" in 2017. The aim is to reduce the level of severe avoidable harm related to medication by 50% over 5 years, globally. The key strategic areas are high-risk situations (settings, patients, medications, etc.), polypharmacy and transitions of care.

- According to the principles of pharmaceutical care, the role of pharmacists in patient care is to ensure the quality of medication therapies and prevent drug-related morbidity, with an emphasis on interprofessional collaborative care and patient interaction. The patient-specific clinical pharmacy services are shown to improve quality, safety, efficiency and reduce costs of care. To ensure the quality of clinical pharmacy services, pharmaceutical care processes should be standardized.

- Particularly in the US and UK hospitals, clinical pharmacists have been integrated into interprofessional medical teams for decades. This has been less common in Finland (including HUS) and in many other European countries. The Council of Europe and the European Directorate for the Quality of Medicines and Healthcare have invited European governments and policymakers to implement the pharmaceutical care philosophy and working methods in their national healthcare systems to develop medication safety and quality of care.

3 AIMS OF THE STUDY

The aim of this study was to explore strategies for medication safety in Finland with a special focus on hospitals by using HUS as a case. The strategic development areas researched from organizational approach were managing high-alert medications and evolving clinical pharmacy services to meet the needs of the organization in ensuring medication safety.

The specific objectives were (number of the original publication is provided in brackets):

1. To demonstrate a method for identifying University Hospital's high-alert medications by applying data from the medication error reporting system (I).

2. To identify organizational high-alert medications by using University Hospital's medication error and adverse drug reaction reports (II).

3. To enhance medication history recording and identify the drug-related problems of older emergency patients with a pharmacist-led medication reconciliation and review procedure (III).

4. To explore the national evolution of clinical pharmacy services to meet the organizational needs in ensuring medication safety in Finnish hospitals (IV).

These objectives were derived and prioritized from the practice development needs of the Finnish healthcare system and HUS as a case organization from a patient and medication safety perspective. They are in line with the aims of the National Medicines Policy 2020 (MSAH 2011) and cover the key areas in the WHO's Patient Safety Challenge "Medication Without Harm" (Figure 2, WHO 2017).

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

This study explored organizational strategies for medication safety and was focused on high-alert medications (Part I) and clinical pharmacy services (Part II, Figure 13). Both quantitative and qualitative research methods were applied and data were collected from various sources. The study applied a systems approach to medication risk management based on the Theory of Human Error as a theoretical framework (Reason 2000).

High-alert medications (Part I)	**Demonstrating a method for identifying high-alert medications (I).**	**Identifying organizational high-alert medications (II)**
	• a retrospective register study • medication error reports • quantitative and qualitative analysis	• a retrospective register study • medication error reports and adverse drug reaction reports • quantitative analysis
Clinical pharmacy services (Part II)	**Enhancing medication history recording and identifying drug-related problems of older emergency patients (III)**	**Exploring the evolution of clinical pharmacy services in ensuring medication safety in Finnish hospitals (IV)**
	• a prospective feasibility study • pharmacist-led medication reconciliation and medication review procedure for older emergency patients • quantitative and qualitative analysis	• a 5-year follow-up study with two national surveys • survey on clinical pharmacy services for hospital pharmacies and medicinel dispensaries • quantitative and qualitative analysis

Figure 13. Study outline.

4.2 IDENTIFYING HIGH-ALERT MEDICATIONS (I-II)

4.2.1 STUDY SETTING, ME AND ADR REPORTING SYSTEMS

Studies I-II were conducted in HUS, which provides tertiary care with approximately 3,000 hospital beds, serving a regional population of 1.6 million in Southern Finland. HUS started to use a voluntary electronic reporting system for patient and medication safety incidents (HaiPro) in pilot units in 2007, extending its use to the entire organization in 2011. The reports can be made by all hospital staff members and are based on narratives (Appendix 1) that are coded according to the stages of the medication use process in the units by the staff members, usually nurses, trained to do the coding. In the HaiPro report form, the reporter is requested to comment on the circumstantial and contributing factors to an error and share ideas on how the error could be prevented in the future. These features make HaiPro comprehensive and system-oriented (Reason 1990, Reason 2000).

At the time of Study I in 2014, medications in HaiPro's ME reports were not structurally documented (e.g., categorized according to Anatomic Therapeutic Codes, ATC). Medications related to MEs were reported in open field narratives, meaning that the sorting of the reports by medications and the creation of top medication lists needed to be performed manually. Conducting Study I revealed a need for developing the structural documentation of medications related to MEs and a top report to the HaiPro tool. These features were added to the HaiPro tool at HUS's request during 2014 and came into use in the beginning of 2015. These improvements in the HaiPro tool enabled effective analysis of larger ME data in Study II.

ADRs are reported to the national pharmacovigilance reporting system maintained by the Finnish Medicines Agency (Fimea) (Directive 2010/84/EU, Fimea 2017a). Fimea provides HUS with an annual ADR report summary upon request. This summary does not include an estimate of the severity of the reported ADRs. Fimea states that "This data cannot be regarded as either quantitatively or qualitatively representative and should not be interpreted as Fimea's statement of a causal connection between a drug and an adverse drug reaction. Comparison of different drugs or products is justified only exceptionally."

4.2.2 DATA COLLECTION

The data from Study I was HUS's ME and near-miss reports from HaiPro database during 2007-2013 (Figure 14). As there were, in total, more than 18,000 ME reports, we did not have sufficient resources to investigate the related medications manually. Accordingly, a targeted sample was used. The study was particularly targeted at those ME reports where the use of specified

medications was reported or coded as a contributing factor leading to a ME or near miss situation (n=263, Figure 14). The medications that related to the reported MEs and near-miss situations were identified and categorized from the report narratives manually.

In HaiPro, reporters report possible circumstantial and contributing factors to an event in a narrative format to an open field, and a trained coder codes these to structured categories. One of the structured categories for contributing factors is *medications*, which is used when a reporter (or a coder) has identified a specific safety risk associated with the medication (e.g. LASA name or package labelling, recent formulary and proprietary name changes, unclear preparation/reconstituting instructions) and thinks that it substantially contributed to an error. In these cases, a specific medication had a larger impact on an error than in other reported MEs, because it had been mentioned as a contributing factor. This targeted sample was later confirmed to include more high-alert medications than a random sample (10% vs. 33%).

HUS's ME reports from the years 2015-2016 were analyzed in Study II. During 2015-2016, a total of 35,610 patient safety incidents were reported in HUS. Of these, 11,668 (33%) were related to medications, infusion fluids, and radio contrast agents. To identify the most commonly reported medications related to these reports, the top report of the HaiPro tool was used. The specific medication related to ME was specified in only 62% of the reports (n=7,201), and the HaiPro system identified a specific ATC code in 43% (n=5,011).

4.2.3 DATA ANALYSIS

Analysis of the quantitative data (I-II)

In Study I, quantitative analysis was conducted to calculate the number and relative proportion of each specific medication involved in MEs and near-misses. Reports without a mention of a specific medication were excluded, as were double reports about the same event (Figure 14). The reports were sorted by ATC codes (World Health Organization, WHO 2011) according to medications involved in MEs to compile larger pharmacotherapeutic groups of ME-related medications. New categories of administration route and high-alert medication were created by using the ISMP's list of High Alert Medications for Acute Care Settings (ISMP 2014). The ISMP's list was chosen because of its internationally widely used high-alert medication list.

The coded ME types related to the specific medications were identified in order to find out the contributing factors and potential root causes in the medication-use process. The medication-use process was divided into 11 sections according to the coded process variables in HaiPro: prescribing; *compounding and preparing; dispensing; administrating; monitoring; unexpected reaction to a patient; ordering; distributing; storage; documenting and information*. Percentages and frequencies were calculated

from the following variables in the HaiPro reports: *consequences to a patient*, *circumstantial and contributing factors* and *ME types* according to the medication-use process.

To calculate the number of reported errors compared to consumption, the drug consumption data were derived from the hospital pharmacy register and linked with HaiPro's ME data. Dispensing units (tablets, capsules, vials, ampoules, injection/infusion bottles, sachets, transdermal patches, etc.) were applied because the hospital drug consumption data were not available in defined daily doses (DDDs). Dispensing units were applicable, because the intention was to compare the number of errors to the consumption volume, not generally report the drug consumption.

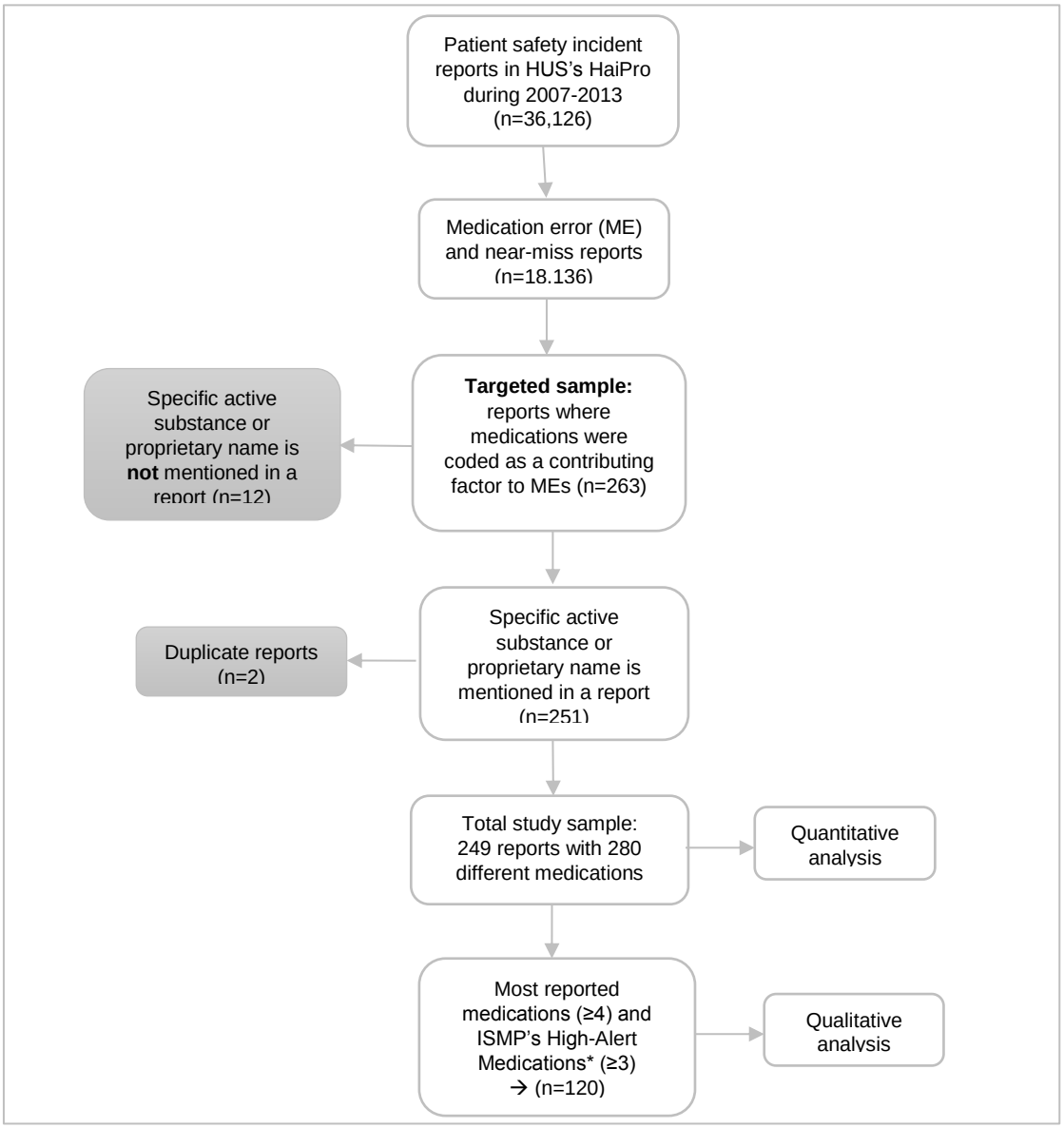

Figure 14. The outline of Study I. The targeted sample was considered to include high-alert medications. *High-alert medication = "Errors may or may not be more common with these drugs than with the use of any others; however, the consequences of the errors are more devastating" (ISMP 2014). ME = medication error.

In Study II, the most commonly reported (top) active substances and ATC groups in HUS's ADR and ME reports in 2015-2016 were analyzed. Fimea has particularly requested that healthcare professionals report all serious and/or unexpected reactions as well as all adverse reactions related to new medicines (Fimea 2017a). Hence, MEs causing severe or moderate harm to a patient and the ME subtype unexpected reaction in a patient were analyzed separately in order to detect possible similarities with ADR reports. ISMP's high-alert medications for acute and ambulatory care settings were identified from each category (ISMP 2010, ISMP 2014). Drug consumption data were derived from the hospital pharmacy register and linked with ADR and ME data. Dispensing units (tablets, injection bottles and pens, hospital pharmacy prepared doses, etc.) were used to compare the number of reported ADRs and MEs with the drug consumption volume. The internationally defined daily doses (DDDs) were not applicable, as most cytotoxic and biological drugs do not have them. Percentages and frequencies were also calculated from the following variables in the HaiPro ME reports: profession of the reporter and ME types according to the medication-use process (as in Study I).

Analysis of qualitative data (II)

In Study I, the most commonly reported medications (n=120) were explored in further detail from a medication safety approach (process and human error view, Figure 14). The objective of the qualitative content analysis of the narrative part of the HaiPro reports was to achieve a more comprehensive understanding of the contributing factors to MEs in order to develop preventable actions in the future. A conventional content analysis (Hsieh and Shannon 2005) was applied in order to identify key safety risks and latent reasons for MEs. Problems which increased the risk of MEs related to specific medications and medication classes were analyzed. Qualitative analysis was targeted to the most commonly reported medications (≥4 reports per medication) and ISMP's High-Alert Medications for Acute Care Settings (≥3 reports per medication, ISMP 2014). As we wished to reveal multi-faceted information and repeated patterns of key safety problems, we used a minimum of 3-4 reports per medication. Reports about oral hypoglycemics (n=6) were analyzed as a group, because they are mentioned as a high-alert medication group in ISMP's list (ISMP 2014).

A qualitative content analysis is a "subjective interpretation of the content of text data through the systematic classification of coding and identifying themes or patterns" (Hsieh and Shannon 2005). The goal is to understand and provide knowledge from the phenomenon under study. The approach to qualitative content analysis is conventional, where the researcher does not use preconceived categories (Hsieh and Shannon 2005). In this study, the coding was inductive: the coding scheme was shaped during the coding process. The advantage of using conventional content analysis is "gaining direct

information without imposing preconceived categories or theoretical perspectives" (Hsieh and Shannon 2005). Content analysis begins by simplifying and reducing the data (Hämeen-Anttila and Katajavuori 2008). At this stage, the intention is to find points that correspond to the research problems. A simplified description will be created from these points. The next stage is categorizing these simplified descriptions into subcategories. Following this, different subcategories will be pooled, where top categories will be created. This is called abstracting: pooling the categories and labelling them so that the name describes both subcategories and top categories. This will be continued as long as it is reasonable and possible in the data. The aim is to create categories that describe the phenomenon under the study, not only to describe categories.

4.3 MEDICATION RECONCILIATION AND REVIEW (III)

4.3.1 STUDY SETTINGS

Study III was conducted in the EDs of two Finnish university hospitals during April 2014 – January 2015. Two EDs were chosen for comparing the feasibility of the pharmacist-led medication reconciliation and medications review process in both settings.

1) Helsinki University Hospital (HUS) provides specialized tertiary medical care, whereby 3,000 hospital beds serve a regional population of 1.6 million in the capital metropolitan area of Finland. The ED in HUS has approximately 80 patient visits per day, with internal, surgical and neurological specialties for patients older than 16 years of age. Clinical pharmacy services were provided in the ED, but the medication reconciliation and review had not been included.

2) Kuopio University Hospital (KUH) provides specialized medical care with 730 beds that serve over 840,000 residents in Eastern Finland. The ED of KUH usually has 200 patient visits per day and provides tertiary, secondary and acute primary care. A clinical pharmacist the KUH-ED has been recording medication histories including medication reconciliations and reviews on a weekly basis since 2013.

4.3.2 PATIENTS

Study III was targeted at older ED patients (n=150) with polypharmacy. The inclusion criteria were: 1) ≥65 years old; 2) Finnish speaking; 3) home-dwelling; 4) oriented to time and place or having a caring close relative who

could be interviewed instead; and 5) using ≥6 medications (including over-the-counter medications, dietary supplements and herbal products) according to the admission medication chart recorded by either the nurse or the physician in the ED. Two clinical pharmacists (one in HUS and the other in KUH), both accredited for conducting medication reviews, worked from Monday to Friday 8 am to 6 pm. They chose the first one or two patients per day who met the inclusion criteria to participate in the study. This was repeated as long as they had 75 participants in both units.

4.3.3 PROCEDURE FOR MEDICATION HISTORY RECORDING INCLUDING MEDICATION RECONCILIATION AND REVIEW

The prospective procedure applied in Study III was designed not to interfere with normal ED routines or passing-times. The starting point of the pharmacist-led medication reconciliation was the admission medication chart taken by a nurse or a physician. In addition, clinical pharmacists checked the possible referral medication chart and medication charts from previous hospital stays.

The information gathered from these charts was used to start the bedside patient interview conducted at ED. In some cases relatives or other caregivers were also interviewed. The structured interview form (Appendix 2) was earlier created and piloted in KUH (Saukkonen 2014, Valkonen 2014) and updated for the purposes of this study. The content of the interview form is based on the clinical interview guide used in the Finnish Comprehensive Medication Review procedure (Leikola et al. 2013). The content of DRP risk-assessment tool, which is targeted at nurses for the identification of the clinically most significant DRPs in older adults, was also reviewed for a content validation of the interview form (Dimitrow et al. 2014).

Medication reviews were conducted by the clinical pharmacists after medication reconciliation. The pharmacists used a medication review form (Appendix 3), which had also been modified from the Comprehensive Medication Review procedure (Leikola et al. 2012) to be appropriate for the emergency setting and was earlier piloted in KUH (Saukkonen 2014, Valkonen 2014). Pharmacists had full access to patients' clinical and medical data, including laboratory results. The applied procedure can be considered as a type III clinical medication review according to Clyne's (2008) typology. Special attention was also paid to problems related to high-alert medications (ISMP 2010, ISMP 2014). These data were later used for identifying the ED's high-alert medications at the admission stage.

4.3.4 CLASSIFICATION OF DRUG-RELATED PROBLEMS IN THE MEDICATION REVIEW PROCEDURE

The classification of the drug-related problems was developed for the study purposes and performed according to the medication review form (Appendix 3) to achieve easy and feasible medication review procedure for ED setting. The identified drug-related problems were divided into three groups:

1) Drug-related problems linked to admission diagnoses. The relationship was judged by comparing the patients' symptoms and signs at admission (e.g. bleeding, constipation, dizziness) to the known adverse drug reactions of used medications with possible impact of clinically problematic interactions and renal insufficiency.

2) The severe drug-related problems that were not related to admission diagnoses, but needed immediate actions at ED (dose adjustment with renal insufficiency, adverse drug reactions) were categorized as acute.

3) The less severe drug-related problems (e.g. reconsidering the need or efficacy of the medication, need for monitoring) that could be resolved later after discharge, e.g. in primary care, were determined to be non-acute.

Before reporting the findings to the ED physicians, all the findings of the cases were approved for clinical relevance by the physicians who performed as supervisors of this study (clinical pharmacology and internal medicine specialist in HUS and internal medicine specialist in KUH). All clinically relevant findings were reported to the ED physicians orally and were documented in the electronic patient information system.

4.3.5 DATA ANALYSIS

The procedure used in Study III in both EDs was assessed by the number of discrepancies and drug-related problems that were identified by the clinical pharmacists. The data were analyzed by using descriptive statistics: 1) patient characteristics; 2) number and frequency of discrepancies in admission medication charts that had been recorded for each patient by nurses or physicians and which were subsequently compared with medication reconciliation procedure conducted by pharmacists; 3) number and frequency of clinically problematic drug-related problems (admission related, acute and non-acute) and their subtypes according to the medication review form. The results from HUS and KUH were analyzed separately in order to find any possible differences in the feasibility of the procedure performed in the ED of either a tertiary (HUS) or secondary (KUH) hospital.

4.4 NATIONAL SURVEY ON CLINICAL PHARMACY SERVICES IN 2011 AND 2016 (IV)

Two national surveys were conducted to explore the extent and range of clinical pharmacy services in Finnish hospitals to promote medication safety: 1) in 2011, when the first National Patient Safety Strategy (MSAH 2009), the new HealthCare Act, and the Medicines Policy 2020 had been recently enacted; and 2) five years later in 2016.

4.4.1 STUDY SETTING AND PARTICIPANTS

The participants of the cross-sectional online surveys were Finnish hospital pharmacies and independent medicine dispensaries (see Chapter 2.6). The number of medicine dispensaries had decreased remarkably from 131 to 51 between 2011 and 2016, while the number of hospital pharmacies (n=24) remained the same (Salminen, personal communication 2012, Fimea 2017b, Fimea 2017c, Tornianen, personal communication 13.4.2017). This is because of a strategic trend to merge small medicinel dispensaries into larger hospital pharmacies in the region, which has freed up resources from administrative and logistic work, and enabled reallocation to more patient care-oriented clinical pharmacy services.

4.4.2 DEVELOPMENT OF THE SURVEY INSTRUMENT

In 2011, six semi-structured theme interviews were conducted to develop the survey instrument (Tyynismaa 2012). The interviewees were selected by strategic sampling to present the widest range of Finnish clinical pharmacy services at that time. The recruitment was facilitated by the Finnish Pharmacists' Association and the Faculty of Pharmacy, University of Helsinki, Finland. Interviewees were working on the wards or as leaders of clinical pharmacy teams in different hospitals and health centers. In addition to the interviews, information gathered from practice development projects in Finland and international scientific literature were used for developing the survey instrument. The survey instrument was piloted for content and face-validity with three clinical pharmacists from separate organizations. Time required for responding to the survey varied between 10-40 minutes depending on the range of the services provided by the respondent's organization.

The final survey instrument was divided into three parts: 1) questions gathering background information on the respondent's healthcare organization; 2) targeted questions to those hospital pharmacies/medicine dispensaries that provided clinical pharmacy services; and 3) targeted

questions to non-providers of clinical pharmacy services (Figure 15, Appendix 4). The questions employed 5-point Likert scales, multiple choices and open fields for responses. Structured questions were used to gather the background information of the responding units, the current range of clinical pharmacy services and the evaluated and perceived benefits and outcomes of these.

The same online survey instrument with some updates was utilized in the follow-up survey in 2016 (Figure 15). Most of the questions remained the same, but some of the open-ended questions were changed to structured questions. The structured list of clinical pharmacy services that assessed their range in the hospital was updated for the 2016 survey by adding such services that had been implemented after the first survey in 2011 e.g. those recommended by the European Statements of Hospital Pharmacy (EAHP 2014). In 2011, the respondents were asked to submit any available reports on the studies they had conducted to show the benefits and outcomes of the services they had provided. These reports were used to develop a structured list of possible benefits and outcomes to the year 2016 survey.

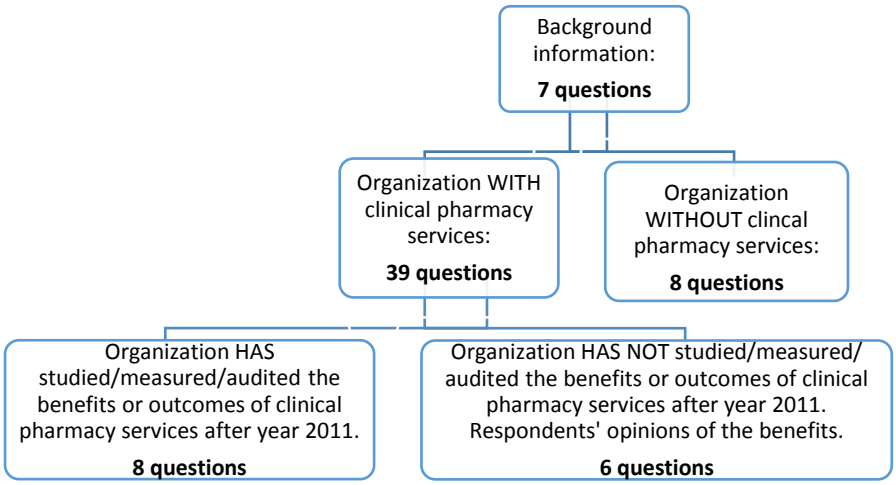

Figure 15. Content of the survey instrument in 2016.

4.4.3 CONDUCTING THE SURVEY IN 2011 AND 2016

The online survey was conducted in 2011 and in 2016. The survey was e-mailed to the chief hospital pharmacists (n=24 in 2011 and 2016) and the managers of the medicine dispensaries (n= 94 in 2011 and n=55 in 2016). The e-mail addresses of the chief hospital pharmacists were received from the Faculty of Pharmacy, the University of Helsinki. The managers of the medicine dispensaries were contacted using the membership register of the Finnish Pharmacists' Association. While there were 55 managers in 2016, only the managers of the independent medicine dispensaries (n=28 out of 55 medicine

dispensaries) were invited to participate in the survey. The chiefs and the managers were asked to forward the survey to the pharmacists in their organization who managed clinical pharmacy services so that that there would be one coordinated response per organization. The survey was open for two weeks and two reminders were sent out during that period. After that, a third e-mail reminder was sent and the survey was open for one more week.

4.4.4 DATA ANALYSIS

The structured questions were analyzed with descriptive statistics using Microsoft Excel (Howell 2013). The responses from hospital pharmacies and medicine dispensaries were analyzed separately in order to identify differences in operation for these units. Equally, in some questions the responses from hospital pharmacies were divided into university hospitals, central hospitals and community hospitals in order to identify differences between these hospital pharmacies. The open-ended questions were analyzed by applying a conventional content analysis (Hsieh and Shannon 2005, see Chapter 4.2.4). Reason's Human Error Theory (2000) was applied to consider reported tasks where clinical pharmacists contributed to medication safety in different stages of medication-use process (see Chapter 2.1).

