9 General discussion
This thesis aims to assess trends in adverse event and preventable adverse event rates in the Netherlands through the time period 2004 – 2012, and to assess patient safety in more detail for specific care processes and patient groups.

**MAIN FINDINGS**

**Part I: Monitoring of adverse events and preventable adverse events 2004-2012**

In total around 16,000 patient records were reviewed in three national adverse event studies using a thorough and systematic assessment of patient records, based on the Harvard Medical Practice Study and the Canadian Adverse Event Study. To assess if the level of patient safety in Dutch hospitals had changed over the years, we assessed the findings through multilevel regression analysis with corrections for clustered data and possible differences in patient mix. These results showed a relatively stable preventable AE rate in 2008 in comparison to 2004 and followed by a statistically non-significant decline of 30% (p=0.10) in preventable adverse events in 2011-2012 in comparison to 2008. This statistically non-significant reduction could primarily be attributed to a lower preventable AE rate in older patients and during the surgical process in 2011/2012 compared to earlier years. In all years the majority of preventable adverse events was related to the surgical process, however the relative contribution increased between 2004 and 2008 and decreased again between 2008 and 2012. Preventable adverse events related to the diagnostic process showed a similar trend. In contrast preventable adverse events related to medication were also common but stayed relatively stable through the years. As can be seen in the intraclass correlation coefficient (ICC) of preventable adverse events, differences between departments were comparable in 2008 and 2011/2012, but were larger than in 2004. This indicates that alongside the national campaigns, some departments may have improved patient safety while others were still lagging behind.

The interrater agreement stayed similar over the years. Part of the 2004 sample was re-reviewed by the same physicians six years later. The results of the intra-rater agreement showed random variation and no systematic shifts, indicating reviewers did not seem to have become stricter or more lenient over the years. Intra-rater agreement scores and kappa statistics were moderate, the intra-rater agreement of preventable adverse events was lowest of all scores.

**Part II: Descriptive studies illustrating patients and processes at risk of experiencing (preventable) adverse events**

Adding to the current body of evidence on processes or patient groups who are at risk of experiencing (preventable) adverse events, we further looked into a number of topics in relation to adverse events and preventable adverse events: patients who eventually died in...
hospital, patients who experienced medication related adverse events, patients treated by multiple physician specialties, and the discharge letter.

*Inpatient deaths:* Patient and admission characteristics between inpatient deaths and patients discharged alive differed. Patients who died in hospital were on average older, admitted for longer periods of time and admitted more often urgently than patients who were discharged alive. Additionally patients who died in hospital were less often admitted to a surgical department.

Twice as many adverse events and preventable adverse events were found in inpatient deaths than in patients discharged alive. Most types of adverse events and preventable adverse events occurred in inpatient deaths as well as in patients discharged alive, however, were differently distributed. Preventable adverse events in inpatient deaths were for example less often related to the surgical process than in patients discharged alive. This was consistent with differences in admission characteristics, as in inpatient deaths there were fewer admissions to surgical departments.

*Medication related adverse events:* Our results showed that 15.2% of all adverse events found in 2008 and 2011/2012 were medication related and that only 18.4% of these adverse events were preventable. Although chemotherapy related adverse events were the most common, these were almost never judged preventable. Preventable medication related adverse events were most often found in relation to anticoagulant treatment, of which most were related to dosage or therapeutic factors.

*Multiple specialties:* The more specialties treating a patient, the higher the risk of experiencing an adverse event or preventable adverse event. This finding was most pronounced in patients treated by three or more specialties. After corrections for patient and health care characteristics the increased risk of harm for patients treated in multiple specialties stayed more visible in preventable adverse events than in non-preventable adverse events. Inadequate care seemed to increase with the number of specialties involved in treatment independent of the complexity of the patient and treatment, but the cross-sectional data cannot confirm a causal relationship.