4.5 STUDY ETHICS

For Studies I-II, a research permit (TYH2014224) was requested from HUS. An ethics committee approval was not needed, because the HUS's ME data in the HaiPro tool and ADR data received from Fimea did not contain any identifiable patient information.

Study III was covered with HUS research permit TYH2014224 and KUH research permit 21//2014. The study followed the World Medical Association's Declaration of Helsinki (2013) and was approved by the ethics committees of HUS (36/13/03/00/14) and KUH (21//2014). All study participants (including interviewed caring close relatives) gave written informed consent before taking part in the study. This study does not contain any indefinable data on individual patients.

According to the scientific ethical guidelines in Finland, an ethics committee approval was not required for a survey (Study IV) without patient data (TENK 2018). The survey participants were informed that their participation was voluntary and responding implied their informed consent. The invitation to the survey was sent by e-mail, including a cover letter with a description of the study and a link to an online survey. Detailed information of the responding organizations was not asked, only whether the unit was a hospital pharmacy or a medicine dispensary and the county in which the unit was located. All responses were confidential

5 RESULTS

5.1 DEMONSTRATING A METHOD FOR IDENTIFYING UNIVERSITY HOSPITAL'S HIGH-ALERT MEDICATIONS (I)

During 2007–2013, a total of 36,126 patient safety incidents and near misses were reported at HUS through the HaiPro tool. Half (50%) of the reports (n=18,136) were related to medications, including infusion solutions, contrast agents, radiopharmaceuticals and blood transfusions. The final targeted sample, in which the specific active substance or proprietary name was identified and medications were coded as a contributing factor to ME, consisted of 249 ME reports (Figure 14). These reports included a total of 280 different medications which were classified into 43 therapeutic subgroups according to ATC codes and compared to the hospital's medication consumption during 2007-2013 (Table 17). The therapeutic groups with the highest number of incidents in the ME reports were antibacterials for systemic use (13% of the reports in the targeted sample), psycholeptics (10%), analgesics (9%), antithrombotic agents (9%) and anesthetics (7%) (Table 17). These five medication groups were involved in almost half (46%) of all reported MEs in the study sample. Drugs for the treatment of bone diseases (M05) were the therapeutic group with the highest number of reported errors compared to the consumption (37.1), followed by antigout preparations (15.6) and anti-Parkinson drugs (9.9). Most commonly reported specific medications were ceftriaxone (n=13) and oxycodone (n=12; Table 18).

Approximately 33% (n=91) of all reported medications in the targeted sample were ISMP's high-alert medications (ISMP 2014). The most commonly reported high-alert medications were oxycodone (n=12), enoxaparin (n=8) and noradrenalin (n=7; Table 18). Half (50%) of all reported medications were used via parenteral route (n=141), including the most commonly reported specific medications, ceftriaxone and oxycodone. Ceftriaxone (administered IV) had the highest number of reported errors of 61.3, followed by insulin (SC, IV; 42.7) and noradrenaline (IV; 31.9) (Table 18).

Table 17. All reported medications (n=280) in the included ME and near-miss reports (n=249) divided in 43 therapeutic classes by ATC codes and compared to the hospital's medication consumption in dispensing units* in 2007-2013.

Therapeutic Group	Number Of Cases n (%)	Consumption 2007-2013 (dispensing units*)	Errors / Consumption (10^{-6})
Antibacterials for systemic use (J01)	35 (12.5)	8 616 351	4.1
Psycholeptics (N05)	27 (9.6)	12 180 221	2.2
Analgesics (N02)	24 (8.6)	17 237 117	1.4
Antithrombotic agents (B01)	24 (8.6)	4 601 147	5.2
Anesthetics (N01)	20 (7.1)	5 295 278	3.8
Psychoanaleptics (N06)	12 (4.3)	2 540 655	4.7
Diuretics (C03)	11 (3.9)	2 990 798	3.7
Cardiac therapy (C01)	11 (3.9)	2 195 909	5.0
Blood substitutes and perfusion solutions (B05)	10 (3.6)	15 234 626	0.7
Agents acting on the renin-angiotensin system (C09)	10 (3.6)	1 818 711	5.5
Calcium channel blockers (C08)	7 (2.5)	1 340 207	5.2
Drugs used in diabetes (A10)	7 (2.5)	1 274 021	5.5
Anti-inflammatory and antirheumatic products (M01)	6 (2.1)	5 160 053	1.2
Antiepileptics (N03)	6 (2.1)	3 224 212	1.9
Muscle relaxants (M03)	6 (2.1)	815 491	7.4
Anti-Parkinson drugs (N04)	5 (1.8)	504 629	9.9
Mineral supplements (A12)	4 (1.4)	3 094 696	1.3
Drugs for acid related disorders (A02)	4 (1.4)	3 586 929	1.1
Drugs for functional gastrointestinal disorders (A03)	4 (1.4)	1 825 389	2.2
Urologicals (G04)	4 (1.4)	832 071	4.8
Beta-blocking agents (C07)	3 (1.1)	3 115 490	1.0
Respiratory system (R)	3 (1.1)	2 949 970	1.0
Corticosteroids for systemic use (H02)	3 (1.1)	2 508 176	1.2
Pituitary, hypotalamic hormones and analogues (H01)	3 (1.1)	734 160	4.1
Antiprotozoals (P01)	3 (1.1)	442 716	6.8
Antigout preparations (M04)	3 (1.1)	192 124	15.6
Drugs for treatment of bone diseases (M05)	3 (1.1)	80 956	37.1
Other therapeutic groups**	22 (1.1)	31 551 905	0.7
TOTAL	**280 (100)**	**135 944 007**	**2.1**

*__Dispensing unit__: tablet, capsule, vial, ampoule, injection/infusion bottle, infusion bag, sachet, transdermal patch, etc.
** **Reported twice:** diagnostic agents (V04), lipid modifying agents (C10), sex hormones and modulators of the genital system (G03), antimycotics for systemic use (J02), antivirals for systemic use (J05) and all other therapeutic groups (e.g. antidotes, V03). **Reported once:** endocrine therapy (L02), dermatologicals (D), antihemorrhagics (B02), immune sera and immunoglobulins (J06), immunosupressants (L04), general nutrients (V06), vaccines (J07), antineoplastic agents (L01), contrast media (V08) and vitamins (A11).

Table 18. Most commonly reported medications (≥3 reports per medication, n=32) and their proportion in the reports (n=249) compared to the hospital's medication consumption in 2007-2013.

Medication (administration route)	ATC Code	Reported Errors n (%)	Consumption 2007-2013 (dispensing units**)	Errors / Consumption (10^{-6})
Ceftriaxone (IV)	J01DD04	13 (5.2)	211 939	61.3
Oxycodone* (IV, PO)	N02AA05	12 (4.8)	2 845 065	4.2
Cefuroxime (IV)	J01DC02	8 (3.2)	2 397 016	3.3
Furosemide (IV, PO)	C03CA01	8 (3.2)	2 309 210	3.5
Enoxaparin* (SC, IV)	B01AB05	8 (3.2)	1 667 588	4.8
Noradrenaline* (IV)	C01CA03	7 (2.8.)	219 495	31.9
Acetaminophen (PO, IV)	N02BE01	6 (2.4)	10 694 876	0.6
Oral hypoglycemics* (PO)	A10B	6 (2.4)	1 180 260	5.1
Propofol* (IV)	N01AX10	6 (2.4)	928 529	6.5
Quetiapine (PO)	N05AH04	4 (1.6)	1 338 320	3.0
Fentanyl* (IV, epidural)	N01AH01, N02AB03	4 (1.6)	1 036 910	3.9
Dalteparin* (SC)	B01AB04	4 (1.6)	752 268	5.3
Ropivacaine* (epidural)	N01BB09	4 (1.6)	497 022	8.1
Citalopram (PO)	N06AB04	4 (1.6)	319 618	12.5
Hydrochlorothiazide (PO)	C03AA03	4 (1.6)	204 921	19.5
Insulin* (SC, IV)	A10A	4 (1.6)	93 761	42.7
Sodium chloride 0,9% (IV)	B05BB01, B05CB01	3 (1.2)	8 390 482	0.4
Clozapine (PO)	N05AH02	3 (1.2)	1 680 402	1.8
Diazepam (PO, per rectum)	N05BA01	3 (1.2)	1 185 457	2.5
Tramadol* (PO)	N02AX02	3 (1.2)	1 103 063	2.7
Acetylsalicylic acid (cardio, PO)*	B01AC06	3 (1.2)	956 301	3.1
Olanzapine (PO)	N05AH03	3 (1.2)	770 428	3.9
Enalapril (PO)	C09AA02	3 (1.2)	390 352	7.7
Metamizol + pitofenone (PO, IV)	A03DA02	3 (1.2)	377 642	7.9
Escitalopram (PO)	N06AB10	3 (1.2)	353 920	8.5
Morphine* (IV, PO)	N02AA01	3 (1.2)	287 232	10.4
Losartan (PO)	C09CA01	3 (1.2)	218 817	13.7
Clopidogrel* (PO)	B01AC04	3 (1.2)	217 304	13.8
Allopurinol (PO)	M04AA01	3 (1.2)	185 027	16.2
Remifentanil* (IV)	N01AH06	3 (1.2)	165 384	18.1
Midazolam* (IV)	N05CD08	3 (1.2)	157 389	19.1
Nifedipine (PO)	C08CA05	3 (1.2)	128 250	23.4
TOTAL		**150 (60.2)**	**43 264 246**	**3.5**

* ISMP's High-Alert Medication for Acute Care Settings (ISMP 2014)
** Dispensing unit: tablet, capsule, vial, ampoule, injection/infusion bottle, infusion bag, sachet, transdermal patch, etc.
IV = intravenous, PO = per oral, SC = subcutaneous

A majority (80%) of the reported medication errors in this study sample actually reached the patients (Figure 16), particularly most of these errors related to oxycodone (n=11) and enoxaparin (n=8). Clearly the most common error type was administration errors (34% of all the reported medication errors, Figure 18). The proportion of actual medication errors reaching the patient was highest in administration errors (96%), while, in other error types, near misses were more common (Figure 18). Administration errors were most common with oxycodone (n=6), enoxaparin (n=6), noradrenalin (n=4) and propofol (n=4). Prescribing errors were usually related to ceftriaxone (n=5) and cefuroxime (n=4), preparing errors to ceftriaxone (n=4) and oxycodone (n=3), and dispensing errors to paracetamol (n=4), hydrochlorothiazide (n=3) and oral hypoglycemics (n=3).

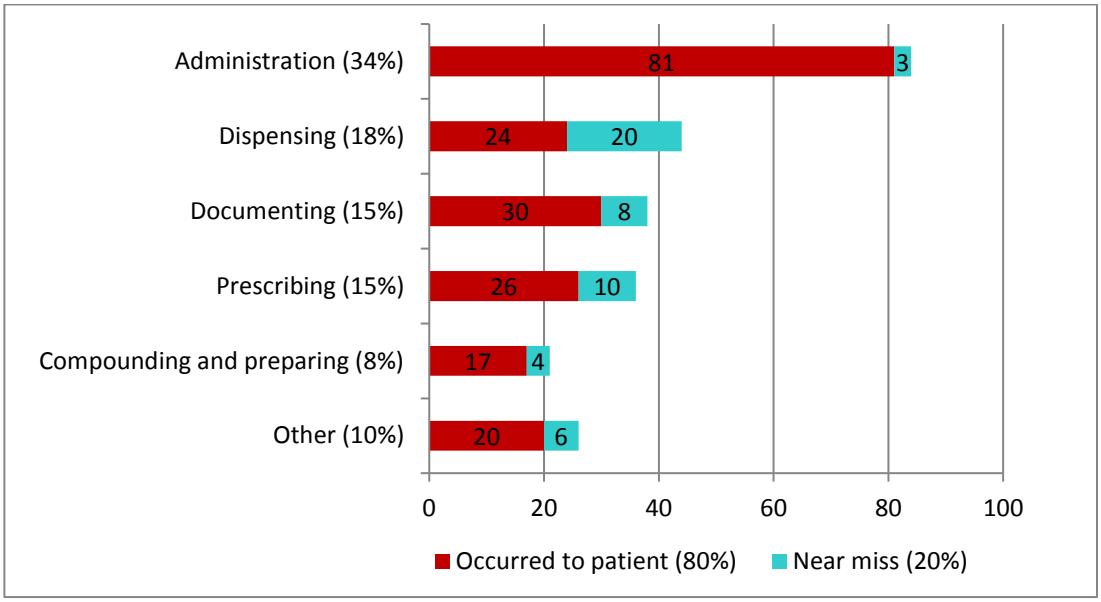

Figure 16. Nature, number and distribution of reported ME types (percentages of all the reported MEs, n=249). Other error types: unexpected reaction to a patient (n=12), information (n=3), monitoring (n=1), storage (n=1), ordering (n=1), distribution (n=1), and other than previously mentioned error type (n=7). ME = medication error.

The consequences to a patient were classified in 225 reports. Usually, the errors did not cause harm to patients (44% of the reports) or the harm was mild (35%). Moderate harm was followed in 17% (n=39) and serious harm in 3% (n=7) of cases, but no fatal medication errors were reported. ISMP's High-Alert Medications (ISMP 2014) were related to half (n=23/46) of the serious or moderate cases. The most common therapeutic groups in these cases were antithrombotic agents (13%; including ASA, clopidogrel, warfarin and enoxaparin and alteplase) and anesthetics (11%; including fentanyl, remifentanil, and propofol). The medications related to cases with serious harm (n=7; 3%) were cefuroxime, enoxaparin (n=2), ibuprofen, midazolam,

propofol and warfarin. The error types in cases usually followed by serious and moderate harm were administration (n=19) and prescribing errors (n=13). The role of prescribing errors is greater in serious or moderate cases (28%) compared to the entire dataset (15%).

In this targeted sample (n=249) medications were always reported or coded to a contributing factor to ME. It was possible to choose several contributing factors: medications alone were specified in 40% of cases and generic medications was the next most commonly specified contributing factor (34%). Other common contributing factors were courses of action (24%), communication (21%), education and induction (16%), working environment and resources (10%), and team-work (9%).

Key safety risks

In total, 120 reports were analyzed using the qualitative method (Figure 14). Key safety risks of most reported and medications included in ISMP's High-Alert List (ISMP 2014), were usually related to LASA nomenclature or packages of the medications (Table 19, Figure 17): cefuroxime/ceftazidim/ceftriaxone; ceftriaxone (Rocephalin®)/ceftriaxone and lidocaine (Rocephalin cum lidocain ®)/rocuronium; citalopram/escitalopram (Cipralex®); enoxaparin/ dalteparin; paracetamol (Panadol®)/paracetamol and codeine (Panacod®); glucosamine/metformin (Glucophage®)/glimepiride; metformin/metoprolol; and clopidogrel (Plavix®)/dabigatran (Pradaxa®). There were also safety risks related to formulary: many different proprietary names for one active substance (quetiapin), no combination tablets available (hydrochlorothiazide) and changes in the formulary (noradrenaline, ropivacaine, tramadol).

Other safety problems were related to confusion in concentrations, milligrams and milliliters (propofol, midazolam, morphine, oxycodone oral solution), confusing normal/enteric coated/slow-release/combination tablets (acetylic salicylic acid, acetaminophen/acetaminophen and codeine, furosemide, oral hypoglycemics, tramadol) and confusing infusion pumps/tubes when patient had several infusions (noradrenaline, propofol, remifentanil).

From the organizational point of view, nurses' workload (fentanyl, morphine), inadequate induction or knowledge of medications (e.g., indication, interactions, incompatibilities and generic names related to ceftriaxone, oral hypoglycaemics, propofol, oxycodone), unclear responsibilities (remifentanil) and lack of double checking (enoxaparin, dalteparin, ASA) were reasons for MEs and near misses (Table 19). In addition, there were problems with labelling syringes, infusions and tubes (fentanyl, noradrenaline) and allergy information was missing or unnoticed (cefuroxime, tramadol). In addition, hand written prescriptions (morphine) and multiphasic documentation process were found (enoxaparin) as safety risks.

Table 19. Key safety risks identified in the qualitative analysis of the medication error reports with most reported (≥4) and ISMP's High-Alert Medications (≥3; n=120).

Medication (administration route)	Key Safety Risks
Ceftriaxone (IV)	Confusing LASA names e.g. cefuroxime or ceftazidime, Rocephalin® > rocuronium, Rocephalin® > Rocephalin cum lidocaine® ceftriaxone combined to lidocaine > lidocaine overdose/poisoning risk, incompatibilities with calcium-containing solutions
Oxycodone* (IV, PO)	Mistakes in concentrations of oral solution e.g. Oxynorm® 5mg > 50 mg, confusion with morphine (oral solution), disorder in ward's medications storage, labelling syringes, hand written prescriptions (0,5mg > 6,5 mg), not noticing interactions, lack of basic knowledge and information of the medication
Cefuroxime (IV)	LASA: other cephalosporins, allergic reactions and missing/not noticing allergy information
Furosemide (IV, PO)	Documenting, administration and dispensing: confusing medications (e.g. Furesis®> Furesis Comp®, Furesis® 10mg/mg > Furesis Special® > Lasix retard® different brand names with different strengths e.g. Furesis® 20 mg and Vesix® 40 mg
Enoxaparin* (SC, IV)	Wrong dose/patient, missing dose, double dose, confusing to dalteparin (same indication, LASA vials), unclear and multiphased documenting process, lack of double checking, missing dose during dialysis
Noradrenaline* (IV)	Confusing infusions/fluid transfer tubes when patient has several infusions (e.g. propofol), insufficient labelling (syringes, infusions and tubes), using different solution concentration (depending on ward/ clinic > transitions), using undiluted noradrenalin, changes in formulary (2 mg/ml > 4 mg/ml), extravasation
Acetaminophen (PO, IV)	LASA: Confusing acetaminophen (PanadolL®) > acetaminophen + codeine (Panacod®), confusing 500 mg tablets to 1 g tablets
Oral hypoglycemics* (PO)	Confusing normal tablet + slow-release tablet; LASA: confusing glucosamine > metformin/glimepiride, metoprolol > metformin; lack of knowledge about generic names and indications; tablets containing multiple active substances > finding same dose from the formulary
Propofol* (IV)	Many concentrations 5 mg/ml; 10 mg/ml; 20 mg/m (LASA), confusing mg to ml, confusing infusion pumps or tubes during anesthesia (> noradrenalin, remifentanil, parenteral nutrition solutions), inadequate inducting
Quetiapine (PO)	Multiple brand names in the formulary, e.g. SeroquelL®, Quetiapin Mylan®, Ketipinor® and stored in an alphabetical order by the brand names in the medication room, confusing normal and slow release tablets, confusing to venlafaxine
Fentanyl * (IV, epidural)	Wrong dose, mistakes in using infusion pumps, insufficient labelling of syringes, workload of nurses
Dalteparin* (SC)	Confusing to enoxaparin (same indication, LASA), missing dose during dialysis, lack of double checking
Ropivacaine* (epidural)	Changes in formulary: Naropin® > Ropivacain Fresenius Kabi®, distributing wrong concentration from the hospital pharmacy, lack of double checking
Citalopram (PO)	Confusing escitalopram > citalopram, confusing generic/brand names, double dosing
Hydrochlorothiazide (PO)	Tablets containing multiple active substances (hydrochlorothiazide is not combined to antihypertensive medications in the formulary) > finding same dose from the formulary
Insulin* (SC, IV)	Wrong patient, confusing concentration and infusion rate, handling of insulin pumps and pens
Tramadol* (PO)	Missing/not noticing allergy information, confusing normal and slow release tablets, wrong patient, changes in formulary
Acetylsalicylic acid (cardio)* (PO)	Wrong patient or dose, confusing normal and enteric coated tablets, lack of double checking
Morphin* (IV, PO)	Confusing concentrations (2 mg/ml > 20 mg/ml), confusing to oxycodone (oral solutions), workload of nurses
Clopidogrel* (PO)	LASA: Plavix® 75 mg > Pradaxa® 75 mg, insufficient medication history taking: activating old medication chart with clopidogrel which was already stopped in primary care, prescribing to a patient with epidural analgesia > delayed discharge
Remifentanil* (IV)	Confusing to propofol or noradrenalin infusion during operation, mistakes in using infusion pumps and labelling infusion tubes, too many persons involved (flow of information, unclear responsibilities)
Midazolam* (IV)	Confusing mg and ml, LASA ampoules with amiodarone

* ISMP's High-Alert Medication for Acute Care Settings (ISMP 2014)
IV = intravenous, PO = per oral, SC = subcutaneous, LASA = lookalike, soundalike

Figure 17. Confusing drug names and packages (lookalike/soundalike = LASA).

5.2 IDENTIFYING ORGANIZATIONAL HIGH-ALERT MEDICATIONS (II)

Adverse drug reactions (ADRs) reported to the national pharmacovigilance system from HUS in 2015-2016

In total, 401 ADRs were reported during 2015 and 2016 by HUS to Fimea. The most numerous ADRs were within ATC group L (Antineoplastic and immunomodulating agents) (n=120; 30%, Figure 18). ATC groups J (Anti-infectives for systemic use) and M (Musculoskeletal system) comprised 15% (n=59) and 13% (n=42) of the reports, respectively. The most common active substances related to reported ADRs were denosumab (n=31, 8%), rivaroxaban (n=25, 6%), zoledronic acid combined with denosumab (n=15, 4%), and influenza vaccine (H1N1)v (n=13, 3%; Table 20). Osteonecrosis of the jaw was the most typically described ADR of denosumab. Rivaroxaban was reported to cause several ADRs, the majority being hemorrhages, low hemoglobin, deep-vein thrombosis, and ineffectiveness. Influenza vaccine (H1N1)v was reported to cause narcolepsy and cataplexy. Denosumab, rivaroxaban, and influenza vaccine (H1N1)v were subject to additional monitoring, as indicated in their summary of product characteristics.

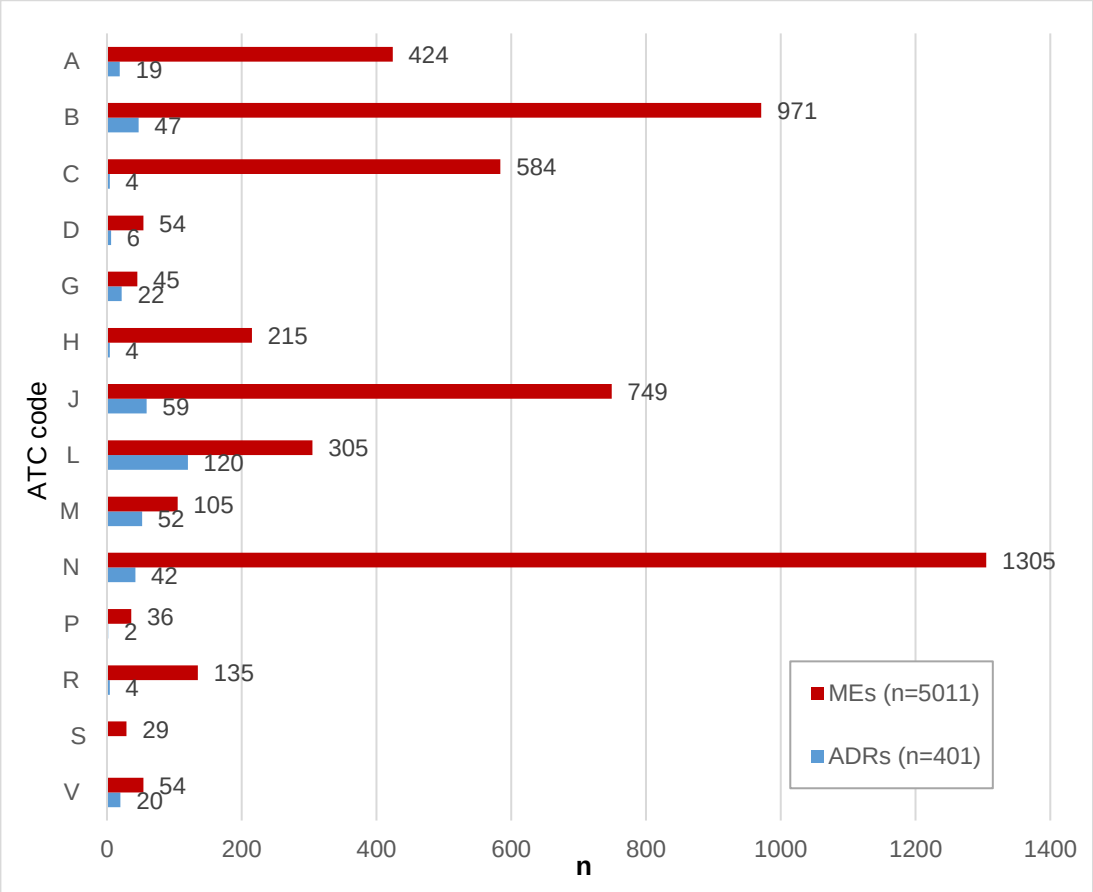

Figure 18. ATC groups of reported adverse drug reactions (ADRs; n=401) and medication error (MEs; n=5011). ATC = Anatomical Therapeutic Chemical classification system [19]. A = alimentary tract and metabolism, B = blood and blood-forming organs, C = cardiovascular system, D = dermatologicals, G = genitourinary system and sex hormones, H = systemic hormonal preparations, excluding sex hormones and insulins, J = anti-infectives for systemic use, L = antineoplastic and immunomodulating agents, M = musculoskeletal system, N = nervous system, P = antiparasitic products, insecticides, and repellents, R = respiratory system, S = sensory organs, V = various.

The highest number of ADRs relative to drug consumption was reported for denosumab (42.52), etanercept (19.23), and dimethyl fumarate (19.05; Table 20). Etanercept was described to cause neurological symptoms such as absence seizure, memory disturbance, and demyelinating disease of the central nervous system. Moreover, injection site pain and extravasation were reported. Dimethyl furmarate caused several gastrointestinal symptoms and rash with eosinophilia; one miscarriage was also reported.