*Discharge letter:* In 2011/2012 nearly 10% of all discharge letters were absent in the patient records. In more than half of the discharge letters that were present one or more relevant components were missing such as changes in medication, follow-up, answers to questions of the referrer and important laboratory results. Discharge letters were more likely to be missing in elective patient admissions, patients with a shorter length of stay, less comorbidity, and in readmissions. Results furthermore showed more differences between departments in missing discharge letters than there were between hospitals.
**METHODOLOGICAL CONSIDERATIONS**

**Strengths and limitations of the studies in this thesis.**

The most important strengths of the studies included in this thesis relate to:

- A large number of patient admissions, 16,000, were included in this study during three national adverse event studies. This is unprecedented in the field of patient safety, and provided us with the data for a good general sense of the burden of preventable harm caused to patients in hospitals over time.

- The method of systematic record review used, following the Harvard Medical Practice Study and the Canadian adverse event study, is a thorough, standardised assessment of patient admission in which physicians assess consecutive events and make a well-considered clinical judgement of adverse events and preventable adverse events, taking all available information into account. Systematic retrospective record review is still regarded as the method that best characterises the overall rate of harm.[1]

- Our study provides information whether judgement of reviewers changes over time. This is of special interest in the light of studies monitoring AEs and preventable AE rates over time. If patient safety improves or worsens over time, it is important to know if this is not caused for example by a more lenient of stricter assessment of AEs and their preventability by the reviewers. The results described in chapter 4 confirmed that this was not the case.

- The results of the studies have increased the sense of urgency to take countermeasures to guarantee the safety of patients in Dutch hospitals. Although this is more a practical strength than a methodological one, the used method and the specific outcome measures together have created this sense of urgency.

The most important general limitations of the studies in this thesis relate to:

- The Dutch adverse event studies showed moderate inter- and intra-rater agreement in kappa values and specific agreements, as is also common for the interrater agreement in other adverse event studies using this structured but relatively implicit review method. [2-7] This is the case for adverse events as well as preventable adverse events, of which the judgement of preventable adverse events seems to be the most difficult. To support the physician reviewers in their judgement of adverse events and preventable adverse events, preparatory questions preceded the causality and preventability score to guide the assessment, all reviewers were extensively trained, received a comprehensive guide and reflection meetings were often organised.
• Although the sample was large, it was not large enough to detect statistically significant decreases in corrected and standardised preventable AE rates over the years. Realistically a preventable adverse event rate of 0% will not be possible, it is thus the question what the lower limit of preventable adverse events is in any country or hospital. This complicates the challenge of reaching statistical significance even further and for our results may even mean that we have approached this lower limit. If attention for a specific topic is high and improvements are made in that specific area, this may coincide with decreasing attention for another area. In this light it may be more important for the future to get an overview of shifts in type of preventable adverse events, more than shifts in the incidence of preventable adverse events.

• It is likely that not all information on adverse events and preventable adverse events has been written down in the patient record, which may lead to information bias. As is the same for information concerning contributing factors as communication and handovers between health care professionals. Also, over the years the patient record has become more and more digital. Advances in electronic patient records on the one hand could make it easier to perform this kind of study because of heightened availability, accessibility and readability. On the other hand, our reviewers commented on the fact that the information written down in electronic patient records is less comprehensive.

• Hindsight bias is the influence of knowing the outcome of the care process of a patient, on the judgment of the preventability of adverse events, and is of influence in any retrospective patient record review study.[8] Especially the severity of the outcome is of influence, for example knowing that the patient has deceased as a result of an adverse event may increase the chance that the adverse events is assessed as preventable.[9] To help our reviewers minimise the effect of hindsight bias the judgement of preventability is preceded by a number of structured questions. This form of bias however can only truly be prevented if the reviewers are blinded for the outcome. This is not possible in this kind of large scaled adverse event studies.
Internal validity and generalisability
Systematic record review currently provides the best characterisation of the overall rate of harm.[1] A well-considered judgement is made by physicians in a method lying close to clinical practice. The method has high face validity with health care workers.[10]