The TOP10 reported ADRs involved six of the ISMP's high-alert medications: rivaroxaban, bevasizumab, iohexol, rituximab, metformin, and vemurafenib (Table 20). The reported ADRs related to bevacizumab were numerous. Iohexol and rituximab were generally reported to cause allergic and anaphylactic reactions. Rituximab was also described to cause atheromatosis and progressive multifocal leukoencephalopathy. Metformin was reported to

cause lactic acidosis. Reports about vemurafenib were usually related to skin reactions (rash, urticaria) and impaired liver function. In addition, gadoteric acid (ATC group V), apixaban (B), warfarin (B), capecitabine (L), erlotinib (L), temozolomid (L), and trastuzumab (L) were ISMP's high-alert medications with four or more ADR reports.

Table 20. TOP active substances in adverse drug reaction (ADR) reports (n=401) in 2015-2016.

	Active substance	ATC code	n (%)	Consumption[b]	ADRs / Consumption x 10^{-3}
1	denosumab ▼	M05BX04	31 (8)	729	42.52
2	rivaroxaban[a] ▼	B01AF01	25 (6)	14 505	0.17
3	zoledronic acid + denosumab ▼	M05BA08, M05BX04	15 (4)	5,098	0.29
4	influenza vaccine (H1N1)v ▼	J07BB02	13 (3)	0*	0.00
5	bevasizumab[a]	L01XC07	12 (3)	23 975	0.05
6	iohexol[a]	V08AB02	11 (3)	63,695	0.02
7	etanercept	L04AB01	10 (3)	52	19.23
	levonorgestrel	G02BA03	10 (3)	3 030	0.33
8	rituximab[a]	L01XC02	9 (2)	6 531	0.14
9	metformin[a]	A10BA02	8 (2)	260 831	0.00
	dimethyl fumarate	N07XX09	8 (2)	42	19.05
	clozapine	N05AH02	8 (2)	375,483	0.00
	vemurafenib[a]	L01XE15	8 (2)	840	0.95
10	tocilizumab	L04AC07	7 (2)	1 542	0.45
	influenza A vaccine (H1N1, H3N2), influenza B vaccine	J07BB02	7 (2)	48 921	0.01

▼ = This medicinal product is subject to additional monitoring. [a] =ISMP's high-alert medications. [b]=Consumption is reported in dispensing units (tablets, injection bottles and pens, hospital pharmacy prepared doses, etc.).
*Marketing authorization of influenza vaccine (H1N1)v and hence its consumption ended in 2009.

Medication errors (MEs) reported through the HUS' HaiPro system in 2015-2016

In 2015-2016, a total of 35,610 patient safety incidents were reported in HUS. Of these, 11,668 (33%) were related to medications, infusion fluids, and radio contrast agents. The majority of ME reports (86%) were made by nursing staff, and only 4% of ME reports came from physicians. Patients were involved in more than half (63%; n=7 321) of the MEs, and 37% (n=4,344) were near misses. The most common ME subtypes were administration (40%), documenting (17%), dispensing (17%), and prescribing errors (12%).

A specific medication related to ME was cited in only 62% of reports (n=7 201), and the HaiPro system identified a specific ATC code in 43% (n=5,011) of the cases. The most numerous ATC group in ME reports was Nervous system (N) (26%), followed by Blood and blood-forming organs (B) (19%) and Anti-infectives for systemic use (J) (15%, Figure 18). The most common active substances related to reported MEs were enoxaparin (n=376, 3%), cefuroxime (n=215, 2%), and acetaminophen (n=174, 2%; Table 21).

Table 21. TOP active substances in all medication error (ME) reports (n=11 668) in 2015-2016.

	Active substance	ATC code	n (%)	Consumption[b]	MEs / Consumption x 10^{-3}
1	enoxaparin[a]	B01AB05	376 (3)	647 245	0.58
2	cefuroxime	J01DC02	215 (2)	795 168	0.27
3	acetaminophen	N02BE01	174 (2)	3 191 627	0.05
4	oxycodone[a], oxycodone + naloxone[a]	N02AA05, N02AA55	159 (1)	849 441	0.19
5	furosemide	C03CA01	151 (1)	701 981	0.22
6	warfarin[a]	B01AA03	93 (<1)	95 716	0.97
7	tinzaparin[a]	B01AB10	87 (<1)	102 132	0.85
8	bisoprolol	C07AB07	81 (<1)	683 711	0.12
9	electrolyte solutions	B05BB01	64 (<1)	4 044 357	0.02
	quetiapine	N05AH04	64 (<1)	411 620	0.16
10	ibuprofen	M01AE01	58 (<1)	1 033 345	0.06

[a] =ISMP's high-alert medications. [b]=Consumption is reported in dispensing units (tablets, injection bottles and pens, hospital pharmacy prepared doses, etc.).

The highest number of MEs relative to drug consumption involved warfarin (0.97; n=93), tinzaparin (0.85, n=87), and enoxaparin (0.58, n=376), all of which are ISMP high-alert medications (Table 21). Oxycodone (n=159) was the fourth ISMP high-alert medication in the TOP10 active substances related to MEs. The TOP20 also contained the following high-alert medications: cyclosporine (0.55; n=56), morphine (0.62; n=53), insulin aspart (4.78; n=52), insulin glargine (4.95; n=51), noradrenaline (0.40; n=50), fentanyl (0.14; n=50), and potassium chloride concentrate (0.25; n=39). The high numbers of MEs relative to drug consumption of insulin aspart (4.78) and insulin glargine (4.95) are due to the consumption unit definition applied in the hospital pharmacy system. One consumption unit of insulin is the entire insulin pen or ampoule, which includes multiple doses, compared with, for example, enoxaparin syringe, where one unit is the syringe, which includes a single dose.

Medication errors caused severe patient harm in 20 cases (0.2%) and moderate patient harm in 376 cases (3%). The most common active substances involved in severe or moderate patient harm were enoxaparin (n=8), cefuroxime (n=7), and insulin aspart (n=6; Table 22). Amphotericin B clearly had the highest number of severe and moderate MEs relative to its consumption (18.52). Of ISMP's high-alert medications, enoxaparin, morphine, oxycodone, insulin aspart, insulin glargine, epirubicin, doxorubicin, and propofol were most commonly associated with MEs causing severe or moderate patient harm (Table 22).

Table 22. TOP reported active substances related to medication errors (MEs) (n=376) causing serious (n=20) or moderate (n=356) harm to a patient in 2015-2016.

	Active substance	ATC code	n (%)	Consumption[b]	MEs / Consumption x 10^{-3}
1	enoxaparin[a]	B01AB05	8 (2)	647 245	0.01
2	cefuroxime	J01DC02	7 (2)	795 168	0.01
3	insulin aspart[a]	A10AB05	6 (2)	10 869	0.55
4	amphotericin B	J02AA01	5 (1)	270	18.52
	epirubicin[a]	L01DB03	5 (1)	4 909	1.02
	morphine[a]	N02AA01	5 (1)	85 009	0.06
	paracetamol	N02BE01	5 (1)	3 191 627	0.00
5	insulin glargine[a]	A10AE04	4 (1)	10 299	0.39
	bisoprolol	C07AB07	4 (1)	683 711	0.01
	oxycodone[a], oxycodone + naloxone[a]	N02AA05, N02AA55	4 (1)	849 441	0.00
6	benzylpenicillin	J01CE01	3 (<1)	126 960	0.02
	doxorubicin[a]	L01DB01	3 (<1)	6 121	0.49
	propofol[a]	N01AX10	3 (<1)	306 821	0.01
	lithium	N05AN01	3 (<1)	114 802	0.03

[a] =ISMP's high-alert medications. [b]=Consumption is reported in dispensing units (tablets, injection bottles and pens, hospital pharmacy prepared doses, etc.).

The ME subtype "unexpected reaction in a patient" was reported 107 times (0.9%). The most commonly reported medications causing an unexpected reaction in a patient were iohexol (n=8) and gadoteric acid (n=6, Table 23). Extravasation (n=27) was the most commonly reported unexpected reaction. It was linked to iohexol (n=8), epirubicin (n=5), doxorubicin (n=5), cisplatin (n=3), bendamustine (n=2), etoposide (n=2), cytarabine (n=1), and acetaminophen (n=1). Hypersensitive reactions (e.g. allergic and anaphylactic reactions) were the second most commonly reported reactions (n=9), and these were related to gadoteric acid (n=6), cefuroxime (n=2), and cisplatin (n=1). Amphotericin B-induced tachycardia and morphine-induced respiratory insufficiency were also noted. Amphotericin B had the highest number of MEs causing unexpected reactions relative to its consumption (18.52). This was followed by bendamustine (1.20) and epirubicin (1.02). The majority (77%) of the TOP active substances causing an unexpected reaction in a patient were ISMP high-alert medications. Although the ME subtype is termed "unexpected reaction in a patient", most of these are known ADRs of the reported medications.

Table 23. TOP reported active substances related to medication error subtype unexpected reaction to a patient (n=107).

	Active substance	ATC Code	n (%)	Consumption**	MEs / Consumption x 10^{-3}
1	iohexol*	V08AB02	8 (8%)	63 695	0.13
1	gadoteric acid*	V08CA02	6 (6%)	27 664	0.22
2	amphotericin B	J02AA01	5 (5%)	270	18.52
2	epirubicin*	L01DB03	5 (5%)	4 909	1.02
3	doxorubicin*	L01DB01	4 (4%)	6 121	0.65
4	cisplatin*	L01XA01	3 (3%)	5 169	0.58
4	olanzapine	N05AH03	3 (3%)	248 347	0.01
5	cefuroxime	J01DC02	2 (2%)	795 168	0.00
5	bendamustine*	L01AA09	2 (2%)	1 670	1.20
5	cytarabine*	L01BC01	2 (2%)	5 516	0.36
5	etoposide*	L01CB01	2 (2%)	7 959	0.25
5	morphine*	N02AA01	2 (2%)	85 009	0.02
5	acetaminophen	N02BE01	2 (2%)	3 191 627	0.00

*ISMP's high-alert medications. **Consumption is reported in dispensing units (tablets, injection bottles and pens, hospital pharmacy prepared doses, etc.)

According to the ADR and ME reports, there are many therapeutic groups and active substances that can be found in the ISMP's list of high-alert medications (ISMP 2010, ISMP 2014). In HUS, antineoplastic agents, anticoagulants and antithrombotics, opioids, insulins and metformin, radio contrast agents, cyclosporine, noradrenaline, potassium chloride concentrate, propofol, and ropivacaine should be considered high-alert medications (Table 24). When high-alert medications were identified from the TOP30 active substances in all ADR and ME reports, warfarin was the only substance found in both lists (Table 24). Iohexol is the only active substance found among TOP10 active substances in the reported ADRs and MEs concerning unexpected reactions (Tables 20 and 23). Additionally, another radio contrast agent, gadoteric acid is the third and last ISMP's high-alert medication which can be found both the TOP30 ADR reports and the TOP30 MEs concerning unexpected reactions (Table 24).

Table 24 ISMP's high-alert medications in TOP30 active substances of adverse drug reaction (ADR) and medication error (ME) reports (divided into all MEs, severe or moderate MEs, and ME subtype unexpected reaction in a patient). Bolded medications are both in ADR and ME reports.

Therapeutic group (ATC code)	TOP high-alert medications in ADR reports (n=401)	TOP high-alert medications in ME reports		
		All MEs (n=11,668)	**MEs causing severe or moderate harm (n=376)**	**MEs causing unexpected reaction in a patient (n=107)**
Anticoagulants and antithrombotics (B)	rivaroxaban (6%,n=25) apixaban (2%, n=6) **warfarin (1%, n=4)**	enoxaparin (3%, n=376) **warfarin (<1%, n=93)** tinzaparin (<1%, n=87)	enoxaparin (2%,n=8) tinzaparin (<1%, n=2)	
Antineoplastic agents (L)	bevasizumab (3%, n=12) rituximab (2%, n=9) vemurafenib (2%, n=8) cabecitabine (2%, n=6) trastuzumab (1%, n=5) erlotinib (1%, n=4) temozolomid (1%, n=4)		epirubicin (1%, n=5) doxorubicin (<1%, n=3) cisplatin (<1%, n=2)	epirubicin (5%, n=5) doxorubicin (4%, n=4) cisplatin (3%, n=3) bendamustine (2%, n=2) cytarabine (2%, n=2) etoposide (2%, n=2)
Insulin and hypoglycemic agents (A)	metformin (2%, n=8)	insulin aspart (<1%, n=52) insulin glargine (<1%, n=51)	insulin aspart (2%, n=6) insulin glargine (1%, n=4) insulin human (<1%, n=2) insulin determir (<1%, n=2)	
Opioids (N)		morphine (<1%, n=53) fentanyl (<1%, n=50)	morphine (1%, n=5) oxycodone (1%, n=4) fentanyl (<1%, n=2)	morphine (2%, n=2)
Radio contrast agents (V)	**iohexol (3%, n=11)** **gadoteric acid (2%, n=6)**			**iohexol (8%, n=8)** **gadoteric acid (6%, n=6)**
Other		cyclosporine (<1%, n=56) noradrenaline (<1%, n=54) potassium chloride concentrate (<1%, n=39)	propofol (<1%, n=3) cyclosporine (<1%, n=2) ropivacaine (<1%, n=2)	

5.3 ENHANCING MEDICATION HISTORY RECORDING AND IDENTIFYING DRUG-RELATED PROBLEMS OF OLDER EMERGENCY PATIENTS (III)

Patient characteristics

A total of 150 ED patients (75 of HUS and 75 of KUH) were included. The patient characteristics are presented in Table 25. The patients in KUH were slightly older and used more medications than those in HUS.

Table 25. Patient characteristics (N=150).

	HUS (n=75)	KUH (n=75)
Age, years		
mean (range)	76 (65–92)	79 (66–98)
Sex, n (%)		
female	46 (61%)	42 (56%)
male	29 (39%)	33 (44%)
Specialty, n (%)		
surgery	30 (40%)	
internal medicine	27 (36%)	NA*
neurology	13 (17%)	
pulmonary	5 (7%)	
Number of used medications, n (range)		
all medications	15 (6–23)	17 (8–27)
long-term medications	9 (4–20)	11 (6–23)
PRN medications**	4 (0–11)	5 (1–14)
medications prescribed in the ER	2 (0–8)	1 (0–4)

* secondary/primary care ED: patients are arriving without a referral and meet general physician first; ** pro re nata = as needed

Accuracy of the medication charts

Every patient in HUS (n=75) and all but one patient in KUH 99% (n=74) had discrepancies in their medication history as taken by the ED nurse or physician when compared to the medication chart reconciled by the clinical pharmacists (Table 26). Nearly four-fifths, 79%, of the patients in HUS and 65% in KUH had at least one omitted long-term medication and the majority of these (63% in HUS and 47% in KUH) were prescription medications. Omissions of PRN (pro re nata, used as needed) medications were even more common: 92% of the patients in HUS and 91% in KUH had these and they were most commonly related to over-the-counter medications (72% in HUS and KUH). In HUS 33% and, in KUH, 48% of the patients had medications in the admission medication chart which were not actually in use. In addition, 56% of the patients in HUS and 43% in KUH had discrepant dose, strength or other incorrect information in their admission medication chart.

Table 26. Discrepancies in admission medication chart obtained by the nurse/ physician compared to the medication charts reconciled by the pharmacists.

Discrepancy	HUS (n=75)	KUH (n=75)
	n (%)	n (%)
Omission of long-term medication	**59 (79%)**	**49 (65%)**
Prescription medications	47 (63%)	35 (47%)
Over-the-counter medications	14 (19%)	24 (32%)
Dietary supplements and herbal products	29 (39%)	13 (17%)
High-alert medication	3 (4%)	1 (1%)
No discrepancies	16 (21%)	26 (35%)
Omission of PRN* medication	**69 (92%)**	**68 (91%)**
Prescription medications	45 (60%)	39 (52%)
Over-the-counter medications	54 (72%)	54 (72%)
Dietary supplements and herbal products	25 (33%)	28 (37%)
High-alert medication	3 (4%)	0 (0%)
No discrepancies	6 (8%)	7 (9%)
Medications on admission chart but not in use	**25 (33%)**	**36 (48%)**
Prescription medications	23 (31%)	30 (40%)
Over-the-counter medications	5 (7%)	16 (21%)
Dietary supplements and herbal products	1 (1%)	0 (0%)
High-alert medication	2 (3%)	1 (1%)
No discrepancies	50 (67%)	39 (52%)
Discrepant dose, strength or other incorrect information	**42 (56%)**	**32 (43%)**
Correct medication chart (no discrepancies)	**0 (0%)**	**1 (1%)**

*PRN = pro re nata, as needed.

Drug-related problems associated to admission diagnoses

As many as 92% (n=69/75) of the patients in HUS and 100% in KUH had clinically relevant drug-related problems (Table 27). Drug-related problems were associated with admission diagnoses of 12 patients (16%) in HUS and 22 patients (29%) in KUH. There were 30 (2.5 per patient) patients in HUS and 43 (2.0 per patient) in KUH for drug-related problems associated to admission diagnoses. The majority of these were adverse drug reactions or clinically problematic interactions (Figure 19 and Figure 20).

Table 27. Clinically relevant drug-related problems (DRPs, HUS: n=316; KUH: n=446) identified in the medication reviews of 150 patients.

	HUS			KUH		
Findings	Patients (n=75)	DRPs (n=316)	DRPs / patients	Patients (n=75)	DRPs (n=446)	DRPs / patients
Drug-related problems certainly or probably related to admissions	n=12 (16%)	n=30 (9%)	2.5	n=22 (29%)	n=43 (9%)	2.0
Acute drug-related problems	n=19 (25%)	n=50 (16%)	2.6	n=54 (72%)	n=111 (25%)	2.1
Non-acute drug-related problems	n=67 (89%)	n=236 (75%)	3.5	n=75 (100%)	n=293 (66%)	3.9
No drug-related problems	n=6 (8%)			n=0 (0%)		

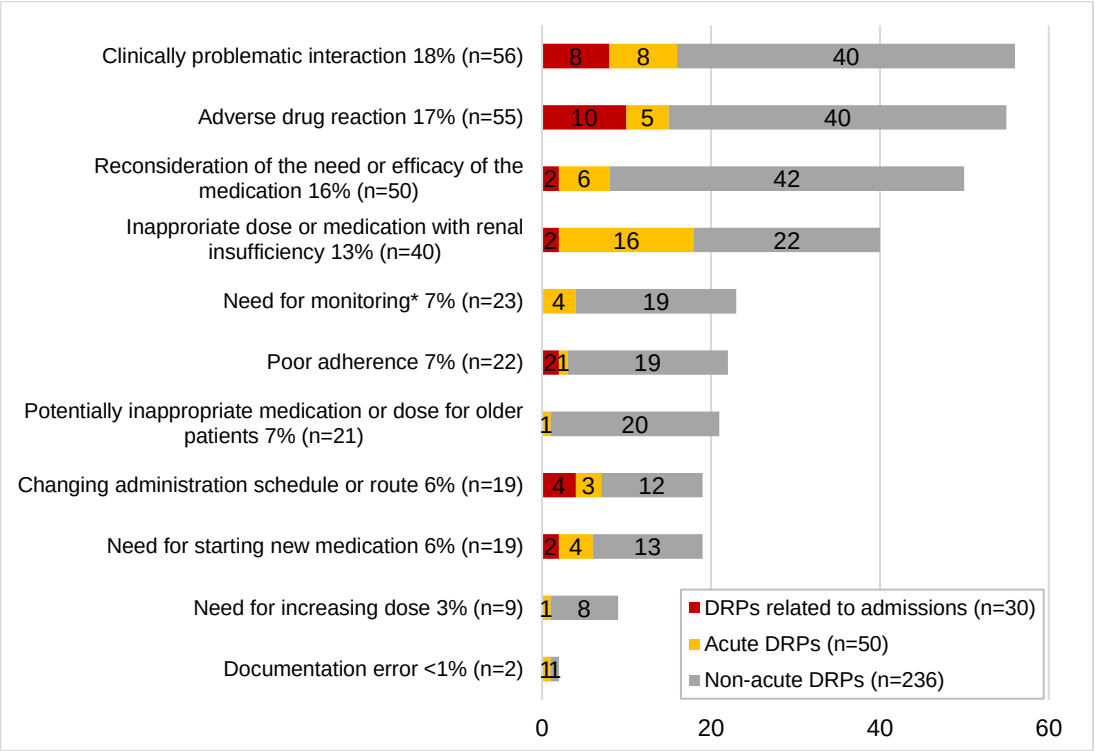

Figure 19. The clinically relevant drug-related problems (DRPs, n=316) obtained from 75 medication reviews in HUS. *Monitoring: therapeutic drug monitoring (n=9), checking laboratory results (n=7), bone mass measurement (n=4), mini-mental state examination (n=3).

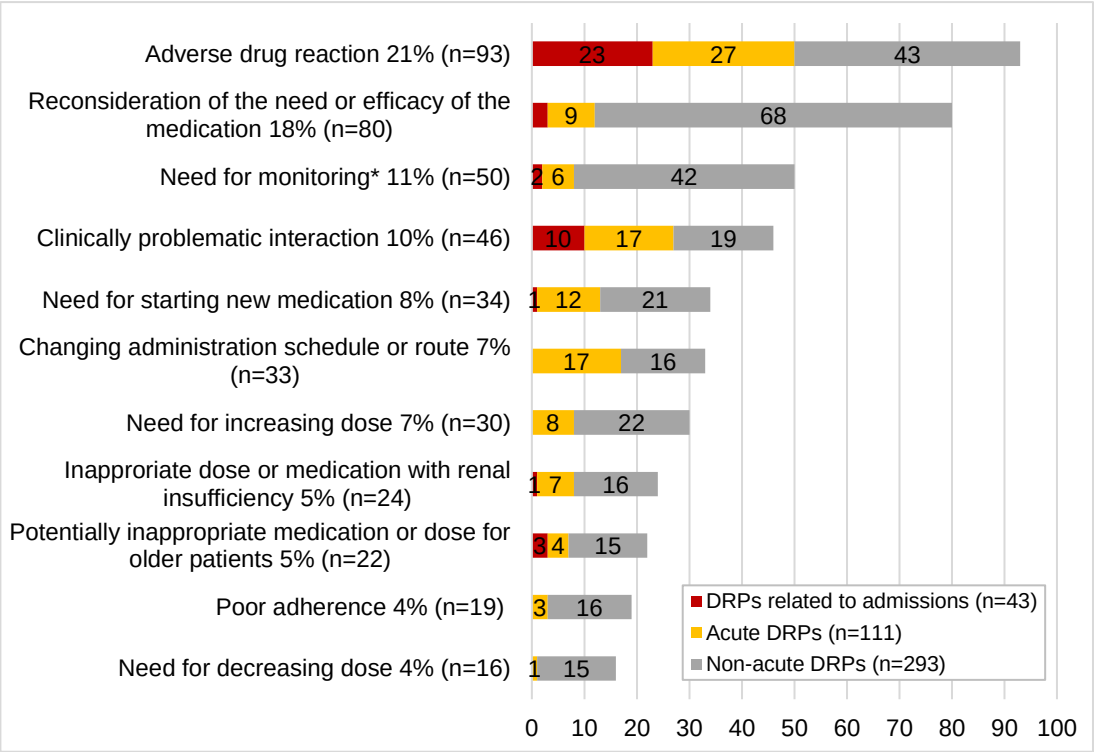

Figure 20. The clinically relevant drug-related problems (DRPs, n=447) obtained from 75 medication reviews in KUH. *Monitoring: checking laboratory results (n=35), orthostatic measurement (n=9), bone mass measurement (n=4), therapeutic drug monitoring (n=2).

ISMP's high-alert medications (ISMP 2010, ISMP 2014) contributed to the admission of eight patients (11%) in HUS and six patients (8%) in KUH (Table 28). These medications included antithrombotics, opioids, oral hypoglycaemic agents and cytostatics. Antithrombotics were related to bleeding in seven patients. Cytostatics were related to infections and fever for two patients. Empirically established ADRs of opioids such as constipation and bile duct spasm were related to admission diagnoses of four patients. Ineffective medications (opioids, oral hypoglycaemic agents) were related to two admissions.

In addition to the high-alert medications, other medications were related to the diagnoses of four patients (5%) in the HUS group and 15 patients (10%) in the KUH group (Table 29). Antihypertensives and diuretics were usually related to a weakened general condition, dizziness, collapses and falls. Anticholinergic agents and benzodiazepines were related to falls, whereas antibiotics were related to diarrhea.

Other acute drug-related problems requiring action in the ED

There were 19 patients (25%) in HUS that presented with 50 acute drug-related problems (2.6 per patient, Table 27) that required action in the ED. The majority of these problems were related to the taking of an inappropriate dose or medication by a patient with renal insufficiency (32%) followed by clinically problematic interactions (16%), reconsidering the need or efficacy of the medications (12%) and ADRs (10%, Figure 19). A typical patient in the HUS group had renal insufficiency with several inappropriate medications or doses (NSAIDs, ACE inhibitors, statins, ASA, codeine, cefuroxime, metformin, digoxin, methotrexate or radio contrast media). Other common suggestions that were made were recommendations for using proton pump inhibitors and paracetamol instead of ibuprofen for analgesia to patients at risk of bleeding.

In the KUH group, there were 54 patients (72%) who had presented with 111 acute drug-related problems (2.1 per patient, Table 27). Acute DPRs were usually related to adverse drug reactions (24%), clinically problematic interactions (15%), change of administration schedule or route (15%) or starting new medications (11%, Figure 20). Typical acute findings in KUH were related to adverse drug reactions which were treated with new medications.

Table 28. Admission diagnoses (HUS: n=8, KUH: n=6) associated with high-alert medications* (ISMP 2010, ISMP 2014).

Unit	Admission diagnoses	Medications	High-Alert Medication Group*
HUS	dyspnoea, anaemia	rivaroxaban* + fluvoxamine	Antithrombotics
HUS	anaemia, melena	warfarin* + ASA*	Antithrombotics
HUS	haematuria	enoxaparin (+ renal insufficiency)	Antithrombotics
HUS	retroperitoneal hemorrhage	warfarin* (+ amitriptyline), methotrexate*, citalopram (+ omeprazole), metylprednisolon, paracetamol	Antithrombotics, Cytostatics
HUS	infection, fever seizure	hydroxyurea*	Cytostatics
HUS	stomach pain, constipation	tramadol* + codeine* + doxepin + hydrochlorothiazide + bisoprolol	Opioids
HUS	bile duct spasms	paracetamol + codeine*	Opioids
HUS	ulcers in left-foot toes, f-P glucose 11	metformin* + pioglitazone* (ineffective)	Oral hypoglycaemic agents
KUH	melena	ASA + low dose ASA + meloxicam + ibuprofen	Antithrombotics
KUH	weakened general condition, anaemia	warfarin* + ASA* + tramadol* + methotrexate* + prednisolon	Antithrombotics, Cytostatics, Opioids
KUH	stomach pain, haematemesis, melena	ASA* + citalopram + tramadol* + metamizole	Antithrombotics, Opioids
KUH	fever	hydroxyurea*	Cytostatics
KUH	leg pain worsening	paracetamol + codeine* (ineffective)	Opioids
KUH	intestinal obstruction	paracetamol + codeine* + atenolol + atorvastatin	Opioids

ASA = acetylsalicylic acid

Table 29. Medications other than high-alert associated with admission diagnoses (HUS: n=4, KUH: n=15).

Unit	Admission diagnoses	Medications	Medication Group
HUS	fever, diarrhea	lymecycline + calcium + magnesium	Antibiotics, Minerals
HUS	stomach pain, high CRP	etoricoxib + low dose ASA (without PPI)	Antithrombotics, NSAIDS
HUS	headache, dizziness, nausea	dipyridamole + bisoprolol + valsartan + mokso-nidine furosemide (ortostatism, temporal relationship)	Antithrombotics, Antihypertensives, Diuretics
HUS	dizziness, nausea	bisoprolol (patient reports, temporal relationship)	Antihypertensives
KUH	diarrhea	several antibiotic regimens	Antibiotics
KUH	atrial fibrillation	metoprolol (non-adherence)	Antiarrythmic agents, Antihypertensives
KUH	high/low blood pressure	amlodipine switched to valsartan two weeks ago (due to swollen ankles)	Antihypertensives
KUH	severe dizziness	candesartan + lercanidipine + hydrochlorothiazide + temazepam	Antihypertensives, Diuretics,Benzodiazepines
KUH	collapse	furosemide + telmisartan + bisoprolol (+ low blood pressure)	Antihypertensives
KUH	fall, urinary tract infection, hyperkalemia	losartan (hyperkalemia) oxybutynin + amitriptyline + chlordiazepoxide	Antihypertensives, Anticholinergics
KUH	fall	valsartan + hydrochlorothiazide + furosemide + spironolactone (+ low blood pressure, dehydration)	Antihypertensives, Diuretics
KUH	fall	amlodipine + bisoprolol + lisinopr	Antihypertensives
KUH	fall	solifenasine + metoprolol + candesartan (+ hyponatremia)	Antihypertensives, Anticholinergics
KUH	fall	oxazepam + diazepam + levomepromazine + tamsulosin	Antipsychotics, Benzo-diazepines, Urologicals, Alpha blockers
KUH	fall, weakened general condition	lisinopril + hydrochlorothiazide + metoprolol + simvastatin	Antihypertensives, Diuretics, Statins
KUH	weakened general condition	furosemide (+ renal insufficiency + dose increase)	Diuretics
KUH	cholecystitis	Dida®	Herbal Supplement
KUH	arrhythmia, nausea, heartburns	digoxin (+ renal insufficiency)	Inotropic medications
KUH	atrial fibrillation	isosorbide mononitrate	Nitrates
KUH	diverticulitis, constipation leg muscle cramps	atorvastatin	Statins

ASA = acetylsalicylic acid, PPI = proton pump inhibitor

Non-acute drug-related problems

Two-thirds (89%, n=67) of patients in HUS had non-acute drug-related problems that required action after discharge e.g. in primary care (Table 27). There were 236 drug-related problems (3.5 per patient), which were predominantly related to the reconsideration of the need or efficacy of the currently used medication (18%), adverse drug reactions (17%), clinically problematic interactions (17%), renal insufficiency (9%) and potentially inappropriate medication or dose for the older patients (9%, Figure 19). Every patient in the KUH group had non-acute drug-related problems (Table 27). There were 293 non-acute DRPs (3.9 per patient), which were typically related to reconsidering the need or efficacy of the medication (23%), adverse drug reactions (15%) and monitoring (14%, Figure 20).

5.4 NATIONAL EVOLUTION OF HOSPITAL CLINICAL PHARMACY SERVICES CONTRIBUTING TO MEDICATION SAFETY IN 2011-2016 (IV)

Survey participants and coverage

In 2011, the responses were received from 20/24 of the hospital pharmacies (83%) and 51/94 medicine dispensaries (54%), yielding an overall response rate of 60% (n=71/118). In 2016, 18/24 of hospital pharmacies (75%) and 9/28 of the independent medicinel dispensaries (32%) responded to the follow-up survey resulting in the overall response rate of 52% (n=27/52, Figure 2). Among the respondents all five university hospital pharmacies, central hospital pharmacies (n=12), a community hospital pharmacy (n=1) and medicine dispensaries in the public sector (n=9, Figure 21).

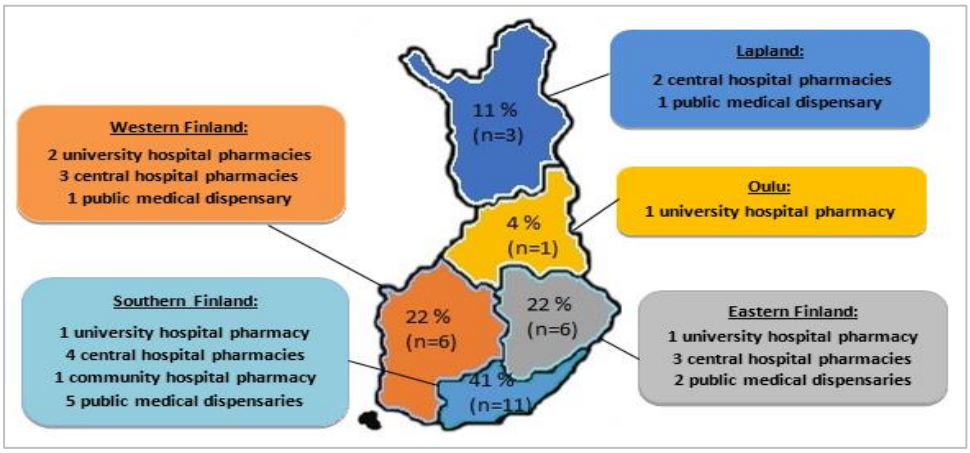

Figure 21. Location of the hospital pharmacies and medicine dispensaries that responded to survey in 2016 (n=27/52) according to the latest Finnish counties.

Clinical pharmacy services in 2016 compared to 2011

In 2016, clinical pharmacy services were provided in 85% (n=23) of the responding units, the majority of which were hospital pharmacies (74%, n=17). The corresponding proportion in 2011 was 51% of the responding units, and more than half (56%) of them were medicinel dispensaries. In 2016, only 15% (n=4) reported not providing clinical pharmacy services (49% in 2011) and these were a central hospital pharmacy and three medicine dispensaries. The main reason for not providing clinical pharmacy services was the small number of pharmacy staff, which is common in medicine dispensaries as each of them typically have a workforce of one-two pharmacists.

The number of clinical pharmacists had increased during the 5-year study period: in 2011, the number of full-time (meaning office hours throughout the paper) working clinical pharmacists was 103 and part-time ones was 54. In 2016, there were 134-215 full-time and 13-65 part-time clinical pharmacists (according to the response scale used in 2016). The variation in the number of clinical pharmacists in 2016 was biggest between university hospitals which all had full-time clinical pharmacists but the number of them varied from 1-50. Some of the clinical pharmacists worked in only one unit (ward, clinic), but typically they divided their work time between two-three units in both 2011 and 2016. The number of hospitals with pharmacy services increased: in 2016, full-time clinical pharmacy services were provided in 179-201 units and part-time in 192-236 units (according to the response scale used in 2016 and in 2011, full-time services were provided in 108 and part-time services in 134 units. According to both surveys, the services were most commonly available in surgical and internal medicine wards. All five university hospitals had clinical pharmacy services in intensive care, pediatric and oncology units in 2016.

Evolution of performed tasks of clinical pharmacists

Tasks performed by clinical pharmacists in 2011 and 2016 are presented in Figure 3. The Figure shows the fast extension and implementation of the new tasks, most of which were related to improving medication safety. Of the 12 new tasks reported in 2016, the most widely performed were developing instructions for medication use and medication therapy (91% reported), taking part in creating and updating medication safety plans (87%), taking part in multiprofessional working groups (87%) and developing medication use processes by using data from medication error reports (78%, Figure 22). In 2016, clinical pharmacy services covered all crucial stages of the medication-use process (Figure 23). The major new contributions during the 5 years are the new role in developing, auditing and instructing medication use-processes with the systems approach (Reason 2000), conducting medication reconciliations (+63%) and counselling patients (+39%, Figure 22).

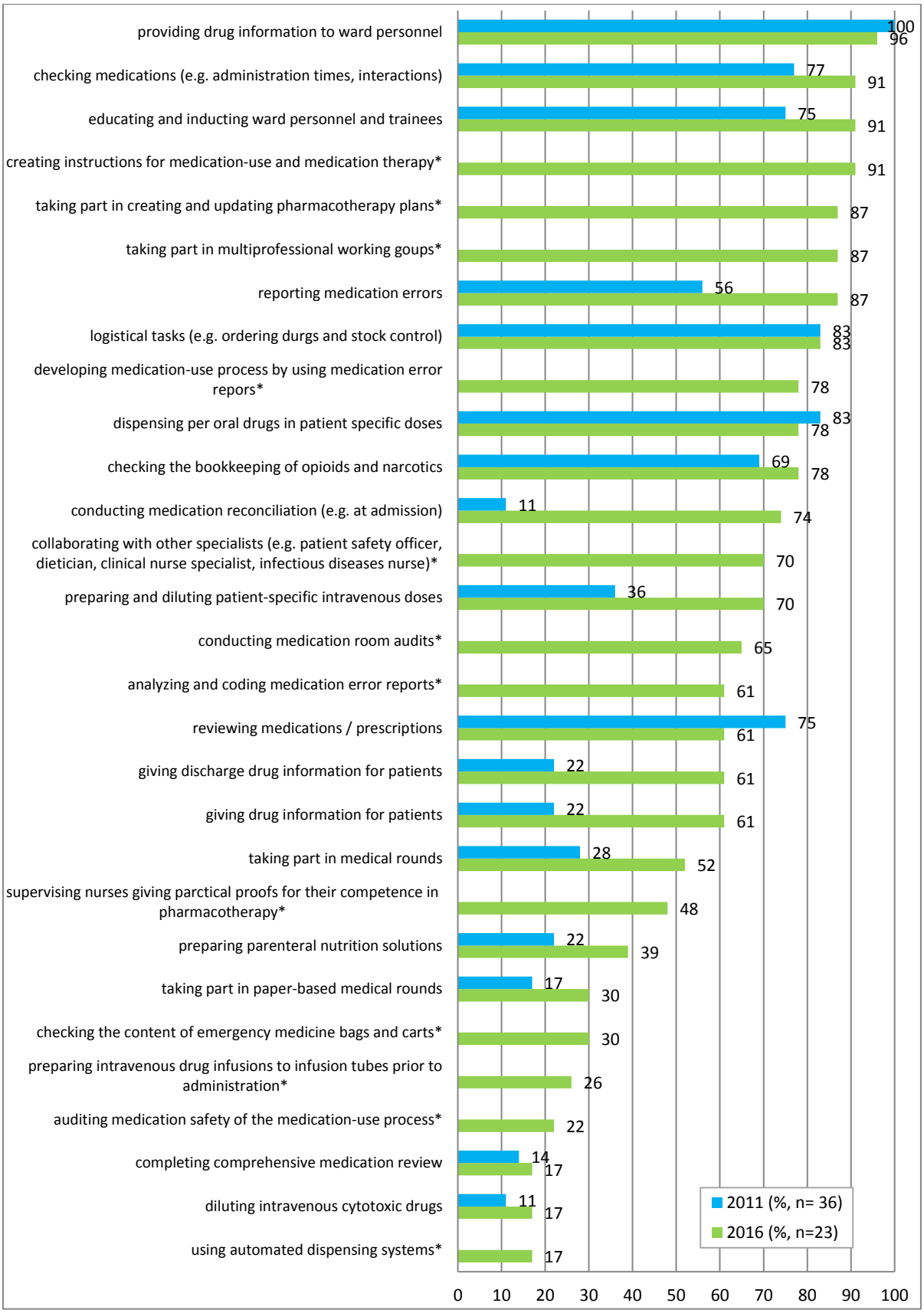

Figure 22. Reported tasks of clinical pharmacists (%) in 2011 and 2016. *New tasks (n=12) added to the year 2016 survey.

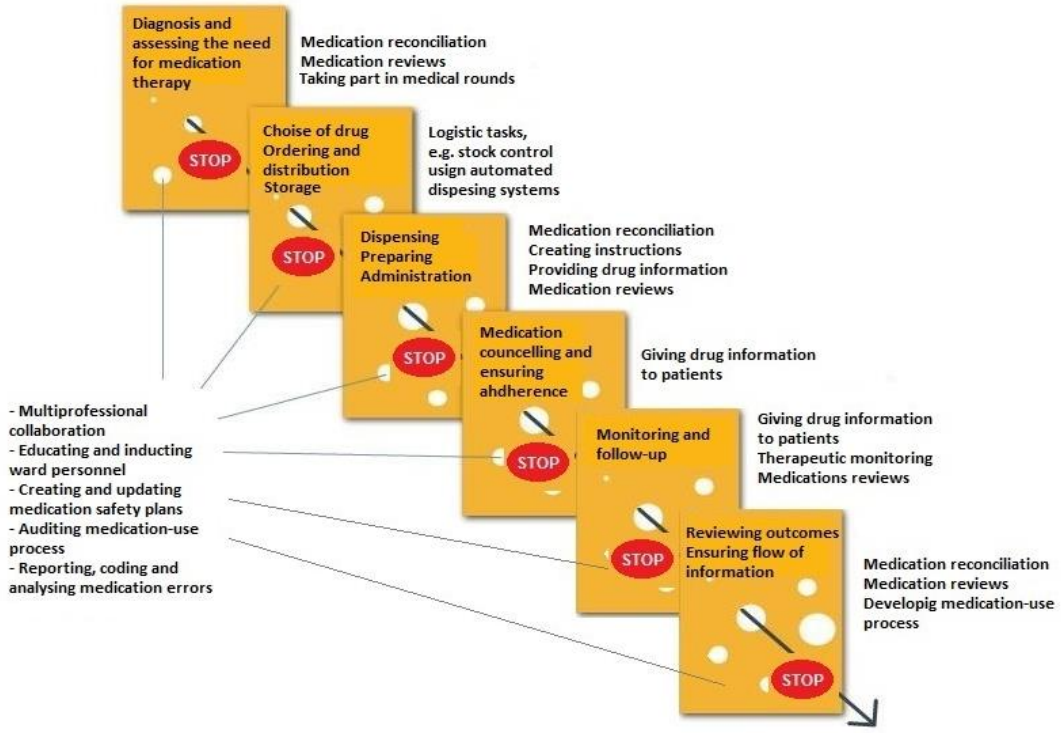

Figure 23. Illustration of the evolution of the tasks of the clinical hospital pharmacists in Finland by 2016 as reported by the responding hospital pharmacies and medicine dispensaries (n=27). The figure demonstrates the coverage of the clinical pharmacy services of the stages of medication use process by applying Reason's Swiss Cheese Model (modified, Reason 2000).

Clinical pharmacists had access to patient records in almost all (96%) and access to laboratory results in the majority (83%) of the responding units in 2016. The proportion of logistical tasks (e.g. ordering and stock control) remained the same (83% reported). In 2016, the respondents were asked to estimate how much time was spent on logistical tasks compared to other tasks. Most respondents (59%, n=16) estimated that at most half (5-50%) of the time was spent on such tasks, while in some units (30%, n=8), only 5% or less of the working time was used on logistical tasks. A variation between the tasks of different clinical pharmacists was reported: some performed only logistical tasks while others did not have any logistical tasks. In an open question the respondents reported their thoughts about the most important tasks of the clinical pharmacists: drug information to ward personnel (48%, n=13), medication reconciliation (33%, n=9), inducting ward personnel (26%, n=7), and developing the medication-use process (22%, n=6).

Strategy, management and future plans

A strategic management of clinical pharmacy services had increased: a plan or strategy for clinical pharmacy services had been devised in 61% of the responding units in 2016, while in 2011 such a plan or strategy existed for only

20% of the responding units. In 2011, only 42% reported having a manager dedicated to clinical pharmacy services while, in 2016, the majority (74%) reported this. In 2016, half of the responding units (52%) were familiar with the European Statements of Hospital Pharmacy (EAHP 2014) that could be utilized to develop a strategy for hospital pharmacy services.

In both 2016 and 2011, the most common plan for the future in the responding hospital pharmacies and medicine dispensaries was extending the clinical pharmacy services to new care units within their healthcare organization. In 2016, almost half (44%) of the responding units had a plan to redevelop and extend clinical pharmacists' role to more clinical and patient-oriented duties. Similar plans were reported already by 2011, but a need for continuing education to adopt a more patient-oriented role was recognized. The use of information and automation technology was seen as the key to change the logistical role of clinical pharmacists in both years. In 2016, 30% of the respondents had the opinion that clinical pharmacy services should increasingly be provided in primary care, nursing homes, homecare and social care units. Additionally, in 2016, almost two-thirds (62%) of the responding units thought that pharmacists could take a position as medication safety coordinators in the future while the remainder (38%) had no opinion.

Importance of continuing education

Participation in long-term continuing education had clearly increased during 2011-2016 (Figure 24). Only one hospital pharmacy and one medicine dispensary reported that their clinical pharmacists had not participated in any long-term continuing education in 2016. It was perceived that the clinical pharmacists were able to use the expertise acquired through the long-term continuing education well (70% of the responding units) or slightly (30%). Almost half (48%) of the respondents thought that participating in continuing education had supported the development of the patient-centered tasks of clinical pharmacists.

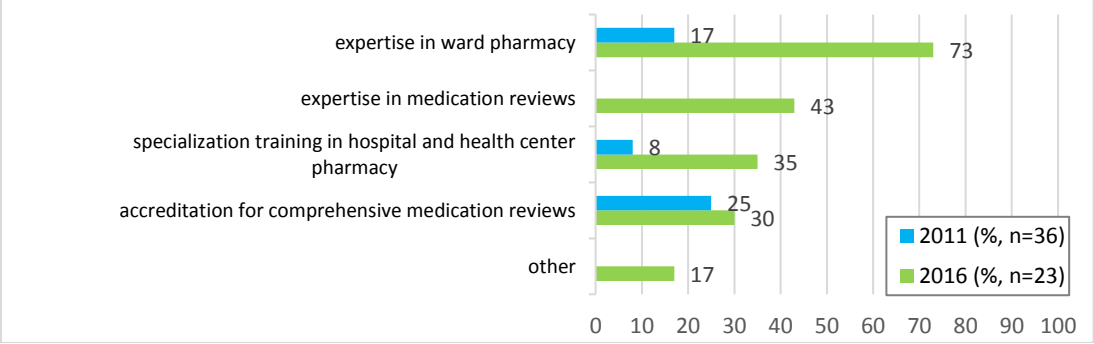

Figure 24. Long-term continuing education of some clinical pharmacists in the responding units (%). Other (n=4): expertise in patient safety (n=2), master of clinical pharmacy (n=1), hospital's internal continuing education program (n=1). Education to expertise in medication reviews was not provided in 2011.

Benefits and outcomes of clinical pharmacy services

Of the responding units, 33% (n=9) had assessed benefits and outcomes of clinical pharmacy services since 2011 (Figure 6). The results were typically reported internally to their own organization (n=7), in the national congresses (n=4) or in national scientific journals (n=2). Increased multiprofessional collaboration, saved working time of nurses, and savings in drug consumption were the most commonly reported assessed and achieved benefits and outcomes in 2011 and 2016. In 2016, common patient safety benefits which were not asked or reported in 2011 were the increased reporting of medication errors (n=5) and increased number of accurate medication charts (n=5).

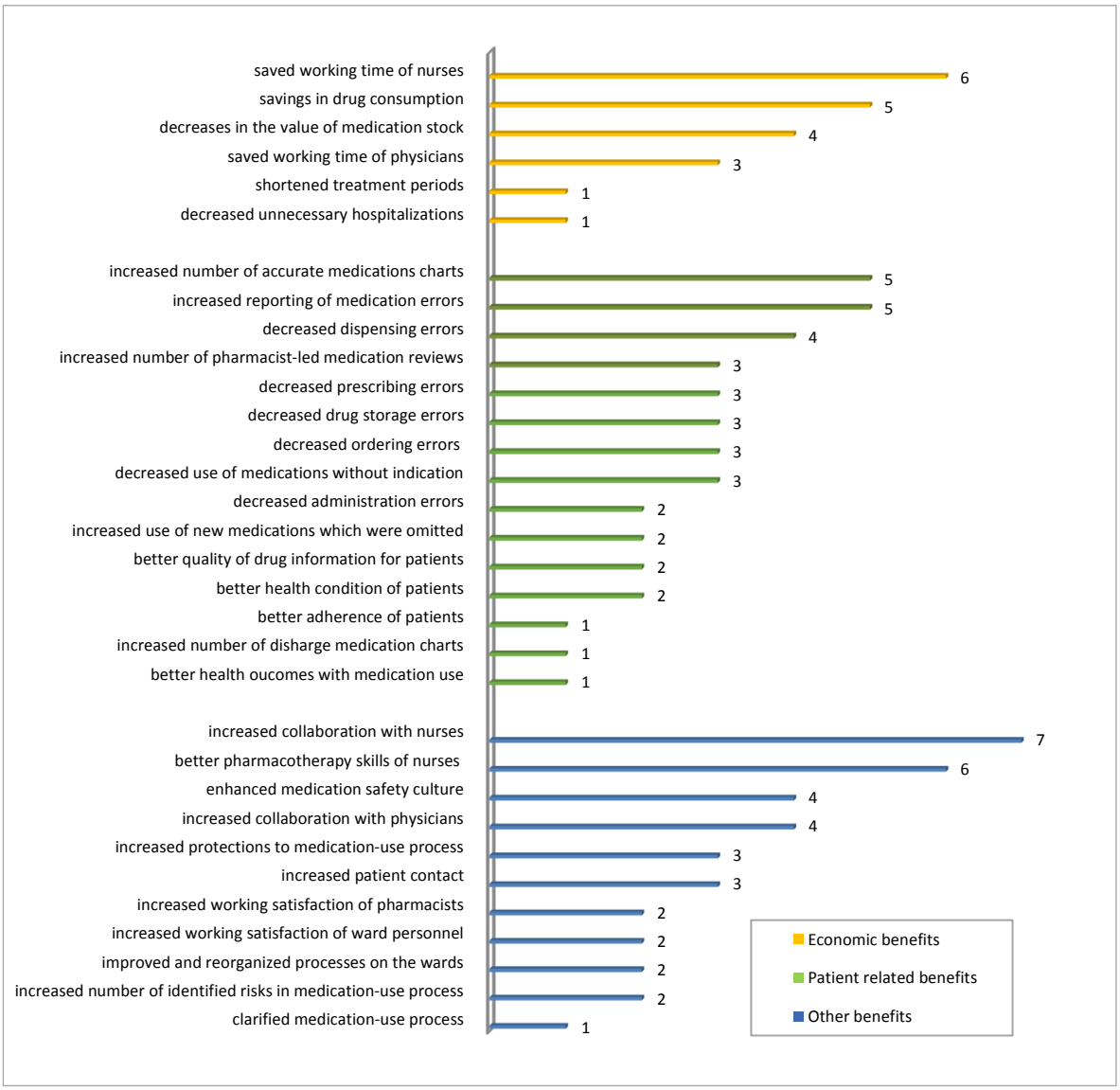

Figure 25. Benefits and outcomes of clinical pharmacy services that were self reported and to have been assessed and achieved in 33% of the responding units (n=9) in 2016.

6 DISCUSSION

6.1 DEMONSTRATING A METHOD FOR IDENTIFYING UNIVERSITY HOSPITAL'S HIGH-ALERT MEDICATIONS BY USING ME REPORTS (I)

This study provided a novel approach to identify organizational high-alert medications by using data on medication error reports (HaiPro). We combined quantitative and qualitative approaches to identify high-alert medications and their key safety risks in a large tertiary care hospital (HUS) by assessing a targeted sample of error reporting data from a longer period of time (7 years). ISMP's list was helpful and worked as a reference tool for our findings (ISMP 2014). Targeting the sample in the pilot study was important in order to condense the data aiming to identify high-alert medications: the targeted sample revealed more high-alert medications (33%) than a random sample (10%), when ISMP's high-alert medication list was used as a reference (ISMP 2014).

Approximately 33% (n=91) of all reported medications in the study sample and 67% of medications related to MEs causing serious patient harm are ISMP's high-alert medications (ISMP 2014). A majority of the most commonly reported high-alert medications in this study, e.g. opioids, anticoagulants and antithrombotics, insulins (Table 18), are identified as high-risk medications in the other studies (Bates et al. 1995, Kanjanrat et a. 2003, Krähenbühl-Melcher et al. 2007, Cousins et al. 2011, Beckett et al. 2012, Saedder et al. 2014). Most commonly reported therapeutic groups and single high-alert medications were also widely used in HUS (Table 17 and 18). However, the highest number of errors compared to consumption were found with therapeutic groups having low consumption, such as drugs for bone diseases, antigout preparations and anti-Parkinson drugs. High-alert medications, such as insulin, noradrenaline, and midazolam had a relatively high number of reported MEs compared to their low consumption. These medications could be considered to have an elevated risk for MEs and actions might be needed to make their use safer.