In all three years, the samples were representative for the total Dutch hospital population after weighting, excluding obstetric admissions, children under 1 and admissions under 24 hours. All proportions were corrected for the oversampling of deceased patients and university hospitals. In our samples, 50% of the patients were inpatient deaths, and in reality this is about 3%. In the results, we weight our 50% back to the actual 3%. The same procedure was followed for the distribution of types of hospitals. This makes the results of the Dutch adverse event studies generalizable to the total Dutch hospital population.

The results of our studies may also be generalizable to other countries. The specific trends in adverse events and preventable adverse events are likely more specific for the Netherlands, however the study also provides information on monitoring preventable adverse events. This information can support other countries in choosing to perform a monitoring study and how to set up such a study. Moreover the results of the more focussed studies looking into patients who eventually died in hospital, patients who experienced medication related adverse events, and patients treated by multiple physician specialties are likely to have a general value.

REFLECTION

Monitoring of adverse events and preventable adverse events 2004-2012
The results we found in regard to the trends in preventable adverse events and adverse events in the Netherlands are encouraging, especially as improvement in specific subpopulations (elderly and surgery) coincided with attention hospitals have given to these topics. Particularly between 2008 and 2012 the surgical process received an increasing amount of attention through surgical checklists, pre, peri and post-surgical guidelines, and attention by the Dutch Health Care Inspectorate.[11-15] Although a causal relation cannot be based on our data, the positive signals in our results combined with the fact that a previous study assessing the effect of implementation of a surgical checklist on surgical complications and mortality found positive results, are promising.[16] Moreover during the safety campaign, care for the complex elderly was also one of the ten medical themes at which interventions were directed and in which subpopulation we found improvements in preventable adverse event rates.

However, as mentioned earlier, hard statistically significant evidence of an improvement in overall patient safety as measured by adverse events and preventable adverse events cannot be supported by our data, as random variation cannot be ruled out. It is further important to realise that not only the quality of health care could have influenced variations in adverse event and preventable adverse event rates, but other factors could also have (partly) sorted
their effect. Over the years the context in health care has changed: on average the length of stay has become shorter and the number of 1-day admissions has increased, while the number of clinical admissions has stayed relatively stable.[17]

Until now only a few other studies of multiple measurements of adverse events have been performed. The most often cited is of Landrigan et al. (2010), who used the Global Trigger Tool to assess temporal trends in rates of patient harm resulting from medical care in 10 hospitals in North Carolina.[18] Their results showed a similar pattern as our study did. They found a reduction in preventable harm that did not reach statistical significance (p=0.06), with no significant change in the overall rate of harms.[18] Wang et al. (2015) recently described national trends in patient safety between 2005 and 2011, for four common conditions, which had received extensive nationwide attention focussed on improving care processes and outcomes. They used a large database of information abstracted from medical records on 21 possible adverse events in patients hospitalised in the United States. Adverse event rates declined substantially among patients hospitalised for AMI or congestive heart failure, but not for pneumonia or conditions requiring surgery.[19] As this study was a database study, no in depth study of the clinical context or assessment of preventability of adverse events could be made.

Often single interventions with a relatively short measurement interval show promising results, where large studies struggle to reproduce the improvements on a large scale over longer periods of time. In a recent study for example, Starmer et al. (2015 NEJM) found changes in preventable adverse event rates using active surveillance after implementation of a handoff programme in nine paediatric hospitals in the US and Canada.[20] Though promising results, it would be interesting to see if such an intervention is sustainable over a longer period of time, when attention for other problems increases and priorities change.