Parenteral medications seem to pose a higher risk than enteral preparations, as half of the medication errors were related to parenteral administration even though the enteral medications are more commonly used. However, parenteral administration is common in tertiary care hospitals. According to the findings of this study, risk factors, such as extravasation, chemical and microbiological stability and incompatibilities with parenteral medications or fluids, and possible confusion with several infusion tubes and pumps, need special consideration (Table 19). Parenteral cefuroxime, ceftriaxone, enoxaparin, insulin, midazolam, noradrenalin and propofol,

which had either the highest error ratios or were causing serious patient harm, are in particular need of safety actions.

As in many earlier studies from a long period of time since the 1990s, administration errors were the most common ME type reported in the current study, and these errors usually (96%) reached the patients (Figure 16) (Bates et al. 1995, Hicks et al. 2004, Krähenbühl-Melcher et al. 2007, Keers et al. 2013). Although frequent, administration errors were seldom reported to have severe consequences for the patient. The case was, however, different with prescribing errors as their proportion was almost 2-fold (28%) in errors causing moderate or serious harm to patients compared to the entire dataset (15%). They also caused relatively more harm than other error types. Prescribing errors and near misses were usually related to ceftriaxone and cefuroxime. Lack of awareness of allergy information with prescribing cefuroxime was highlighted in this study. Patients' allergy information should thus be better documented and made available for prescribers, e.g., electronic prescribing systems should warn the prescribers about contraindicated medications (ISMP 2011).

Qualitative analysis of ME reports revealed the confusion with drug nomenclature and formulations, e.g. confusing normal and enteric coated, slow-release or combination tablets (Table 19). How the generic and proprietary drug names are pronounced and written poses a risk when the drug is selected from the drug storage or processed in IT systems. Confusion related to product names is found to be one of the major risks to MEs (Kohn et al. 2000, CoE 2006a, Aspden et al. 2007, Hoffman and Proulx 2003, ISMP 2015). The ISMP has published a list of confused drug names (ISMP 2015) but it cannot be fully transferred to a Finnish context because of the different proprietary names in the US. The use of Tall Man lettering is suggested to highlight the differences in spelling of drug names (e.g. ceFTRIAxone – ceFUROxime). Moreover, the safe storage of LASA medications (not side by side) should be considered.

Due to public tendering, formularies are changing every 2-3 years in Finland. Changing formulary proprietary names are risky (Table 19), because nurses have to do the generic substitution during the medication-use process. This was found in the qualitative analysis of ME reports, and the same problem has been identified in Norway (Håkonsen et al. 2017). Generic prescribing is not common in Finland, although generic substitution has been in use since 2003. The HUS's patient information system suggests prescribers use formulary proprietary names, but it is not mandatory. Regarding formulary management, medication safety aspects are lacking in the current formulary selection criteria, which makes it difficult to rate them in public tendering. Thus, European collaboration would be needed to create medication safety rating scales applicable to public tendering purposes.

6.2 IDENTIFYING ORGANIZATIONAL HIGH-ALERT MEDICATIONS: COMPARISON BETWEEN ME AND ADR REPORTS (II)

The most commonly reported (TOP10) active substances in ADR and ME reports are entirely different from each other (Tables 20 and 21). The most commonly reported ATC groups in ADR and ME reports were had very few similarities (Figure 18). When high-alert medications were identified from the TOP30 active substances in all ADR and ME reports, warfarin was the only substance found on both lists (Table 24). In addition, the most commonly reported active substances (TOP10) in ADR reports and in MEs causing severe/moderate harm or an unexpected reaction (Tables 20 and 22) differed. Interestingly, iohexol is the only active substance found among TOP10 active substances in the reported ADRs and MEs concerning unexpected reactions (Tables 20 and 23). This is an important finding because Fimea has particularly requested that healthcare professionals report all serious and/or unexpected ADRs (Fimea 2017). Are these MEs somehow regarded differently by the reporters than the unexpected ADRs that are reported to Fimea? Alarmingly, amphotericin B, which clearly had the highest number of MEs causing severe/moderate harm and unexpected reactions relative to its consumption (Tables 22 and 23), had no ADR reports.

In the EU Directive 2010/84EU1, which came into force in July 2012, the term 'adverse drug reaction' is redefined as 'a response to a medicinal product that is noxious and unintended, resulting not only from the authorized use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse, off-label use, and abuse of the medicinal product'. This is confusing, because ADR reporting is drug and molecule oriented. For example, high-alert medications are safe when they are used in correct way, but if any errors in their use occur, the consequences are usually devastating for patients (ISMP 2014). Medication error reporting systems are needed for learning and to provide information on the real-life medication-use process, including human error, and they are the key element in developing patient and medication safety (Kohn et al. 2000, CoE 2006a, Holmström et al. 2015a).

International efforts have been made to expand the role and scope of national pharmacovigilance centers to include also MEs (The Erice Manifesto 2007, Bencheikh and Benabdallah 2009, Pal et al. 2015, Cousins et al. 2015). In the UK, the National Health Service (NHS) and the Medicines and Healthcare Products Regulatory Authority (MHRA) have started a collaboration, sharing ADR and ME incident data (Cousins et al. 2015). The aim is to simplify and increase ME reporting, improve data report quality, and maximize learning and guide practices to minimize harm from MEs. They are also jointly issuing a web-based Patient Safety Alert, which provides feedback to reporters and motivates them to report.

There is a need for similar collaborations in other countries. In Finland, ADR reports are collected nationally by Fimea and ME reports are collected within organizations. Although MEs can also be reported through ADR reports, the information gathered with these two separate systems is clearly very different. One reason for this might be the profession of the reporters: ADR reports are primarily created by physicians, while the majority of ME reports come from nursing staff. In Finland, only physicians and pharmacists are able to report ADRs to Fimea with an electronic reporting form that can be submitted online. A traditional, paper-based reporting by mail option is possible for all, including nurses and patients. Perhaps the unexpected reactions reported to the ME system (Table 23) originate from nurses who have easier access to the ME reporting system than the paper-based ADR system. Furthermore, it is typical that only a small portion of the ADRs are reported to the authorities, which can also be seen in this data: the total number of reported ADRs from HUS in 2015-2016 was considerably lower (n=401) than the number of reported MEs (n=11,668).

According to the ADR and ME reports, there are many therapeutic groups and active substances that can be found in the ISMP's list of high-alert medications (ISMP 2010, ISMP 2014). In HUS, antineoplastic agents, anticoagulants and antithrombotics, opioids, insulins and metformin, radio contrast agents, cyclosporine, noradrenaline, potassium chloride concentrate, propofol, and ropivacaine should be considered high-alert medications (Table 24). The results of this study are somewhat similar to those of a pilot study (I) with smaller data from HUS's ME reports. However, some well-known high-alert medications, such as digoxin and methotrexate, were missing from both the pilot study and this study (Krähenbühl-Melcher 2007, DMA 2010, NPSA 2011, Saedder et al. 2014, CEC 2015).

In addition, there are high-risk active substances that are not regarded as high-alert medications by ISMP, but are nevertheless known to cause severe ADRs, e.g. clozapine, non-liposomal amphotericin B, and lithium (Tables 20 and 22). Moreover, medicinal products that are subject to additional monitoring (e.g. new active substances, biological medicines) should receive special attention from clinicians. In contrast, cefuroxime, acetaminophen, furosemide, and bisoprolol are medications that are widely used, but usually well tolerated. Due to their high consumption volume, the possibility of making errors is also higher, explaining their presence on the TOP lists of reported MEs (Table 21).

6.3 ENHANCING MEDICATION HISTORY RECORDING AND IDENTIFYING DRUG-RELATED PROBLEMS OF OLDER EMERGENCY PATIENTS (III)

The accurate medication history recording and the medication chart is the basis for safe pharmacotherapy (JCAHO 2005, IHI 2011, WHO 2017) and a starting point for medication reviews. We found that the current process of medication reconciliation at the admission of older ED patients is not satisfactory in Finland and the older patients had clinically problematic DRPs, of which a remarkable number also contributed to ED visits. The magnitude of the medrec problem is illustrated by the finding that only one patient out of the study sample of 150 had an accurate admission medication chart in two study sites in HUS and KUH. Incorrect medication history recorded at admission has been found to lead to prescription errors (Dobrzanski et al. 2002) and may complicate the identification of the correct admission diagnosis (Tam et al. 2005).

This risk has now also been identified in the Rational Pharmacotherapy Action Plan (MSAH 2018a), which is aiming to ensure an accurate medication chart with establishing a patient-specific electronic medication chart to the national patient data repository (Kanta) and with collaborative medication reconciliation procedures in all transitions of care. Implementing good practices related to medication reconciliations has also been in focus in the joint action of European Union Network for Patient Safety and Quality of Care (PaSQ 2012). In general, adequate resources (time and staff) are not allocated to the medication reconciliation process in hospitals. Moreover, responsibilities between healthcare professionals have not been explicitly demarked or agreed upon. Clinical pharmacists are not widely assigned for recording medication history and the medication reconciliation processes in Finland even though there is evidence of the benefits of their involvement from other countries with more advanced clinical pharmacy practices (De Winter et al. 2010, Mueller et al. 2012).

Our study showed that it is possible to prospectively identify and solve clinically relevant drug-related problems of older ED patients with a pharmacist-led medication reconciliation and review. The medication review procedure used is applicable to acute care settings, because it does not impede or slow down the ED admission or the processing times. We have no exact data on the time spent per patient in the ED admission process, but the process was designed not to prolong the treatment time of the patients. The medication reconciliation process took approximately 10-30 minutes per patient and medication reviews usually took 1-2 hours per patient. It should be noted that using the knowledge of clinical pharmacists at this level will save time in the long run because it allows more time for the nurses and physicians to concentrate on treating the patient.

Earlier studies have shown that 10-30% of hospital stays for older patients are drug-related (Hanlon et al. 1997, Beijjer and Blaey 2002). In this study 16%

of HUS patients and 29% of KUH patients had drug-related problems that were certainly or probably linked to admissions (Table 27). In addition, other acute drug-related problems that required actions at ED were identified for 19% of HUS patients and 72% of KUH patients. As many as 89% in HUS and every patient in KUH had drug-related, non-acute problems, which should be resolved later after ED discharge, e.g. in primary care. This reveals that medication reviews should also be conducted on older patients with polypharmacy in non-acute settings.

The clinical pharmacists were able to identify the patients with clinically relevant drug-related problems by using the agreed upon criteria. Hence, there is no urgent need for a referral for a medication review by a physician or nurse. All the reported drug-related problems were accepted by the study's supervising physicians and are thus clinically relevant. The clinical pharmacists were able to perform an effective medication review after only a short period of training. Earlier studies show that medication reviews reduce ED visits and an inpatient medication review conducted by pharmacists in close contact with physicians might lead to fewer admissions and lower morbidity (Gillespie et al. 2009, Chistensen and Lund 2016. An inpatient clinical pharmacist service in the ED setting may also improve the safety of prescribing drugs and the patients' health-related quality of life (Bladh et al. 2011).

The results of medication reconciliations were similar in both study EDs, but the results of the medication reviews showed some differences between HUS and KUH groups. These disparities between the two centers can be explained by the differences in the patient characteristics and the method of operation between the two ED units. Patients are admitted at HUS tertiary ED only by referral or are taken there by ambulance. The findings for HUS were, therefore, characteristic of a more severe setting (e.g. more severe admission diagnoses and more high-alert medications related to admissions; Table 28) and there were more drug-related problems per patient than that found for the KUH group (Table 27). Moreover, there were also primary care patients in the secondary/primary ED of KUH who had come directly from home with several admission diagnoses of symptoms and signs e.g. dizziness, weakened general condition and falls (Table 28 and 29) and the patients at KUH were slightly older and used more medications (Table 25) than their HUS counterparts. Although the findings at KUH were less severe compared to HUS, they are no less important. If these drug-related problems are not resolved, the patients will burden the healthcare system with repeated visits and readmissions.

This study (III) provided additional information about high-alert medications of older ED patients at the admission stage. The drug-related problems identified in the medication reviews accumulated for certain specific medications, which enabled the identification of unit-specific high-alert medications. High-alert medications listed in the ISMP were involved in the admission of eight patients (11%) in HUS and six patients (8%) in the KUH group (Table 28) (ISMP 2011, ISMP 2014). These included antithrombotics,

cytostatics, opioids and oral hypoglycaemic agents. The antithrombotics and cytostatics were also the leading causes of inadvertent drug-related deaths in HUS in 2000 and in 2012 (Juntti-Patinen et al. 2006, Lapatto-Reiniluoto et al. 2015). Regarding the non-high-alert medications, antihypertensives and diuretics were commonly related to admission diagnoses in this study (Table 29). When drug-related visits to a HUS district hospital ED were studied in 2001-2002, cardiovascular drugs were one of the leading causes for ADRs (Juntti-Patinen et al. 2006).

6.4 NATIONAL EVOLUTION OF HOSPITAL CLINICAL PHARMACISTS' CONTRIBUTIONS TO MEDICATION SAFETY WITHIN 2011-2016 (IV)

This national study showed a remarkable change in the pharmacists' involvement in patient care and ensuring medication safety in the Finnish hospitals within a relatively short time period of 5 years in 2011-2016. This change can be seen in the workforce resources and tasks performed by clinical pharmacists in care units (Figure 22, Figure 23). Their contributions have, remarkably, extended towards interventions prioritized in international and national patient and medication safety recommendations (Kohn et al. 2000, CoE 2006a+b, MSAH 2009, THL 2011, MSAH 2011, WHO 2017. Moreover, clinical pharmacists' competences have evolved to support patient and medication safety initiatives (Figure 24).

The relatively rapid improvement has been possible with the support of national patient and medication safety initiatives and guidelines (MSAH 2005, MSAH 2009, THL 2011, MSAH 2011), pharmacists' involvement in establishing these policies and making long-term continuing education and accreditation programs available for pharmacists with a focus on a systems approach to patient and medication safety (Reason 2000, WHO 2011). A crucial element in this development has been the establishment of the HaiPro system and the involvement of hospital pharmacies and medicine dispensaries in analyzing the data for learning purposes within their organizations. Reporting medication errors and related research have revealed medication safety risks and their characteristics in the Finnish healthcare system, which have laid the foundation for managing the risks (Juntti-Patinen et al. 2002, Mustajoki 2005, Lindén-Lahti et al. 2009, Pitkä 2009, Ruuhilehto et al. 2011, Eronen 2015, Lapatto-Reiniluoto et al. 2015, Härkänen et al. 2016, Holmström 2017, Tyynismaa et al. 2017, Hakoinen et al. 2017) and facilitated pharmacists' contributions to ensuring safe medication practices in hospitals.

Recommended system-based actions to improve medication safety were widely performed by clinical pharmacists in Finnish hospitals in 2016 (Figure 3) and they amply cover the crucial stages of medication-use process (Figure 4). The actions are in line with the European hospital pharmacy statements, particularly with those concerning pharmacists, ensuring quality assurance

strategies for medicine use processes (5.2), reporting of adverse drug reactions and medication errors (5.4), and ensuring that the information needed for safe medicines use, including both preparation and administration, is accessible at the point of care (5.9; EAHP 2014).

During the last 5 years, the most notable increase has taken place with conducting medication reconciliations, for example, at admission (+63%) despite it not being reported as a future plan in 2011. Medication reconciliation was not explicitly mentioned as a concept in patient safety and medicines policy documents published in Finland in the beginning of the 2000s (MSAH 2005, MSAH 2011). The Medicines Policy 2020 had set a goal for collaborative medication reviews and medication lists, particularly for older people and those using multiple medications (MSAH2 2011). In many other countries and international recommendations, medication reconciliation has been prioritized as one of the key strategies to prevent ADEs and improve patient safety at all transitions in care (IHI 2011, WHO 2017). In the US, medication reconciliation was recommended already by 2005 in the Hospitals' National Patient Safety Goals established by the US Joint Commission on Accreditation of Healthcare Organizations (JCAHO) which also established guidelines for performing medrec (JCAHO 2005). In Europe, medrec has been prioritized, for instance by the second EU Patient Safety and Quality program, PASQ (PASQ 2012).

Despite recommendations and guidelines, medication reconciliation practices are challenging to perform and EAHP evaluated that it was the most poorly implemented statement (4.4) in Europe in 2015 (EAHP 2014, Underhill and Gibbons 2015). The reasons for poor implementation were that pharmacists did not generally have access to patient information systems or direct contact to patients. According to this study, in 2016, clinical pharmacists had access to patient records in almost all (96%) responding units, which is in line with the European hospital pharmacy statement 4.3 (EAHP 2014). Pharmacists should also ensure an accurate recording of all allergy and other relevant medicine-related information in the patient's health record (5.8, EAHP 2014). The importance of updated and accurate medication charts has recently been addressed in Finland in the Rational Pharmacotherapy Action Plan by 2023, which also covers the development of electronic patient information systems and establishing a patient-specific electronic medication chart to the national patient data repository (Kanta) (MSAH 2018a, MSAH 2018b). The goal of the program is to facilitate implementation of rational pharmacotherapy in the ongoing social and healthcare reform in Finland (Kangas and Kalliomaa-Puha 2018).

Our follow-up study revealed that positive development had occurred in strategic planning and managing clinical pharmacy services in hospitals during 2011-2016. However, the content and quality of clinical pharmacy services are not uniform even inside the same organization. It was also positive that more than half (52%) of the responding units were familiar with the European Statements of Hospital Pharmacy (EAHP 2014) that could also be

utilized to standardize clinical pharmacy services in Finland. A common goal in the future plans of the responding units in our national survey was to shift the focus of pharmacists' work from logistics to patient care-oriented tasks. Automation technology (e.g. automated dispensing systems) is arriving in Finnish hospitals, which releases time of clinical pharmacists from drug logistics to be reallocated for patient care tasks supporting rational pharmacotherapy and medication safety (MSAH 2017c, MSAH 2018c). Furthermore, Finnish healthcare reform (Kangas and Kalliomaa-Puha 2018) will enable the reform or current legislation (Medicines Act 395/87) related to the number of hospital pharmacies (MSAH 2017c, MSAH 2018c). This allows the merging of hospital pharmacies with overlapping responsibilities and will release hospital pharmacy staff to patient care (MSAH 2017c, MSAH 2018c). It is crucial to be prepared with clinical pharmacy skills in order to be able to provide pharmaceutical care at this point.

Our national follow-up study revealed that pharmacists' participation in long-term continuing education and accreditation training related to pharmaceutical care and system-based medication safety work had increased remarkably during the last 5 years (Figure 24). The majority (70%) of the respondents reported that they are able to use their expertise achieved from long-term continuing education well and almost half (48%) of the respondents thought that continuing education had helped them to adopt a more patient-oriented role. The history of long-term continuing education of clinical pharmacy and medication safety is not lengthy in Finland: during the first decade of the 21st century, the Faculty of Pharmacy in the University of Helsinki started to systematically study and educate about patient and medication safety issues. A clinical pharmacy-oriented hospital pharmacy specialization program has been available since 2010 (Laaksonen et al. 2011). Practice and competence development methods and research of practices are in focus (Holmström 2015b). Postgraduate accreditation training for comprehensive medication review (CRM) started in 2008 (Leikola et al. 2009, Leikola et al. 2016). Later, a shorter, one-year training program for medication reviews and accreditation training for ward pharmacy has also been available. Furthermore, the education of basic degrees in pharmacy is in reform to meet the growing need for clinical pharmacy skills. The latter is also addressed in the European hospital pharmacy statement 6.1 (EAHP 2014).

In addition to enhancing the skills and knowledge of clinical pharmacists, outcome research related to the clinical pharmacy services is crucial for the development. The relative number of responding organizations which had evaluated the benefits or outcomes of clinical pharmacy services increased from 16% to 33% during 2011-2016. The most commonly reported achieved benefits in 2016 were related to work of nurses, e.g. saving their working time, improving their pharmacotherapy skills and increasing their collaboration with pharmacists (Figure 6). Moreover, savings in drug consumption, increased number of accurate medication charts and increased medication error reporting were common. However, only a few organizations had

published their results nationally and international publications were missing. This area needs development according to European hospital pharmacy statement 6.4. (EAHP 2014) and has also been identified in in the Rational Pharmacotherapy Action Plan (MSAH 2018d). Furthermore, documenting clinical pharmacy interventions to the patient's health record according to European hospital pharmacy statement 4.3 (EAHP 2014), enables the more rigorous evidence of outcomes related to clinical pharmacy services' impact on, for instance, readmissions, treatment periods and mortality. These should be studied and published nationally and internationally.

6.5 RELIABILITY AND VALIDITY OF THE RESEARCH METHODS (I-IV)

Studies I-II provided a novel, hospital-specific approach to high-alert medications and complements the earlier studies in Finland (Lindén-Lahti et al. 2009, Pitkä 2009, Ruuhilehto et al. 2011, Eronen 2016). This study demonstrates how data of medication-error reporting systems can be used to develop medication safety, which needs improvement in many countries (Holmström 2012, Holmström 2015a). At the time of Study I, HaiPro did not create structural data of specific medications related to MEs. We had no resources to analyze the entire dataset from 2007-2013 (n=18,136) manually, so we performed a pilot study and used reports where medications were reported or coded as contributing factor to MEs (n=263). Those were confirmed to include more high-alert medications than a random sample. However, this sample represented only 1.5% of the entire dataset (n=18,136) and further research with a more extensive dataset was needed. Hence, we applied the same method Study II with the entire organizational dataset on ADR (n=401) and ME (n=11,668) reports in 2015-2016.

ADR and ME reports cannot be regarded as prevalence data because the reporting is voluntary. It has been estimated that only 14% of actual MEs are reported to ME systems (Levonson 2012) and the percentage of reported ADRs seems to be even lower (Lapatto-Reiniluoto et al. 2015). Moreover, limitations in the classification of ME data have been identified (Holmström 2017), but Studies I-II concentrated on medications related to MEs, and not, for instance, to the stage of medication use-process or on severity of MEs.

Many earlier studies about high-risk medications are carried out with quantitative methods to measure error ratios, types and medications related to errors (Krähenbühl-Melcher et al. 2007, Cousins et al. 2011, CEC 2012). In the Study I, the qualitative analysis of ME reports revealed the latent reasons (key safety risks) for MEs in the medication use-process, which could not be discovered using only quantitative methods (Table 19). This enables the development of safer medication-use processes, which is important as 25-44% of MEs are estimated to be preventable (Nebeker et al. 2004, Aspden et al. 2007, Levinson 2010, Beckett et al. 2012).

We identified several high-alert medications (I-II), but some well-known high-alert medications, e.g. digoxin, methotrexate, and theophylline, were missing in both studies (Krähenbühl-Melcher 2007, DMA 2010, NPSA 2011, ISMP 2014, Saedder et al. 2014, CEC 2015). Further studies are needed to gain a more comprehensive understanding of these multifaceted safety problems of high-alert medications in different settings and specialties in HUS (e.g., pediatrics, intensive care, emergency, and oncological wards). A literature search and expert opinions should also be employed when compiling hospital-specific high-alert medication lists. The results of Study II, combined with the further qualitative analysis of MEs, were used to compile a hospital-specific list of high-alert medications.

Study III focused only on Finnish, home-dwelling older (≥65 years old) ED patients, which might be regarded as a limitation. The aim, however, was to demonstrate the need for enhancing the recording of medication history and identification of DRPs at admission of older ED patients. Classification of DRPs was conducted practice-oriented with the medication review form (Appendix 3) to achieve easy and feasible medication review procedure for ED setting. However, using published DRP classification systems (Strand 1990, (Basger et al. 2015) would have made the results more comparable to other similar studies.

Patients receiving homecare were excluded, because their medication charts were considered to be better managed. According to a recent Finnish study, the majority of the homecare clients had discrepancies between in-home interview data and electronic medical records, and 40% of these discrepancies were clinically important (Tiihonen et al. 2015). Hence, homecare patients might also benefit from medication reconciliation and medication reviews. The differences between the findings of the medication reviews conducted in HUS and KUH can be explained by the differences in the patient details and in the respective ED unit procedures. Medication reviews were conducted in HUS and KUH by different teams, which may have affected the findings. The clinical pharmacist for KUH introduced the clinical pharmacist for HUS to the medication review procedure before the study commenced in order to harmonize the medication reviews and minimize the risk of discrepancy due to differences in procedures. The teams had several meetings during the study and the analyses of these data were made in close collaboration with the study personnel of both centers.

The results of Study IV can be generalized nationally due to the good response rates 2011: 60% and 2016: 52%. Additionally, the coverage of hospital pharmacies serving university and central hospitals, providing the majority of the clinical pharmacy services, was 83% in 2011 and 75% in 2016. The survey method was applicable and provided a good understanding of the evolution of the Finnish clinical pharmacy services during 2011-2016 and future prospects. We sent only one survey per unit, which may have caused difficulties in responding due to the wide variety between the tasks of the pharmacists in each unit.

6.6 PRACTICAL IMPLICATIONS

Organizational level

At the time of Study I, HaiPro did not create structural data for specific medications related to MEs. This study revealed a need for a development of the HaiPro tool. For HUS's request, since the beginning of 2015, it has been possible to structurally document medications involved in MEs by using proprietary names and ATC codes and create top reports related to these. This makes the identification of high-alert medications related to all reported MEs considerably more effective and we were able to start compiling the organizational and specialty-specific lists of high-alert medications for HUS. In addition, organizations would need real-time information on ADRs and we have started a discussion to develop ADR reporting through future patient information systems. Hence, organizations could have copies of each ADR report and could follow the situation in real time.

Applying the method from Studies I-II and the results from Studies I-III, a multiprofessional expert group compiled an organizational list of high-alert medications for adult patients in HUS as part of the organizational patient safety strategy. Local ADR and ME data (quantitative and qualitative) were used and compared with earlier literature and internationally published high-alert and high-risk medication lists. Anticoagulants and antithrombotics, insulins, opioids, immunosuppressants, and oral cytotoxic drugs were categorized as high-alert medications in all units for adult patients. The instructions for high-alert medications also included key safety risks from a drug and medication safety perspective and a suggested course of action to prevent errors. Furthermore, healthcare units in HUS have been given instructions to complement this general list within each specialty with their specific medications (e.g. intensive care, pediatric, and oncology settings). High-alert medications, such as radio contrast agents, parenteral cytotoxic drugs, propofol, and noradrenaline, are only used in selected units, which is why they do not appear on the general list.

After Study III, HUS developed a guideline to standardize the medication reconciliation process at admission, discharge and transitions of care as a part of patient safety plan in 2015. HUS also increased the clinical pharmacy services in the study ED from a half-day to a full-day (office hours) and the additional time is now allocated to medication reconciliation and prescription reviews for the patients with polypharmacy, high-alert medications, renal insufficiency and/or continuing ED visits. Later, clinical pharmacy services have also been expanded in other EDs in HUS hospitals and primary care EDs in the HUS area and it has also been piloted in the oncology ambulatory clinic (Kähkönen 2017). Medication reconciliations and reviews have been conducted by the clinical pharmacist in the ED of KUH on a weekly basis before and after this study.

Additionally, Study III showed that a modified comprehensive medication review procedure is also applicable in hospital settings. HUS and KUH Pharmacy have been provided clinical medication reviews by clinical pharmacists working on wards and other care units as well as a centralized consulting service from the hospital pharmacy to tertiary, secondary and primary and homecare units. To ensure the competence of clinical pharmacists to conduct clinical medication reviews, HUS Pharmacy developed in-house continuing education program, which takes one year on the side of working. This has been possible with a clinical teacher's post, which is shared with the Faculty of Pharmacy, University of Helsinki.

The results of Studies III-IV and European Hospital Pharmacy statements (EAHP 2014) have been be used to develop and standardize clinical pharmacy services towards patient care and system-based medication safety work in HUS and HUS Pharmacy. This can been seen in the strategic indicators for clinical pharmacy (Table 16), which came into use in all five university hospitals in the beginning of 2018. Clinical pharmacy interventions will be better documented in the new patient information system (Apotti), which will be in use in HUS and many primary and social care units in the Helsinki and Uusimaa area in 2018-2020. This enables more effective outcome research related to clinical pharmacy services. Furthermore, in the 2016 survey (Study IV), 62% of the responding organizations thought that pharmacists could be working as medication safety officers in the future. The first post for medication safety officer (pharmacist) was launched in the HUS in 2017.

National level

The method developed to identify organizational high-alert medications using ME and ADR data (Studies I-II) can also be used in other organizations in Finnish healthcare. The knowledge of high-alert medications should be increased and defenses to medication-use process should be developed in order to ensure the safe use of high-alert medications. HUS's list of high-alert medications have also been exploited in the primary care units in the Helsinki and Uusimaa area and it was applied when the high-risk over-the-counter medications were identified in the Finnish community pharmacy setting (Ylä-Rautio et al. 2017). Moreover, the new features which were requested for the HaiPro tool by HUS (structurally documented medications involved in MEs and top reports related to these) are available for all HaiPro users.

ME data should be used to develop medication safety and new effective methods, e.g. data mining, should be exploited. ADR reporting through future patient information systems should be possible for all healthcare professionals. A national collaboration is needed to share ADR and ME data to maximize learning and guide practices to minimize harm from ADRs and MEs. There is a need for a national focal point for coordinating medication safety research, practice and competence development was identified in this

thesis (Studies II and IV) and in other Finnish publications and policy documents (Härkänen 2014, Schepel et al. 2017, Hakoinen et al. 2017, MSAH 2018a, MSAH 2018c). This has already been recommended by the CoE by 2006 and repeated by other key documents guiding patient and medication safety work.

The medication reconciliation process should be standardized and responsibilities should be clarified in Finnish healthcare organizations, especially in ED settings. Furthermore, collaborative medication reviews should also be conducted in hospital settings. Clinical pharmacists should have a role in medication mediconciliation and review procedures. A more patient-centered role of clinical pharmacists including system-based medication safety work is in line with international and national patient safety guidelines and policy initiatives and should be continued in the Finnish hospitals.

6.7 TOPICS FOR FUTURE RESEARCH

Research related to high-alert medications in different settings should be continued to increase awareness and to develop defenses to these in the medication-use process. Data on ME reporting systems include valuable information on risks in the medication-use process and new effective methods, for example, data mining, should be applied to increase the understanding of these. Evolution of clinical pharmacy services (including medication reconciliations and reviews) to ensure medication safety and their impact on patient care outcomes should also be followed-up regularly in the future with rigorous methodology.

7 CONCLUSIONS

- Organizational ME-reporting data is applicable when organizational high-alert medications are identified, but it should be complemented with a literature search and by local expert opinions. In addition to quantitative methods, qualitative methods deepen the understanding of the key safety risks related to high-alert medications and enable the development of safer medication-use processes. The use of ADR reports alone will provide a narrow picture of high-alert medications, even though the definition of ADR has been extended to include MEs. ME reports, which reflect the real-life medication-use process, the presence of human error, and the consequences of both, must be taken into account.

- In HUS, antineoplastic agents, anticoagulants and antithrombotics, opioids, insulins and metformin, radio contrast agents, cyclosporine, noradrenaline, potassium chloride concentrate, propofol, and ropivacaine should be considered as high-alert medications.

- ED medication history-taking procedure must not only be further developed in tertiary hospital EDs, but also in primary and secondary hospital EDs in Finland. Clinical pharmacists' involvement in medication reconciliation and review at admission is beneficial and allows nurses and physicians to concentrate on the assessment and treatment of the patient.

- Modified comprehensive medication review procedure is applicable to hospital settings. The drug-related problems identified with regard to medication reviews accumulated specific medications. Medication reviews helped to identify the high-alert medications at the ED admission.

- The provision of clinical pharmacy services increased remarkably between 2011 and 2016 and a more patient-centered role of clinical pharmacists including system-based medication safety work has become clearly more common and planned in Finnish hospitals. This development is in line with international and national system-based patient safety guidelines and policy initiatives and should be continued. Availability of patient-centered and system-based continuing education and accreditation training has had a crucial impact in this shift towards patient-oriented services.

- A need for organizational and national coordination of medication safety development was identified in this thesis as well as in other national and international publications and policy documents. Furthermore, national collaboration is needed to combine the information gathered from ADR and ME incident data to better understand the risks of medication use.

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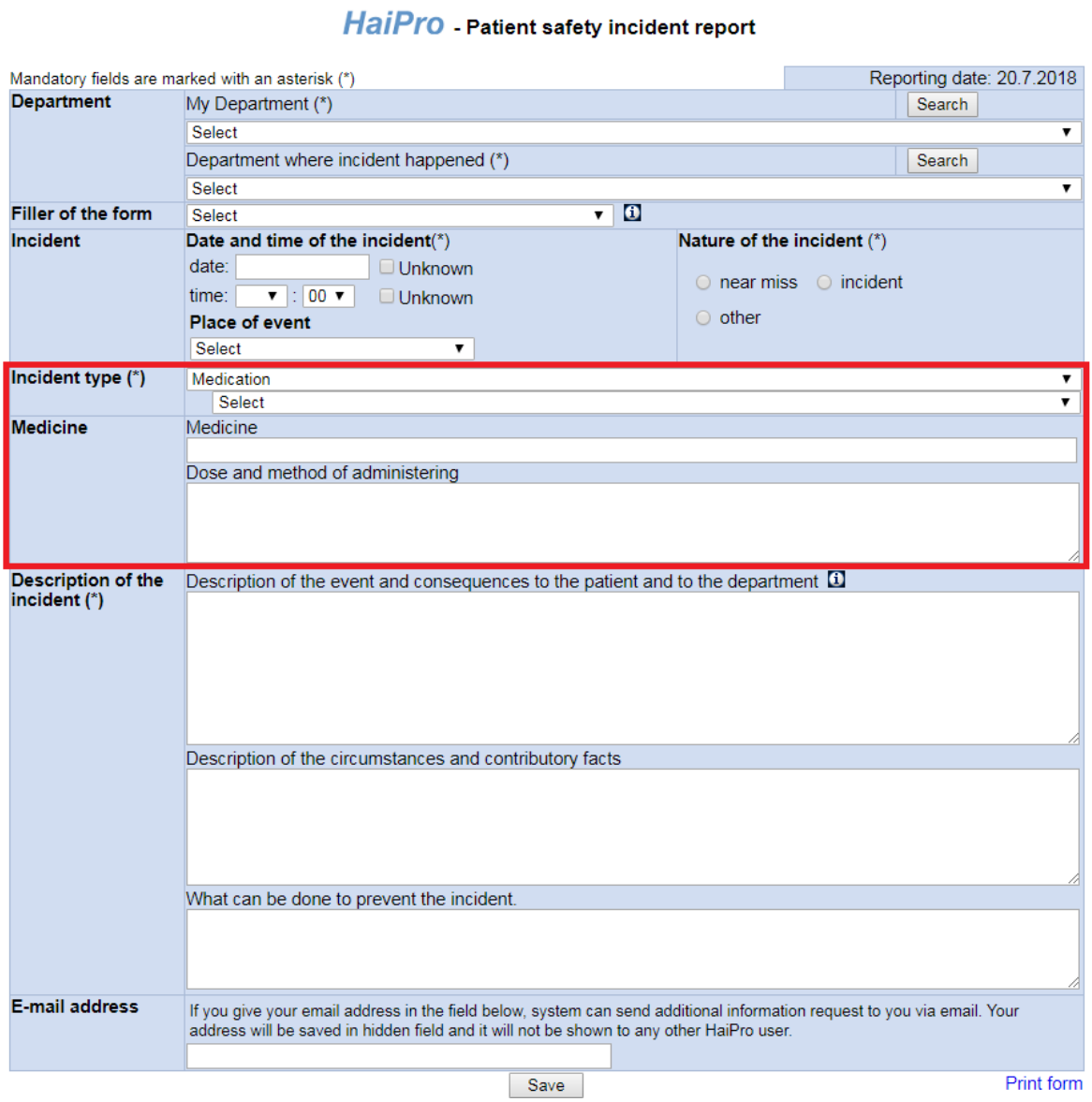
APPENDIXS

Appendix 1. HaiPro medication error report form in English (studies I-II)



HaiPro - Patient safety incident report

Mandatory fields are marked with an asterisk (*)

Reporting date: 20.7.2018

Department

My Department (*) Search

Select

Department where incident happened (*) Search

Select

Filler of the form

Select

Incident

Date and time of the incident(*)

date: Unknown

time: : 00 Unknown

Place of event

Select

Nature of the incident (*)

near miss incident

other

Incident type (*)

Medication

Select

Medicine

Medicine

Dose and method of administering

Description of the incident (*)

Description of the event and consequences to the patient and to the department

Description of the circumstances and contributory facts

What can be done to prevent the incident.

E-mail address

If you give your email address in the field below, system can send additional information request to you via email. Your address will be saved in hidden field and it will not be shown to any other HaiPro user.

Save

Print form

Appendix 2. Medication reconciliation form (Study III).

MEDICATION RECONCILIATION FORM

Date: _____ Time: _____

Patient code number: _____
Admission diagnosis (e.g. triage form): _____
Other diagnoses: _____
_____
_____

Weight: _____kg, Height: _____cm, Plasma creatinine: _____(date), RR and pulse _____(date)
Other relevant laboratory results: _____
Allergies: _____
Recent diet changes: _____
Smoking: no ___yes ____ ____cigarettes/day Alcohol use: no ___yes ____ _____ doses/week

Patient's medications:

[1]Prescription (R), OTC (I)
[2]Patient chart (SK), Medication card (L), Interview (H), Prescriptions (R), Dose dispensing (A), Hospice care (HP), Electronic archives (E), Relative (O), -Other (M)_____
[3]Long-term (S) and PRN, pro re nata = as needed (T)

Drug, strength and formulation (R/I[1])	Reference (code[2])	Dosing (eg. 1 tbl x 3)	Dosing times	S/T[3]	Comments, and if needed the indication for the medication

Check-list for medication reconciliation: Does patient use:

medications that affect blood clotting___
medication for flu___
allergy medication ___
cough medicine___
1x/week or 1x/month etc.
administrated medications___
heartburn medication___
pain killers___
vitamins___
herbal product ___
medical patches (nicotine,
nitro, hormone, dementia)___
medication for constipation___
medicinal cream___
injectable medication (insulin etc.)___
eye medication (drops)___
aerosols (asthma, nitro etc.) ___
drugs that belong to someone else ___

Have your medications been altered during the last month? No ___ Yes ___, what?

_____

_____

Medication administration and adherence outside of the hospital

Do you take your medications according to your medication plan? Yes ___ No ___
Have you made changes to your medications? Yes ___ No ___

Why? _____

_____

Possible problems (fill in the comment section of the patient's medication list):

Problems in swallowing ___
Medication costs ___
Side effects ___
Fear ___
Dementia ___
Difficult dispensing (e.g. package opening)____
Difficulties with administration ___
Inefficacy or excessive efficacy ___
Missing or unclear instructions ___
Inappropriate use of OTC medications ___
Several caregivers, unclear responsibility ___
Other, what? _____

Check-list for the detection of side effects:

Acid reflux ___	Nausea ___	Dry mouth ___	Diarrhoea ___	Constipation ___
Pain ___	Sweating ___	Dysuria ___	Itching___	Amnesia ___
Stiffness ___	Falls ___	Dyspnoea___	Chest pain___	Arrhythmias ___
Dizziness ___	Walking difficulties ___	Insomnia ___	Anxiety ___	Confusion ___
Swelling ___	Cough ___	Visual disturbances ___	Restless legs, cramps, leg pain ___	

Description:

_____

_____

_____

_____

When did you last take your medications? _____

Do you have any medication with you? _____

Interviewers comments:

_____

_____

_____

_____

_____

Additional information:

_____

_____

_____

_____

Interviewer: _____

Appendix 3. Medication review form (Study III).

MEDICATION REVIEW FORM

Patient code number: _____

- GFR (CKD-EPI): _____ ml/min.
- Admission diagnosis:
- Detected adverse drug reactions in the patient interview:

DRUG-RELATED PROBLEMS:

1. Adverse drug reactions[1,2]	
2. Overlapping medications[2,3]	
3. Clinically problematic interactions[2-5]	
4. Dose (including inappropriate doses with renal insufficiency)[2,6]	
5. Dosing schedule[2,7]	
6. Missing medications compared to diagnoses[2,8]	
7. Potentially inappropriate medications for older patients (≥75 years)[9]	
8. Problems with adherence[1]	
9. High-alert medications[10-11]	
10. Other important findings (e.g. need for monitoring, inappropriateness of the hospital drugs with home medication, costs and reimbursement aspects, availability, dosing technique, length of treatment, no indication)	

SUMMARY OF THE FINDINGS FOR THE PHYSICIAN
(documented and sent to the patient information system):

1. **Drug-related problems certainly or probably linked to admission diagnoses:**
2. **Other acute drug-related problems (needing actions in the emergency department):**
3. **Non-acute drug-related problems (needing actions later after discharge):**

Date, completed by:
Summary delivered to physician (date and physician):

References

1 Patient interview
2 Duodecim Medication database (summaries of product characteristics). https://verkkokauppa.duodecim.fi/890.html (accessed 20 Dec 2017).
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4 Medbase Ltd. Swedish, Finnish Interaction X-referencing – SFINX http://www.medbase.fi/en/professionals/sfinx (accessed 20 Dec 2017).
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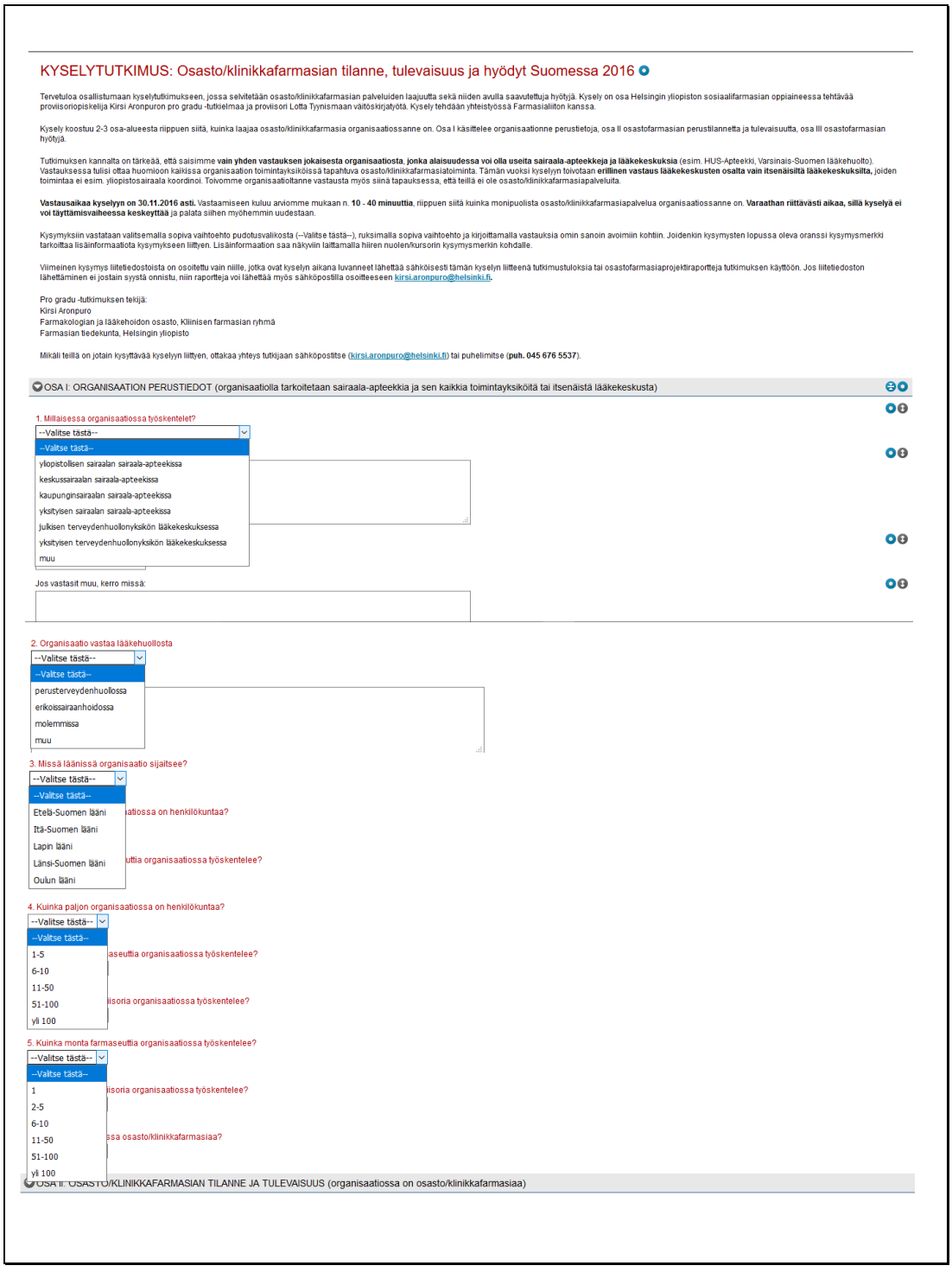
10 Institute for Safe Medication Practices (ISMP). ISMP's List of High Alert Medications in Acute Care Settings, 2014. www.ismp.org/tools/institutionalhighAlert.asp (accessed 20 Dec 2017).
11 Institute for Safe Medication Practices (ISMP). ISMP's List of High Alert Medications in Community/Ambulatory Healthcare, 2011. https://ismp.org/communityRx/tools/ambulatoryhighalert.asp (accessed 20 Dec 2017).

Appendix 4. Online survey in 2016 (Study IV).



KYSELYTUTKIMUS: Osasto/klinikkafarmasian tilanne, tulevaisuus ja hyödyt Suomessa 2016

Tervetuloa osallistumaan kyselytutkimukseen, jossa selvitetään osasto/klinikkafarmasian palveluiden laajuutta sekä niiden avulla saavutettuja hyötyjä. Kysely on osa Helsingin yliopiston sosiaalifarmasian oppiaineessa tehtävää provisoriopiskelija Kirsi Aronpuron pro gradu -tutkielmaa ja proviisori Lotta Tyynismaan väitöskirjatyötä. Kysely tehdään yhteistyössä Farmasialiiton kanssa.

Kysely koostuu 2-3 osa-alueesta riippuen siitä, kuinka laajaa osasto/klinikkafarmasia organisaatiossanne on. Osa I käsittelee organisaationne perustietoja, osa II osastofarmasian perustilannetta ja tulevaisuutta, osa III osastofarmasian hyötyjä.

Tutkimuksen kannalta on tärkeää, että saisimme **vain yhden vastauksen jokaisesta organisaatiosta**, **jonka alaisuudessa voi olla useita sairaala-apteekkeja ja lääkekeskuksia** (esim. HUS-Apteekki, Varsinais-Suomen lääkehuolto). Vastauksessa tulisi ottaa huomioon kaikissa organisaation toimintayksiköissä tapahtuva osasto/klinikkafarmasiatoiminta. Tämän vuoksi kyselyyn toivotaan **erillinen vastaus lääkekeskusten osalta vain itsenäisiltä lääkekeskuksilta,** joiden toimintaa ei esim. yliopistosairaala koordinoi. Toivomme organisaatioltanne vastausta myös siinä tapauksessa, että teillä ei ole osasto/klinikkafarmasiapalveluita.

Vastausaikaa kyselyyn on 30.11.2016 asti. Vastaamiseen kuluu arviomme mukaan n. **10 - 40 minuuttia**, riippuen siitä kuinka monipuolista osasto/klinikkafarmasiapalvelua organisaatiossanne on. **Varaathan riittävästi aikaa, sillä kyselyä ei voi täyttämisvaiheessa keskeyttää** ja palata siihen myöhemmin uudestaan.

Kysymyksiin vastataan valitsemalla sopiva vaihtoehto pudotusvalikosta (--Valitse tästä--), ruksimalla sopiva vaihtoehto ja kirjoittamalla vastauksia omin sanoin avoimiin kohtiin. Joidenkin kysymysten lopussa oleva oranssi kysymysmerkki tarkoittaa lisäinformaatiota kysymykseen liittyen. Lisäinformaation saa näkyviin laittamalla hiiren nuolen/kursorin kysymysmerkin kohdalle.

Viimeinen kysymys liitetiedostoista on osoitettu vain niille, jotka ovat kyselyn aikana luvanneet lähettää sähköisesti tämän kyselyn liitteenä tutkimustuloksia tai osastofarmasiaprojektiraportteja tutkimuksen käyttöön. Jos liitetiedoston lähettäminen ei jostain syystä onnistu, niin raportteja voi lähettää myös sähköpostilla osoitteeseen kirsi.aronpuro@helsinki.fi.

Pro gradu -tutkimuksen tekijä:
Kirsi Aronpuro
Farmakologian ja lääkehoidon osasto, Kliinisen farmasian ryhmä
Farmasian tiedekunta, Helsingin yliopisto

Mikäli teillä on jotain kysyttävää kyselyyn liittyen, ottakaa yhteys tutkijaan sähköpostitse (kirsi.aronpuro@helsinki.fi) tai puhelimitse (**puh. 045 676 5537**).