The question rises if systematic record review is a suitable candidate for the monitoring of adverse events and preventable adverse events through time. The outcomes of our and other monitoring studies shows that monitoring adverse event rates through systematic record review also brings along some challenges. In the Dutch adverse event study, despite the considerable amount of in total nearly 16,000 reviewed patient records in three time periods, with already low rates of preventable adverse events the sample was not large enough to detect a statistically significant decrease in corrected and standardised preventable adverse event rates. Random variation therefore cannot be ruled out as the explanation for the non-significant reduction. Shojania & Mheen have mentioned this as a plausible explanation in the light of a Bayesian perspective.[21] However as afore mentioned, other considered methods have their own challenges and systematic record review still seems the best possible candidate. Moreover, it is also important to realise that the benefits of national adverse event
studies are not merely scientific. The results have also been an important tool for stressing the need for attention to patient safety and preventing harm to patients and herewith also have a more societal impact. Repeatedly making preventable adverse event rates public over the last 10-15 years has helped to repeatedly put patient safety on the agenda of hospitals in the Netherlands. The scientific as well as the societal impact should be considered when thinking of monitoring adverse events through time.

In a Health Foundation report on measurement and monitoring of safety, Vincent and colleagues describe that information from different dimensions is needed to get a full picture of organisational (conditions for) safety management and monitoring (figure 1).[22]

1. Past Harm: both psychological and physical measures
2. Reliability: measures of behaviour and systems
3. Sensitivity to operations: information and capacity to monitor safety on an hourly or daily basis
4. Anticipation and preparedness: ability to anticipate and be prepared for problems
5. Integration and learning: the ability to respond to and improve from safety information.

Figure 1: The five dimensions of patient safety measurement and monitoring
Our adverse event studies, by repeatedly reporting on past harm, provide important information on one of these dimensions. Safety I (what and why did it go wrong) as well as the more recent Safety II (what goes right) thinking can be placed within these dimensions. Organisations need outcomes of safety as well as information on preconditions for patient safety. Furthermore the aim of safety I and II is the same: safer healthcare for patients. The focus how to reach this primarily differs, as the focus of patient safety II lies on the resilience of an organisation and what goes right instead of what goes wrong. Outcomes of adverse event studies will stay important, for Safety I and II likewise, as results provide information on presence as well as absence of adverse events.

When choosing a type of measurement, one must take into account the goal, strategy and involved stakeholders. The goal of our study was a more policy driven one: to monitor hospital wide patient safety on a national level. This in light of a comprehensive safety programme in which all Dutch hospitals had to implement an accredited safety management system and additionally improve their clinical practice on ten medical themes known to contribute to harm to patients. If the goal had been obtaining information more specifically on causes of adverse events as to help hospitals in their search for ways to increase patient safety, then the chosen method could have been a different one. As Vincent and Amalberti discuss, adverse event studies provide a very general sense of the burden of “disease”. If one for example would want to evaluate specific treatments, or the outcome of a specific intervention, often more specific measures are chosen.[23]

Descriptive studies illustrating patients and processes at risk of experiencing (preventable) adverse events

A large amount of effort has been put into gathering the data for the successive national adverse event studies. These data have also been used to further study patients and processes at risk of experiencing adverse events and preventable adverse events. What can be learned from these focussed secondary analyses?

Studying inpatient deaths with patient record review seems an efficient way to identify preventable AEs in comparison with patients discharged alive and may be a practical new direction for future adverse event studies, as for example the UK has done.[24] However, when only studying inpatient deaths, awareness of the fact that some problems remain under- or unexposed is important, and that on certain hospital wards, patients rarely die.