OSA I: ORGANISAATION PERUSTIEDOT (organisaatiolla tarkoitetaan sairaala-apteekkia ja sen kaikkia toimintayksiköitä tai itsenäistä lääkekeskusta)

1. Millaisessa organisaatiossa työskentelet?
--Valitse tästä--
--Valitse tästä--
yliopistollisen sairaalan sairaala-apteekissa
keskussairaalan sairaala-apteekissa
kaupunginsairaalan sairaala-apteekissa
yksityisen sairaalan sairaala-apteekissa
julkisen terveydenhuollonyksikön lääkekeskuksessa
yksityisen terveydenhuollonyksikön lääkekeskuksessa
muu

Jos vastasit muu, kerro missä:

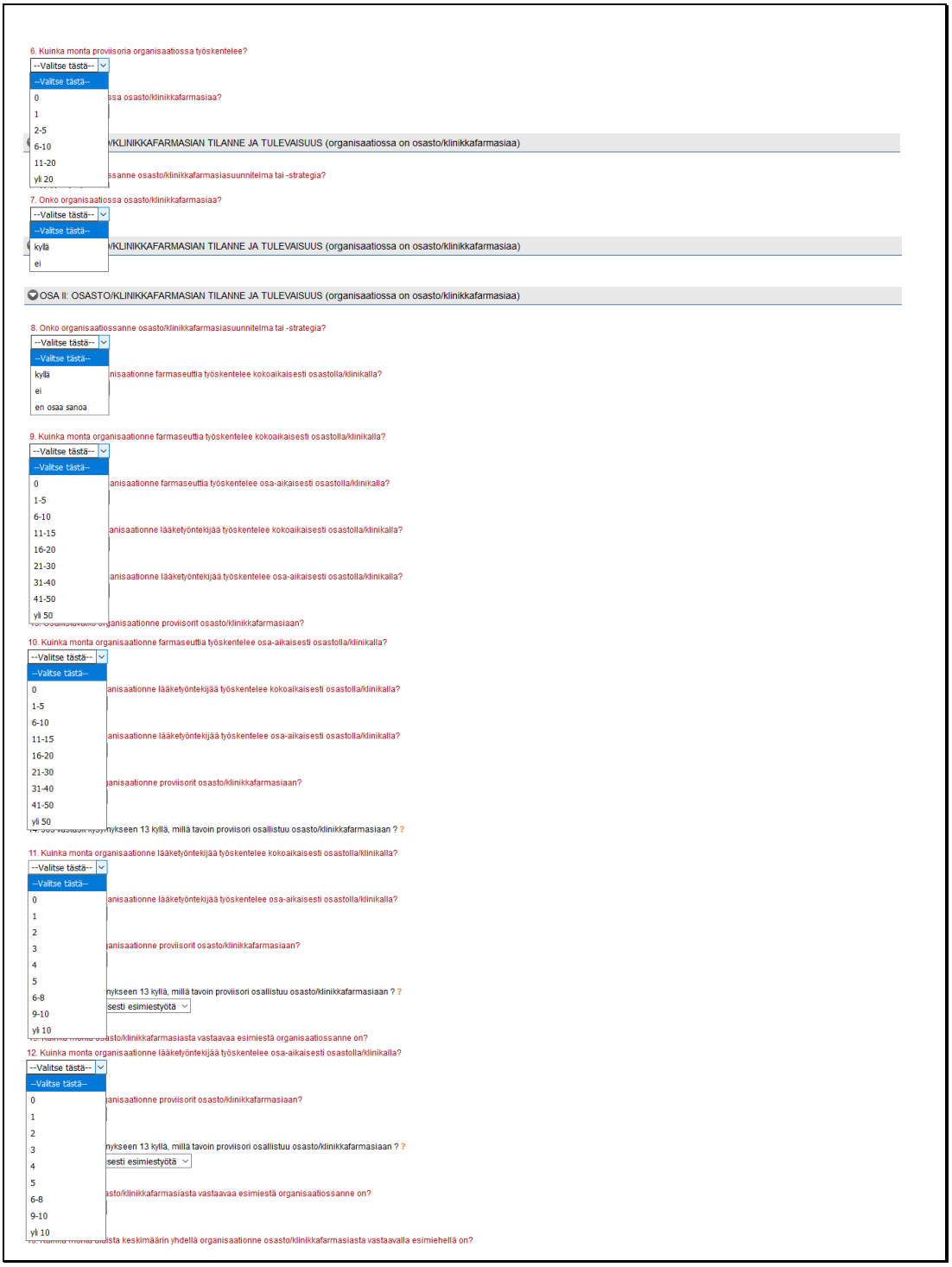
2. Organisaatio vastaa lääkehuollosta
--Valitse tästä--
--Valitse tästä--
perusterveydenhuollossa
erikoissairaanhoidossa
molemmissa
muu

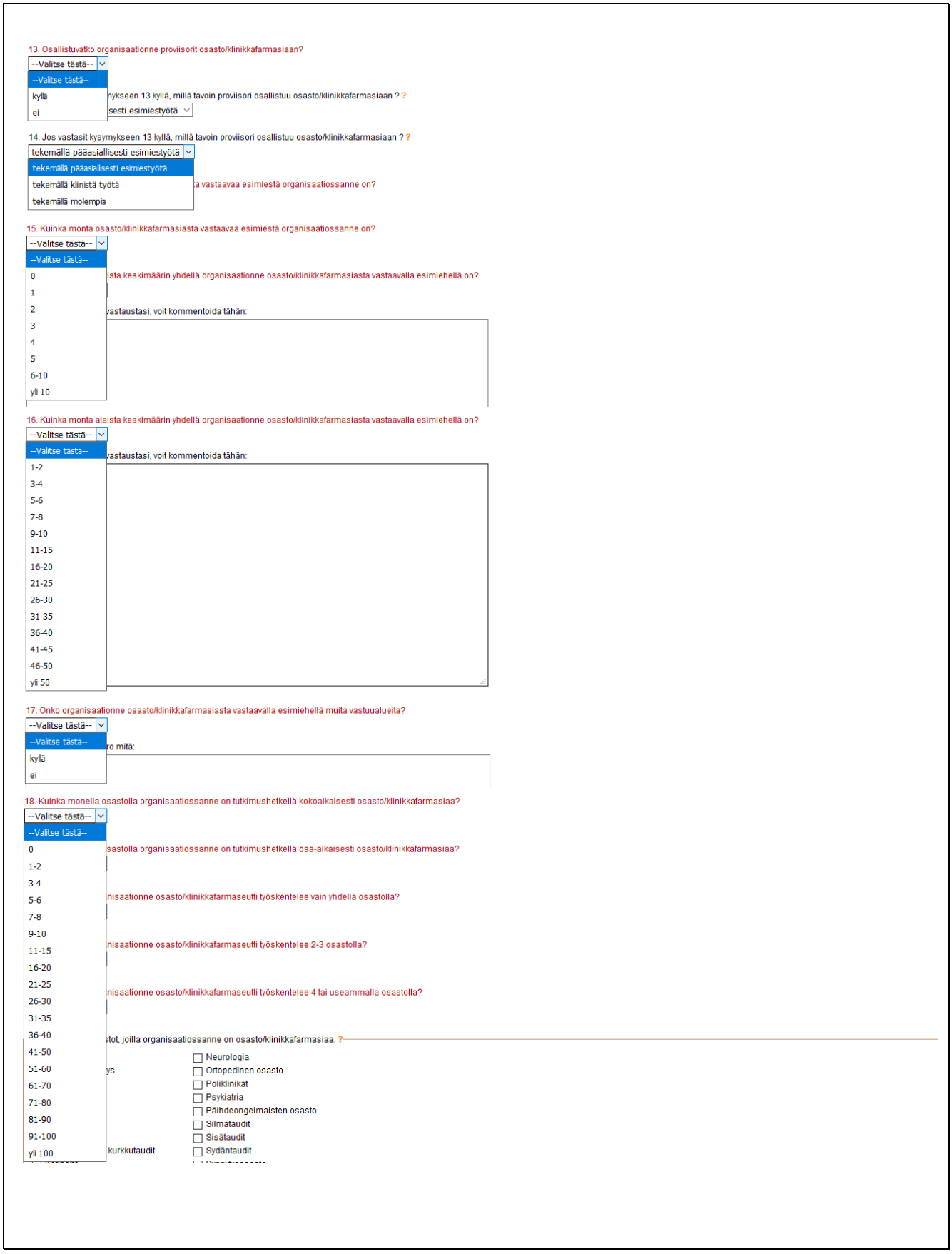
3. Missä läänissä organisaatio sijaitsee?
--Valitse tästä--
--Valitse tästä--
Etelä-Suomen lääni
Itä-Suomen lääni
Lapin lääni
Länsi-Suomen lääni
Oulun lääni

4. Kuinka paljon organisaatiossa on henkilökuntaa?
--Valitse tästä--
--Valitse tästä--
1-5
6-10
11-50
51-100
yli 100

5. Kuinka monta farmaseuttia organisaatiossa työskentelee?
--Valitse tästä--
--Valitse tästä--
1
2-5
6-10
11-50
51-100
yli 100

OSA II: OSASTO/KLINIKKAFARMASIAN TILANNE JA TULEVAISUUS (organisaatiossa on osasto/klinikkafarmasiaa)


6. Kuinka monta proviisoria organisaatiossa työskentelee?
--Valitse tästä--
--Valitse tästä--
0
1
2-5
6-10
11-20
yli 20
ssa osasto/klinikkafarmasiaa?
/KLINIKKAFARMASIAN TILANNE JA TULEVAISUUS (organisaatiossa on osasto/klinikkafarmasiaa)
ssanne osasto/klinikkafarmasiasuunnitelma tai -strategia?
7. Onko organisaatiossa osasto/klinikkafarmasiaa?
--Valitse tästä--
--Valitse tästä--
kyllä
ei
/KLINIKKAFARMASIAN TILANNE JA TULEVAISUUS (organisaatiossa on osasto/klinikkafarmasiaa)
OSA II: OSASTO/KLINIKKAFARMASIAN TILANNE JA TULEVAISUUS (organisaatiossa on osasto/klinikkafarmasiaa)
8. Onko organisaatiossanne osasto/klinikkafarmasiasuunnitelma tai -strategia?
--Valitse tästä--
--Valitse tästä--
kyllä
ei
en osaa sanoa
nisaationne farmaseuttia työskentelee kokoaikaisesti osastolla/klinikalla?
9. Kuinka monta organisaationne farmaseuttia työskentelee kokoaikaisesti osastolla/klinikalla?
--Valitse tästä--
--Valitse tästä--
0
1-5
6-10
11-15
16-20
21-30
31-40
41-50
yli 50
anisaationne farmaseuttia työskentelee osa-aikaisesti osastolla/klinikalla?
anisaationne lääketyöntekijää työskentelee kokoaikaisesti osastolla/klinikalla?
anisaationne lääketyöntekijää työskentelee osa-aikaisesti osastolla/klinikalla?
10. Kuinka monta organisaationne farmaseuttia työskentelee osa-aikaisesti osastolla/klinikalla?
--Valitse tästä--
--Valitse tästä--
0
1-5
6-10
11-15
16-20
21-30
31-40
41-50
yli 50
anisaationne lääketyöntekijää työskentelee kokoaikaisesti osastolla/klinikalla?
anisaationne lääketyöntekijää työskentelee osa-aikaisesti osastolla/klinikalla?
anisaationne proviisorit osasto/klinikkafarmasiaan?
nykseen 13 kyllä, millä tavoin proviisori osallistuu osasto/klinikkafarmasiaan ? ?
11. Kuinka monta organisaationne lääketyöntekijää työskentelee kokoaikaisesti osastolla/klinikalla?
--Valitse tästä--
--Valitse tästä--
0
1
2
3
4
5
6-8
9-10
yli 10
anisaationne lääketyöntekijää työskentelee osa-aikaisesti osastolla/klinikalla?
anisaationne proviisorit osasto/klinikkafarmasiaan?
nykseen 13 kyllä, millä tavoin proviisori osallistuu osasto/klinikkafarmasiaan ? ?
sesti esimiestyötä
sto/klinikkafarmasiasta vastaavaa esimiestä organisaatiossanne on?
12. Kuinka monta organisaationne lääketyöntekijää työskentelee osa-aikaisesti osastolla/klinikalla?
--Valitse tästä--
--Valitse tästä--
0
1
2
3
4
5
6-8
9-10
yli 10
anisaationne proviisorit osasto/klinikkafarmasiaan?
nykseen 13 kyllä, millä tavoin proviisori osallistuu osasto/klinikkafarmasiaan ? ?
sesti esimiestyötä
sto/klinikkafarmasiasta vastaavaa esimiestä organisaatiossanne on?
dusta keskimäärin yhdellä organisaationne osasto/klinikkafarmasiasta vastaavalla esimiehellä on?


13. Osallistuvatko organisaationne proviisorit osasto/klinikkafarmasiaan?
--Valitse tästä--
--Valitse tästä--
kyllä
ei
nykseen 13 kyllä, millä tavoin proviisori osallistuu osasto/klinikkafarmasiaan ? ?
sesti esimiestyötä
14. Jos vastasit kysymykseen 13 kyllä, millä tavoin proviisori osallistuu osasto/klinikkafarmasiaan ? ?
tekemällä pääasiallisesti esimiestyötä
tekemällä pääasiallisesti esimiestyötä
tekemällä kliinistä työtä
tekemällä molempia
a vastaavaa esimiestä organisaatiossanne on?
15. Kuinka monta osasto/klinikkafarmasiasta vastaavaa esimiestä organisaatiossanne on?
--Valitse tästä--
--Valitse tästä--
0
1
2
3
4
5
6-10
yli 10
ista keskimäärin yhdellä organisaationne osasto/klinikkafarmasiasta vastaavalla esimiehellä on?
vastaustasi, voit kommentoida tähän:
16. Kuinka monta alaista keskimäärin yhdellä organisaationne osasto/klinikkafarmasiasta vastaavalla esimiehellä on?
--Valitse tästä--
--Valitse tästä--
1-2
3-4
5-6
7-8
9-10
11-15
16-20
21-25
26-30
31-35
36-40
41-45
46-50
yli 50
vastaustasi, voit kommentoida tähän:
17. Onko organisaationne osasto/klinikkafarmasiasta vastaavalla esimiehellä muita vastuualueita?
--Valitse tästä--
--Valitse tästä--
kyllä
ei
ro mitä:
18. Kuinka monella osastolla organisaatiossanne on tutkimushetkellä kokoaikaisesti osasto/klinikkafarmasiaa?
--Valitse tästä--
--Valitse tästä--
0
1-2
3-4
5-6
7-8
9-10
11-15
16-20
21-25
26-30
31-35
36-40
41-50
51-60
61-70
71-80
81-90
91-100
yli 100
sastolla organisaatiossanne on tutkimushetkellä osa-aikaisesti osasto/klinikkafarmasiaa?
nisaationne osasto/klinikkafarmaseutti työskentelee vain yhdellä osastolla?
nisaationne osasto/klinikkafarmaseutti työskentelee 2-3 osastolla?
nisaationne osasto/klinikkafarmaseutti työskentelee 4 tai useammalla osastolla?
tot, joilla organisaatiossanne on osasto/klinikkafarmasiaa. ?
ys
kurkkutaudit
Neurologia
Ortopedinen osasto
Poliklinikat
Psykiatria
Päihdeongelmaisten osasto
Silmätaudit
Sisätaudit
Sydäntaudit

19. Kuinka monella osastolla organisaatiossanne on tutkimushetkellä osa-aikaisesti osasto/klinikkafarmasiaa?

--Valitse tästä--
--Valitse tästä--
0
1-2
3-4
5-6
7-8
9-10
11-15
16-20
21-25
26-30
31-35
36-40
41-50
51-60
61-70
71-80
81-90
91-100
yli 100

nisaationne osasto/klinikkafarmaseutti työskentelee vain yhdellä osastolla?

nisaationne osasto/klinikkafarmaseutti työskentelee 2-3 osastolla?

nisaationne osasto/klinikkafarmaseutti työskentelee 4 tai useammalla osastolla?

tot, joilla organisaatiossanne on osasto/klinikkafarmasiaa. ?

ys

kurkkutaudit

- Neurologia
- Ortopedinen osasto
- Poliklinikat
- Psykiatria
- Päihdeongelmaisten osasto
- Silmätaudit
- Sisätaudit
- Sydäntaudit
- Synnytysosasto
- Syöpätaudit
- Teho-osasto
- Terveyskeskuksen vuodeosasto

20. Kuinka moni organisaationne osasto/klinikkafarmaseutti työskentelee vain yhdellä osastolla?

--Valitse tästä--
--Valitse tästä--
0
1-2
3-4
5-6
7-8
9-10
11-15
16-20
yli 20

nisaationne osasto/klinikkafarmaseutti työskentelee 2-3 osastolla?

nisaationne osasto/klinikkafarmaseutti työskentelee 4 tai useammalla osastolla?

tot, joilla organisaatiossanne on osasto/klinikkafarmasiaa. ?

ys

- Neurologia
- Ortopedinen osasto
- Poliklinikat

21. Kuinka moni organisaationne osasto/klinikkafarmaseutti työskentelee 2-3 osastolla?

--Valitse tästä--
--Valitse tästä--
0
1-2
3-4
5-6
7-8
9-10
11-15
16-20
21-25
26-30
31-40
41-50
yli 50

nisaationne osasto/klinikkafarmaseutti työskentelee 4 tai useammalla osastolla?

tot, joilla organisaatiossanne on osasto/klinikkafarmasiaa. ?

ys

kurkkutaudit

- Neurologia
- Ortopedinen osasto
- Poliklinikat
- Psykiatria
- Päihdeongelmaisten osasto
- Silmätaudit
- Sisätaudit
- Sydäntaudit
- Synnytysosasto
- Syöpätaudit
- Teho-osasto
- Terveyskeskuksen vuodeosasto

22. Kuinka moni organisaationne osasto/klinikkafarmaseutti työskentelee 4 tai useammalla osastolla?

--Valitse tästä--
--Valitse tästä--
0
1-2
3-4
5-6
7-8
9-10
11-15
16-20
21-25
26-30
31-40
41-50
yli 50

tot, joilla organisaatiossanne on osasto/klinikkafarmasiaa. ?

ys

kurkkutaudit

- Neurologia
- Ortopedinen osasto
- Poliklinikat
- Psykiatria
- Päihdeongelmaisten osasto
- Silmätaudit
- Sisätaudit
- Sydäntaudit
- Synnytysosasto
- Syöpätaudit
- Teho-osasto
- Terveyskeskuksen vuodeosasto
- Urologian osasto
- Vastasyntyneiden teho-osasto
- Muu

23. Luettele ne osastot, joilla organisaatiossanne on osasto/klinikkafarmasiaa. ?

- ☐ Akuuttiosasto
- ☐ Ensiapu/Päivystys
- ☐ Geriatria
- ☐ Ihotaudit
- ☐ Infektiotaudit
- ☐ Keuhkotaudit
- ☐ Kirurgia
- ☐ Korva-, nenä- ja kurkkutaudit
- ☐ Kotihoito
- ☐ Kuntoutus
- ☐ Lastentaudit
- ☐ Leikkausosasto
- ☐ Maksataudit
- ☐ Munuaistaudit
- ☐ Naistentaudit
- ☐ Neurologia
- ☐ Ortopedinen osasto
- ☐ Poliklinikat
- ☐ Psykiatria
- ☐ Päihdeongelmaisten osasto
- ☐ Silmätaudit
- ☐ Sisätaudit
- ☐ Sydäntaudit
- ☐ Synnytysosasto
- ☐ Syöpätaudit
- ☐ Teho-osasto
- ☐ Terveyskeskuksen vuodeosasto
- ☐ Urologian osasto
- ☐ Vastasyntyneiden teho-osasto
- ☐ Muu

Jos vastasit muu, kerro missä/millaisilla muilla osastoilla:

Jos vastasit poliklinikat, kerro missä/millaisilla poliklinikoilla:

Lisäkommentteja: ?

24. Kuuluuko organisaationne osasto/klinikkafarmasiapalveluun sijaistuspalvelu?

--Valitse tästä--

--Valitse tästä--
kyllä
ei

ro millainen:

25. Mitä organisaationne osasto/klinikkafarmaseutin työtehtäviin kuuluu? ?

- [ ] logistiset tehtävät (tilaaminen, varastonhallinta)
- [ ] huumausainekorttien tarkistaminen ja kirjanpito
- [ ] lääkeautomaatioon liittyvät työtehtävät (esim. älylääkekaapit)
- [ ] elvytyslaukkujen/-kärryjen lääkkeiden tarkastus
- [ ] osastotarkastukset
- [ ] suun kautta annosteltavien lääkkeiden jako potilasannoksiin
- [ ] suonensisäisesti annettavien potilasannosten käyttökuntoon saatto
- [ ] solunsalpaajien käyttökuntoon saatto
- [ ] parenteraalisten ravitsemusliuosten käyttökuntoon saatto
- [ ] suonensisäisesti annettavien potilasannosten letkutus
- [ ] lääkeinformaatio potilaille
- [ ] lääkeinformaatio hoitohenkilökunnalle
- [ ] lääkehoitoon liittyvien ohjeiden laatiminen
- [ ] osaston henkilökunnan kouluttaminen (esim. osastotunnit)
- [ ] osaston uusien työntekijöiden perehdytys (sairaanhoitaja, lähihoitaja)
- [ ] osaston opiskelijoiden (sairaanhoitaja, lähihoitaja) perehdytys
- [ ] LOVe-näytön (tai muun lääkelupanäytön) vastaanottaminen
- [ ] potilaan lääkityslistan ajantasaistaminen (esim. tulovaiheessa)
- [ ] potilaan kotiuttamisen yhteydessä annettu lääkeinformaatio
- [ ] osallistuminen lääkärin kierroille
- [ ] osallistuminen ns. paperikierroille
- [ ] lääkityksen tarkistus
- [ ] lääkityksen arviointi
- [ ] lääkehoidon kokonaisarviointi (LHKA)
- [ ] Haipro-ilmoitusten tekeminen
- [ ] Haipro-ilmoitusten käsittely
- [ ] lääkehoitoprosessin kehittäminen Haipro-ilmoitusten perusteella (esim. suojaukset)
- [ ] osallistuminen moniammatillisiin työryhmiin
- [ ] yhteistyö muiden asiantuntijoiden kanssa (esim. kliinisen hoitotyön asiantuntija, potilasturvallisuuspäällikkö, ravitsemusterapeutti, hygieniahoitaja)
- [ ] osallistuminen lääkehoitosuunnitelman laatimiseen/päivittämiseen
- [ ] lääkitysturvallisuusauditoinnit
- [ ] muuta

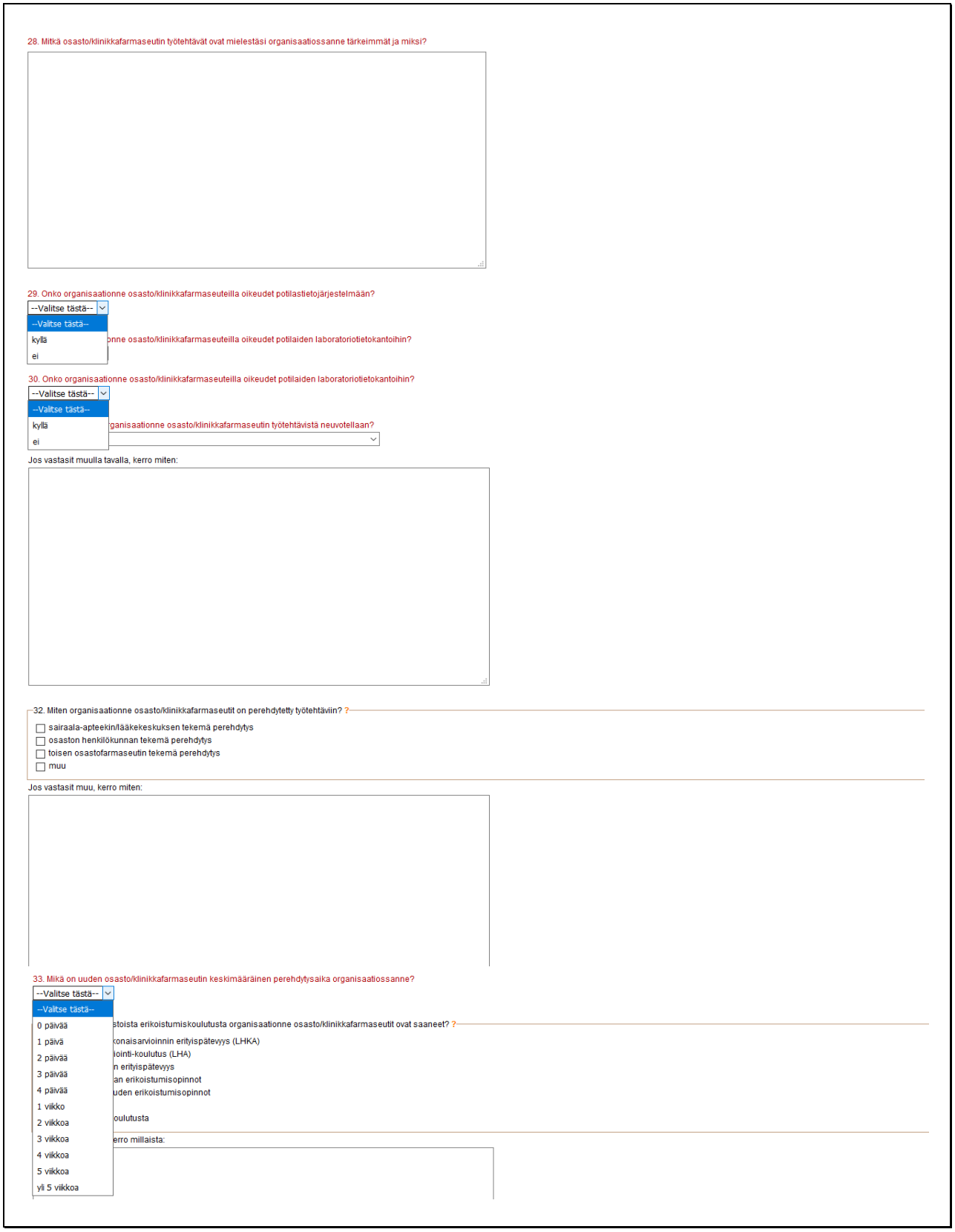
Jos vastasit muuta, kerro mitä:

26. Jos organisaatiossanne on osastolääketyöntekijöitä, mitä työtehtäviä he tekevät? ?

- [ ] logistiset tehtävät (tilaaminen, varastonhallinta)
- [ ] huumausainekorttien tarkistaminen ja kirjanpito
- [ ] lääkeautomaatioon liittyvät työtehtävät (esim. älylääkekaapit)
- [ ] avustavat tehtävät iv-lääkkeiden käyttökuntoon saattamisessa
- [ ] siivous (LIV-kaapin puhdistus, lääkekaappien hyllyjen puhdistus, lääkehuoneen yleinen siisteys)
- [ ] toimistotehtävät (esim. lääkelainojen kirjaaminen, lääkehävikin kirjaaminen, taulukointi)
- [ ] muuta

Jos vastasit muuta, kerro mitä:

27. Arvioi, kuinka paljon (%) organisaatiossanne keskimäärin osasto/klinikkafarmaseutin työajasta kuluu logistisiin työtehtäviin. Jos tässä on paljon vaihtelua, kuvaile millaista.



28. Mitkä osasto/klinikkafarmaseutin työtehtävät ovat mielestäsi organisaatiossanne tärkeimmät ja miksi?

29. Onko organisaationne osasto/klinikkafarmaseuteilla oikeudet potilastietojärjestelmään?

--Valitse tästä--
--Valitse tästä--
kyllä
ei

onne osasto/klinikkafarmaseuteilla oikeudet potilaiden laboratoriotietokantoihin?

30. Onko organisaationne osasto/klinikkafarmaseuteilla oikeudet potilaiden laboratoriotietokantoihin?

--Valitse tästä--
--Valitse tästä--
kyllä
ei

ganisaationne osasto/klinikkafarmaseutin työtehtävistä neuvotellaan?

Jos vastasit muulla tavalla, kerro miten:

32. Miten organisaationne osasto/klinikkafarmaseutit on perehdytetty työtehtäviin? ?

- [ ] sairaala-apteekin/lääkekeskuksen tekemä perehdytys
- [ ] osaston henkilökunnan tekemä perehdytys
- [ ] toisen osastofarmaseutin tekemä perehdytys
- [ ] muu

Jos vastasit muu, kerro miten:

33. Mikä on uuden osasto/klinikkafarmaseutin keskimääräinen perehdytysaika organisaatiossanne?

--Valitse tästä--
--Valitse tästä--
0 päivää
1 päivä
2 päivää
3 päivää
4 päivää
1 viikko
2 viikkoa
3 viikkoa
4 viikkoa
5 viikkoa
yli 5 viikkoa

stoista erikoistumiskoulutusta organisaationne osasto/klinikkafarmaseutit ovat saaneet? ?

konaisarvioinnin erityispätevyys (LHKA)
iointi-koulutus (LHA)
n erityispätevyys
an erikoistumisopinnot
uden erikoistumisopinnot

oulutusta

erro millaista:

34. Millaista pitkäkestoista erikoistumiskoulutusta organisaationne osasto/klinikkafarmaseutit ovat saaneet? ?

- ☐ lääkehoidon kokonaisarvioinnin erityispätevyys (LHKA)
- ☐ lääkehoidon arviointi-koulutus (LHA)
- ☐ osastofarmasian erityispätevyys
- ☐ sairaalafarmasian erikoistumisopinnot
- ☐ potilasturvallisuuden erikoistumisopinnot
- ☐ muuta
- ☐ ei erikoistumiskoulutusta

Jos vastasit muuta, kerro millaista:

35. Kuinka monella organisaationne osasto/klinikkafarmasiaan osallistuvalla henkilöllä on erikoistumiskoulutus?

--Valitse tästä--
--Valitse tästä--
0
1-2
3-4
5-6
7-8
9-10
yli 10

llä mainitut henkilöt pystyvät työssään hyödyntämään erikoisosaamistaan organisaatiossanne?

vää keskimäärin vuoden aikana organisaationne osasto/klinikkafarmaseutti osallistuu
nyskoulutukseen?

n täydennyskoulutus vaikuttanut osasto/klinikkafarmaseuttien toimenkuvaan organisaatiossanne?

36. Missä määrin edellä mainitut henkilöt pystyvät työssään hyödyntämään erikoisosaamistaan organisaatiossanne?

hyvin
hyvin
jossain määrin
ei lainkaan

äivää keskimäärin vuoden aikana organisaationne osasto/klinikkafarmaseutti osallistuu
nnyskoulutukseen?

37. Kuinka monta päivää keskimäärin vuoden aikana organisaationne osasto/klinikkafarmaseutti osallistuu ammatilliseen täydennyskoulutukseen?

--Valitse tästä--
--Valitse tästä--
0 päivää
1 päivä
2 päivää
3 päivää
4 päivää
5 päivää
enemmän kuin 5 päivää

nyskoulutus vaikuttanut osasto/klinikkafarmaseuttien toimenkuvaan organisaatiossanne?

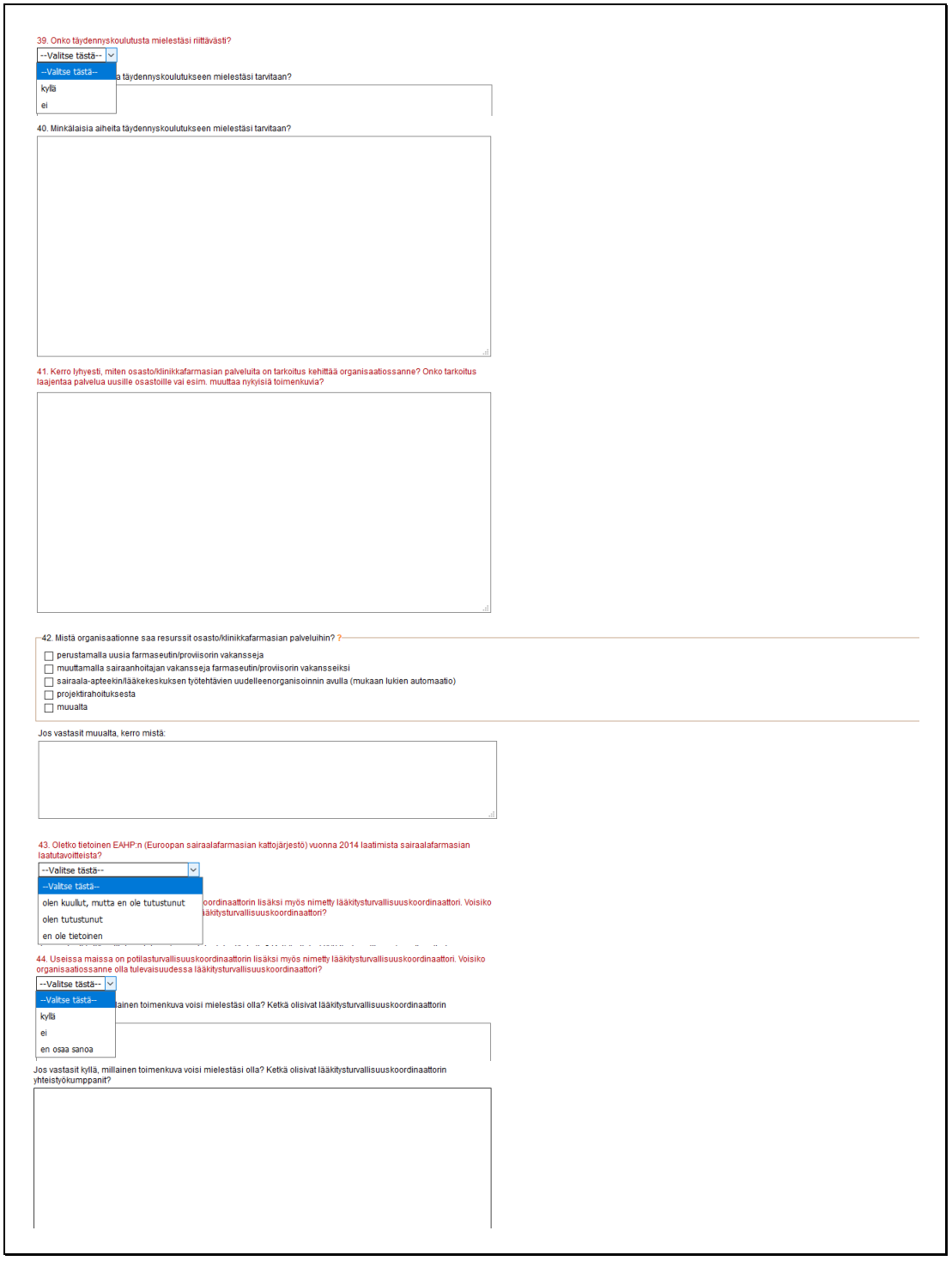
?

38. Onko ammatillinen täydennyskoulutus vaikuttanut osasto/klinikkafarmaseuttien toimenkuvaan organisaatiossanne?

--Valitse tästä--
--Valitse tästä--
kyllä
ei
en osaa sanoa

ro miten?

Jos vastasit kyllä, kerro miten?



39. Onko täydennyskoulutusta mielestäsi riittävästi?

--Valitse tästä--
--Valitse tästä--
kyllä
ei

a täydennyskoulutukseen mielestäsi tarvitaan?

40. Minkälaisia aiheita täydennyskoulutukseen mielestäsi tarvitaan?

41. Kerro lyhyesti, miten osasto/klinikkafarmasian palveluita on tarkoitus kehittää organisaatiossanne? Onko tarkoitus laajentaa palvelua uusille osastoille vai esim. muuttaa nykyisiä toimenkuvia?

42. Mistä organisaationne saa resurssit osasto/klinikkafarmasian palveluihin? ?

- [ ] perustamalla uusia farmaseutin/proviisorin vakansseja
- [ ] muuttamalla sairaanhoitajan vakansseja farmaseutin/proviisorin vakansseiksi
- [ ] sairaala-apteekin/lääkekeskuksen työtehtävien uudelleenorganisoinnin avulla (mukaan lukien automaatio)
- [ ] projektirahoituksesta
- [ ] muualta

Jos vastasit muualta, kerro mistä:

43. Oletko tietoinen EAHP:n (Euroopan sairaalafarmasian kattojärjestö) vuonna 2014 laatimista sairaalafarmasian laatutavoitteista?

--Valitse tästä--
--Valitse tästä--
olen kuullut, mutta en ole tutustunut
olen tutustunut
en ole tietoinen

oordinaattorin lisäksi myös nimetty lääkitysturvallisuuskoordinaattori. Voisiko
lääkitysturvallisuuskoordinaattori?

44. Useissa maissa on potilasturvallisuuskoordinaattorin lisäksi myös nimetty lääkitysturvallisuuskoordinaattori. Voisiko organisaatiossanne olla tulevaisuudessa lääkitysturvallisuuskoordinaattori?

--Valitse tästä--
--Valitse tästä--
kyllä
ei
en osaa sanoa

ainen toimenkuva voisi mielestäsi olla? Ketkä olisivat lääkitysturvallisuuskoordinaattorin

Jos vastasit kyllä, millainen toimenkuva voisi mielestäsi olla? Ketkä olisivat lääkitysturvallisuuskoordinaattorin yhteistyökumppanit?

45. Kuvaa lyhyesti, miten näet organisaationne osasto/klinikkafarmasian ja kliinisen farmasian palvelut tulevaisuudessa vuonna 2025. Esim. mikä voisi olla sote-uudistuksen vaikutus?

46. Onko organisaatiossanne tutkittu/mitattu/auditoitu osasto/klinikkafarmasian avulla saavutettuja hyötyjä vuoden 2011 jälkeen?

--Valitse tästä--
--Valitse tästä--
kyllä
ei

/KLINIKKAFARMASIAN HYÖDYT (hyötyjä on selvitetty/tutkittu organisaatiossa). Vastaa tutkimustenne tulosten perusteella.

en olette asiaa organisaatiossanne tutkineet:

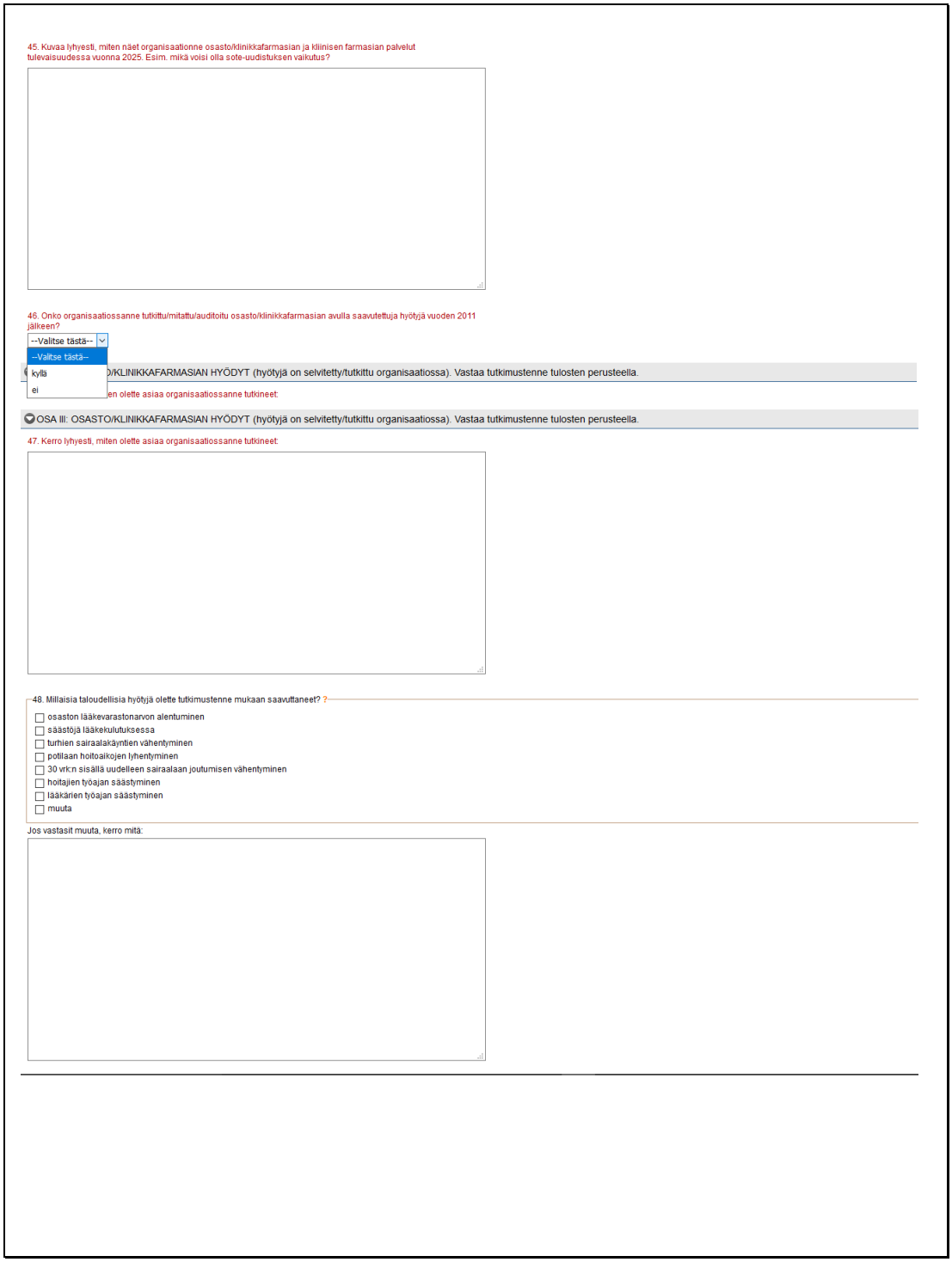
OSA III: OSASTO/KLINIKKAFARMASIAN HYÖDYT (hyötyjä on selvitetty/tutkittu organisaatiossa). Vastaa tutkimustenne tulosten perusteella.

47. Kerro lyhyesti, miten olette asiaa organisaatiossanne tutkineet:

48. Millaisia taloudellisia hyötyjä olette tutkimustenne mukaan saavuttaneet? ?

- [ ] osaston lääkevarastonarvon alentuminen
- [ ] säästöjä lääkekulutuksessa
- [ ] turhien sairaalakäyntien vähentyminen
- [ ] potilaan hoitoaikojen lyhentyminen
- [ ] 30 vrk:n sisällä uudelleen sairaalaan joutumisen vähentyminen
- [ ] hoitajien työajan säästyminen
- [ ] lääkärien työajan säästyminen
- [ ] muuta

Jos vastasit muuta, kerro mitä:



45. Kuvaa lyhyesti, miten näet organisaationne osasto/klinikkafarmasian ja kliinisen farmasian palvelut tulevaisuudessa vuonna 2025. Esim. mikä voisi olla sote-uudistuksen vaikutus?

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--Valitse tästä--
--Valitse tästä--
kyllä
ei

/KLINIKKAFARMASIAN HYÖDYT (hyötyjä on selvitetty/tutkittu organisaatiossa). Vastaa tutkimustenne tulosten perusteella.

en olette asiaa organisaatiossanne tutkineet:

OSA III: OSASTO/KLINIKKAFARMASIAN HYÖDYT (hyötyjä on selvitetty/tutkittu organisaatiossa). Vastaa tutkimustenne tulosten perusteella.

47. Kerro lyhyesti, miten olette asiaa organisaatiossanne tutkineet:

48. Millaisia taloudellisia hyötyjä olette tutkimustenne mukaan saavuttaneet? ?

- [ ] osaston lääkevarastonarvon alentuminen
- [ ] säästöjä lääkekulutuksessa
- [ ] turhien sairaalakäyntien vähentyminen
- [ ] potilaan hoitoaikojen lyhentyminen
- [ ] 30 vrk:n sisällä uudelleen sairaalaan joutumisen vähentyminen
- [ ] hoitajien työajan säästyminen
- [ ] lääkärien työajan säästyminen
- [ ] muuta

Jos vastasit muuta, kerro mitä:

49. Millaisia potilaaseen liittyviä hyötyjä olette tutkimustenne mukaan saavuttaneet? ?

- ☐ lääkkeen tilaamiseen liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeen säilytykseen/varastointiin liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkemääräykseen liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeenjakoon liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeen käyttökuntoonsaattoon liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeen antoon liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeiden aiheuttamien haittojen vähentyminen
- ☐ turhien lääkkeiden käytön vähentyminen
- ☐ tarpeellisten uusien lääkkeiden aloittaminen
- ☐ potilaan sairaalassaolopäivien vähentyminen
- ☐ turhien sairaalakäyntien vähentyminen
- ☐ potilaiden kuolleisuuden vähentyminen
- ☐ potilaiden parempi hoitoon sitoutuminen
- ☐ potilaan voinnin parantuminen
- ☐ lääkeohjauksen laadun parantuminen
- ☐ potilaiden henkilökohtaisten lääkehoitosuunnitelmien lisääntyminen
- ☐ farmasistin tekemän lääkehoidon arviointien lisääntyminen
- ☐ kaatumisten vähentyminen
- ☐ lääkehoidon tavoitteiden parempi toteutuminen (esim. verenpaine tavoitearvossa, kipu hallinnassa)
- ☐ ajantasaisten lääkityslistojen lisääntyminen
- ☐ kotiutuvalle potilaalle annettavien kotilääkekorttien lisääntyminen
- ☐ lääkityspoikkeamien raportoinnin lisääntyminen
- ☐ monitoroinnin paranturninen ja parempi lääkehoidon seuranta (laboratoriomittaukset, pitoisuusmääritykset)
- ☐ muuta

Jos vastasit muuta, kerro mitä:

50. Millaisia muita hyötyjä olette tutkimustenne mukaan saavuttaneet? ?

- ☐ hoitajien lääkeosaamisen lisääntyminen
- ☐ yhteistyön lisääntyminen lääkäreiden kanssa
- ☐ yhteistyön lisääntyminen hoitajien kanssa
- ☐ yhteistyön lisääntyminen potilaiden kanssa
- ☐ eri ammattiryhmien työnjaon selkiytyminen lääkehoidossa
- ☐ lääkehoitoprosessin selkiytyminen
- ☐ lääkitysturvallisuuskulttuurin parantuminen
- ☐ lääkehoitoprosessin riskien tunnistaminen
- ☐ lääkehoitoprosessin suojauksien lisääntyminen
- ☐ osaston toiminnan kehittyminen ja/tai osaston voimavarojen uudelleensuuntaaminen
- ☐ osaston muun henkilökunnan työtyytyväisyyden lisääntyminen
- ☐ osasto/klinikkafarmaseuttien/proviisorien työtyytyväisyyden lisääntyminen
- ☐ muuta

Jos vastasit muuta, kerro mitä:

51. Miten olette raportoineet saamianne tuloksia? ?

- ☐ sairaala-apteekissa/lääkekeskuksessa
- ☐ sairaalassa/terveyskeskuksessa/hoitoyksikössä
- ☐ kansallisesti (esim. koulutuspäivillä, kongresseissa, seminaareissa)
- ☐ kansallisissa julkaisuissa
- ☐ kansainvälisesti (esim. koulutuspäivillä, kongresseissa, seminaareissa)
- ☐ kansainvälisissä julkaisuissa
- ☐ emme ole raportoineet tuloksia
- ☐ muuten

Jos vastasit muuten, kerro miten:

52. Voisiko saamistanne tuloksista saada yhteenvedon tämän tutkimuksen käytöön? ?

- ☐ kyllä, toimitamme ne tutkijalle sähköisesti kyselyn vastausten liitteenä (kyselyn lopussa)
- ☐ ei

53. Millaisia muita hyötyjä olette mielestänne organisaatiossanne osasto/klinikkafarmasian avulla saavuttaneet, vaikka ette ole niitä tutkineet?

54. Otamme mielellämme vastaan kommenttejanne ja ajatuksianne osasto/klinikkafarmasiaan liittyen:

Seuraavassa vaiheessa voit lähettää liitetiedostona tutkimustuloksianne (koskee vain niitä, jotka ovat tutkineet hyötyjä) ja tallentaa lopulliset vastauksesi kyselyyn.

Kiitos, että osallistuit tähän kyselytutkimukseen!

OSA II: OSASTO/KLINIKKAFARMASIAN TILANNE JA TULEVAISUUS (organisaatiossa ei ole osasto/klinikkafarmasiaa)

8. Kerro lyhyesti, miksi organisaatiossanne ei ole osasto/klinikkafarmasiaa?

9. Oletteko suunnitelleet aloittavanne osasto/klinikkafarmasiaa organisaatiossanne?

--Valitse tästä--
--Valitse tästä--
kyllä
ei

ro miten:

Jos vastasit kyllä, kerro miten:

10. Mitkä asiat ovat mielestäsi helpottaneet tai vaikeuttaneet osasto/klinikkafarmasian suunnittelua ja aloittamista organisaatiossanne?

11. Missä yksiköissä/mille osastoille organisaatiossanne osasto/klinikkafarmasiaa mielestäsi eniten tarvittaisiin? Miksi?

12. Oletko tietoinen EAHP:n (Euroopan sairaalafarmasian kattojärjestö) vuonna 2014 laatimista sairaalafarmasian laatutavoitteista?

--Valitse tästä--
--Valitse tästä--
olen kuullut, mutta en ole tutustunut
olen tutustunut
en ole tietoinen

oordinaattorin lisäksi myös nimetty lääkitysturvallisuuskoordinaattori. Voisiko
äkitysturvallisuuskoordinaattori?

13. Useissa maissa on potilasturvallisuuskoordinaattorin lisäksi myös nimetty lääkitysturvallisuuskoordinaattori. Voisiko organisaatiossanne olla tulevaisuudessa lääkitysturvallisuuskoordinaattori?

--Valitse tästä--
--Valitse tästä--
kyllä
ei
en osaa sanoa

lainen toimenkuva voisi mielestäsi olla? Ketkä olisivat lääkitysturvallisuuskoordinaattorin

14. Kuvaa lyhyesti, miten näet organisaationne osastofarmasian ja kliinisen farmasian palvelut tulevaisuudessa vuonna 2025. Esim. mikä voisi olla sote-uudistuksen vaikutus?

15. Otamme mielellämme vastaan kommenttejanne ja ajatuksianne osasto/klinikkafarmasiaan liittyen:

Seuraavassa vaiheessa voit lähettää liitetiedostona tutkimustuloksianne (koskee vain niitä, jotka ovat tutkineet hyötyjä) ja tallentaa lopulliset vastauksesi kyselyyn.

Kiitos, että osallistuit tähän kyselytutkimukseen!

OSA III: OSASTO/KLINIKKAFARMASIAN HYÖDYT (hyötyjä ei ole selvitetty/tutkittu organisaatiossa)

47. Jos hyötyjä ei ole tutkittu, millaisia taloudellisia hyötyjä olette oman henkilökohtaisen näkemyksenne mukaan pystyneet osasto/klinikkafarmasian avulla saavuttamaan? ?

- ☐ osaston lääkevarastonarvon alentuminen
- ☐ säästöjä lääkekulutuksessa
- ☐ turhien sairaalakäyntien vähentyminen
- ☐ potilaan hoitoaikojen lyhentyminen
- ☐ 30 vrk:n sisällä uudelleen sairaalaan joutumisen vähentyminen
- ☐ hoitajien työajan säästyminen
- ☐ lääkärien työajan säästyminen
- ☐ muuta

Jos vastasit muuta, kerro mitä:

48. Millaisia potilaaseen liittyviä hyötyjä olette oman henkilökohtaisen näkemyksenne mukaan pystyneet osasto/klinikkafarmasian avulla saavuttamaan? ?

- ☐ lääkkeen tilaamiseen liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeen säilytykseen/varastointiin liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkemääräykseen liittyvien lääkityspoikkeamien vähentyminen
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- ☐ lääkkeen käyttökuntoonsaattoon liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeen antoon liittyvien lääkityspoikkeamien vähentyminen
- ☐ lääkkeiden aiheuttamien haittojen vähentyminen
- ☐ turhien lääkkeiden käytön vähentyminen
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- ☐ lääkityspoikkeamien raportoinnin lisääntyminen
- ☐ monitoroinnin parantuminen ja parempi lääkehoidon seuranta (laboratoriomittaukset, pitoisuusmääritykset)
- ☐ muuta

Jos vastasit muuta, kerro mitä:

49. Millaisia muita hyötyjä olette mielestänne osasto/klinikkafarmasian avulla saavuttaneet? ?

- ☐ hoitajien lääkeosaamisen lisääntyminen
- ☐ yhteistyön lisääntyminen lääkäreiden kanssa
- ☐ yhteistyön lisääntyminen hoitajien kanssa
- ☐ yhteistyön lisääntyminen potilaiden kanssa
- ☐ eri ammattiryhmien työnjaon selkiytyminen lääkehoidossa
- ☐ lääkehoitoprosessin selkiytyminen
- ☐ lääkitysturvallisuuskulttuurin parantuminen
- ☐ lääkehoitoprosessin riskien tunnistaminen
- ☐ lääkehoitoprosessin suojauksien lisääntyminen
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- ☐ osaston muun henkilökunnan työtyytyväisyyden lisääntyminen
- ☐ osasto/klinikkafarmaseuttien/proviisorien työtyytyväisyyden lisääntyminen
- ☐ muuta

Jos vastasit muuta, kerro mitä:

50. Aiotteko tulevaisuudessa organisaatiossanne tutkia osasto/klinikkafarmasian avulla saavutettuja hyötyjä?

--Valitse tästä--

--Valitse tästä--
kyllä
ei
en osaa sanoa

ro miten:

Jos vastasit kyllä, kerro miten:

51. Oletteko tehneet osasto/klinikkafarmasiaprojekteja ja onko niistä tehty loppuraportteja? Olisiko projektiraportteja mahdollista saada tämän tutkimuksen käyttöön? ?

- ☐ kyllä, toimitamme ne tutkijalle sähköisesti kyselyn vastausten liitteenä
- ☐ kyllä, mutta emme voi toimittaa raportteja tutkijalle
- ☐ olemme tehneet projekteja, mutta niistä ei ole loppuraportteja
- ☐ emme ole tehneet projekteja

52. Otamme mielellämme vastaan kommenttejanne ja ajatuksianne osasto/klinikkafarmasiaan liittyen:

Seuraavassa vaiheessa voit lähettää liitetiedostona tutkimustuloksianne (koskee vain niitä, jotka ovat tutkineet hyötyjä) ja tallentaa lopulliset vastauksesi kyselyyn.

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ARTICLES