Delivering care to more complex patients, not surprisingly, often seems to be associated with a higher risk of experiencing preventable adverse events.[25,26] Patients in need of multiple specialties, simultaneously or in sequence, are a good example hereof. As even after corrections the effect remains most visible in preventable adverse events, it is likely that this is not only dependent on the patients complexity and suboptimal care also plays a role. Communication problems between professionals during handoffs, or between the patient and professionals could play a role.[27,28] Handover studies most commonly focus on the
sign out, and rarely evaluate the quality of handover practices.[28] Discharge of a patient from in hospital care is also considered as a high risk process in patient safety terms.[29] The discharge letter is one of the handover methods for the outpatient carer, but are not always sufficient, as important information or the entire discharge letter is often missing. The (preventable) adverse events resulting from this lack of information during transitions in care will not always be visible in the results of the in hospital adverse event studies, as these rely on the information in the patient record of the hospital. These adverse events will only be found in the case that the adverse event leads to a readmission to the same hospital, or through studying patient records of the GP after discharge of a patient.

Although the study was not set up for these specific research questions, it would have been a waste of data and resources not to look into secondary data analysis possibilities. If the specific research questions had been the main research questions, then systematic record review and the specific data collected for the studies may not have been the preferred method to facilitate the particular research questions in all cases. Especially for the studies of multiple specialties treating a patient and adverse events related to medication other or additional research methods could have provided additional meaningful information. Although the results that we have assessed may lack some desired information, information from patient records contain powerful and valuable data and we believe that our studies are a valuable intermediate step in acquiring information on what the next important questions on a topic are.

**RECOMMENDATIONS**

**Recommendations for future research**

- Adverse event studies play an important role in highlighting the need to maintain high levels of patient safety in hospitals. However, given the already low rates of preventable adverse events in our country and taking the limited resources into account, it may not seem advisable to perform a fourth generic measurement for patients discharged alive. Future large scaled adverse event studies should therefore be directed at on the one hand specific patient groups at high risk for experiencing preventable adverse events, such as patients undergoing surgery or inpatient deaths. In this case, it is important not to lose attention for patient safety on wards where there are only few hospital deaths, or non-surgical units. On the other hand future studies could optimise the data collection to further facilitate in depth analysis possibilities, besides the assessment of (preventable) adverse events.
- Retrospective patient record review of (preventable) adverse events is performed using a structured method. Inter- and intra- rater agreement scores in our studies, as is also
the case in other research, however remain moderate. Future research could be set up to study the possibilities of making the preventability of adverse events more explicit.

- The results of chapter 7 and 8 warrant further research into communication between caregivers, intramural as well as extramural.
- Patients treated by multiple specialties have an increasing risk of experiencing preventable adverse events, however the underlying causes and suitable solutions should be the subject of further research.
- Continuity of care between the hospital and the primary care setting does not seem to be guaranteed through the discharge letters of patients, putting them at risk for experiencing adverse events and readmissions. Further research is needed directed towards patient safety and transmural care.
- The results of chapter 6 shows that future research is needed to further examine the complex nature of MRAEs, especially focussing on suboptimal integrated care and anticoagulant treatment.

**Recommendations for practice and policy**

Monitoring of adverse events in the Netherlands shows that there are indications that patient safety is increasing in Dutch hospitals. Although the results cannot be causally linked to the large scaled quality and safety programmes in our country, these positive signals do encourage to continue improvement efforts. Moreover maintaining a high level of patient safety is and will remain a continuous challenge as scientific and technological progress, and older and sicker patients, make hospital care increasingly complex. High quality and safety of patient care should be and remain a self-evident top priority.

Systematic record review provides relevant information on problems and difficulties in the provision of hospital care. The nurses and physicians who performed the reviews for our adverse event studies often commented on the fact that it is also a useful quality measure for hospitals themselves. Currently nearly a quarter of all Dutch hospitals perform systematic record review as a part of their quality cycle, often focussing on hospital deaths. In hospitals not the number of adverse events is the most important outcome, but more the underlying problems leading to preventable adverse events and the focus on learning possibilities. Besides a focus on inpatient deaths, hospitals could also focus on other areas at high risk for experiencing preventable adverse events such as patients undergoing surgery, or even directed towards specific problems such as patients using specific medication types or vulnerable (elderly) patients.
REFERENCE LIST