Development and application of measurement methods focusing on medication related problems in elderly hospitalised patients
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Citation for published version (APA):
Wierenga, P. C. (2013). Development and application of measurement methods focusing on medication related problems in elderly hospitalised patients

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Development and application of measurement methods focusing on medication related problems in elderly hospitalised patients

Peter Wierenga
DEVELOPMENT AND APPLICATION OF MEASUREMENT METHODS FOCUSING ON MEDICATION RELATED PROBLEMS IN ELDERLY HOSPITALISED PATIENTS
Wierenga, Peter C.

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Thesis, University of Amsterdam – with summary in Dutch

The research described in this thesis was supported by grants of the Netherlands Organization for Health Research and Development (ZonMw) for the Bow-Tie (#8120.0005), WINGS/CAREFUL (#SG0000001), PROFIT (#300020010) and ICOVE (#311020302) projects.

The research was conducted at the Department of Clinical Pharmacy of the Academic Medical Center Amsterdam in close collaboration with the Department Internal and Geriatric Medicine and the Department of Medical Informatics of the same hospital.

Funding for the publication of this thesis was kindly provided by the Stichting KNMP-fondsen and the Academic Medical Center Amsterdam.

ISBN 978-94-6182-355-7

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DEVELOPMENT AND APPLICATION OF MEASUREMENT METHODS FOCUSING ON MEDICATION RELATED PROBLEMS IN ELDERLY HOSPITALISED PATIENTS

ACADEMISCH PROEFSCHRIFT

der verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. D.C. van den Boom
ten overstaan van een door het college voor promoties ingestelde commissie, in het openbaar te verdedigen in de Aula der Universiteit
op vrijdag 8 november 2013, te 13.00 uur
door Peter Christiaan Wierenga
geboren te Hengelo
Promotiecommissie:

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Faculteit der Geneeskunde
A cause worth fighting for is worth fighting for to the end

- Grover Cleveland
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1

General introduction
Medication related problems

Each patient expects the best and safest medical treatment when needed. It is the obligation of each caregiver to deliver safe and effective care. “Primum non nocere”, Latin for “first, do no harm”. In real life however, medical care has the danger of causing unintended harm besides serving the patient. In several countries the magnitude of unintended harm has been assessed and confirmed in large multi-center studies. In 1991 researchers from Harvard (USA) published the first in the row of landmark studies[1]. Other countries, such as Canada, UK, Australia, New Zealand, Denmark, and the Netherlands soon followed[2-8]. Medication has shown to be a key factor in the majority of cases of unintended harm.

Pharmaceutical care covers all processes of medical care where medication is applied and in which the pharmacist directly or indirectly plays a role. On of the most commonly applied medical interventions is the application of medication. In general drugs have contributed significantly to the increase of quality of medical practice, of life expectancy and health of people. However, the application of medication can also cause problems, can be erroneous and last but not least can cause (unintended) harm[9-11]. Among medical errors, medication errors make up the largest part and of the medical adverse events (harmful events), adverse drug events (ADEs) are the most frequent type in patients[12]. Furthermore, a considerable part of hospital admissions are related to ADEs[13]. ADEs may occur during the normal use of medication as a result of an unavoidable pharmacological effect (side effects or Adverse Drug Reactions (ADRs)) or as a result of a medication error (preventable ADEs). ADEs are associated with extra length of stay, increased morbidity and mortality, and considerable extra costs[11,14,15]. Since pharmaceutical care is an essential component of healthcare; prevention, monitoring and a profound understanding of medication related problems is an important condition for the consecutive improvement of the quality and safety of medical care.

Elderly

The elderly (patient) population will continue to grow in the next decades. Compared to younger patients, patients aged 65 years or older are at a four-fold higher risk for ADEs[16,17]. The following factors play an important role in the vulnerability of this population:

• elderly often use multiple drugs (polypharmacy), thereby increasing the
chance for drug-drug and drug-disease interactions, adverse drug events, or medication errors\[18\].

• due to physiological changes, elderly often have altered pharmacokinetics and pharmacodynamics, necessitating individual drug dose adjustments.

• elderly often have multiple co-morbidities (conditions). These conditions may influence each other and influence each other’s indicated drug therapy. Due to this multi-morbidity several guidelines can be applicable to a patient and may conflict in drug therapy recommendations. Individual drug therapy adjustments are often necessary.

• elderly are treated concurrently by several medical specialists. Each doctor focuses on the care and drug therapy concerning the morbidity in which he/she is specialized\[19\]. A general overview for every elderly patient is often lacking, despite the fact that many hospitals structurally have employed geriatricians.

• elderly can suffer from cognitive, social and functional problems, further increasing the risk for medication related problems. For example, if such an elder is not able to distinguish his/her medication anymore or is not able to remember the correct use of their medication.

• elderly often transfer from one care setting to the other (hospital-nursing home, hospital-home) thereby increasing the risk for drug therapy information errors and consequently medication errors and adverse drug events. Continuity of care is an important point of attention\[20-22\].

Measuring quality and safety of pharmaceutical care

There is an abundance of studies in the field of medication safety research. Especially since the nineties of the 20th Century, after the worldwide attention for patient safety after the publication of the Institute of Medicine’s report ‘To err is human\[23\], there has been a strong increase of medication safety studies. Furthermore, there is an increasing obligation to measure quality and safety. Firstly, issued by professional societies for benchmarking between institutions; secondly, by the health inspectorate for gauging whether minimal standards of care are met; and thirdly, by health insurance companies for evaluation of key hospital data and possible financial consequences. Several interventions have been developed and applied in order to improve the quality of pharmaceutical care. To measure the effect of these interventions on medication safety the application of the right measurement method is essential. In order to facilitate the right
choice for a measurement method an overview of the main foci of approach and their pros and contras is needed.

Taking Donabedian’s (figure 1) framework in mind one can postulate that there are

*Figure 1. Donabedian’s model; adapted from[^14]*

three different types of focus in measuring medication safety: a focus on the system (the structure), a process focus, and a focus on outcome. The model shows how the three parts of the triad are related and how outcomes are influenced by structure and processes.

In a systems focus the subject is the structure of the organisation, e.g. the manner in which the care processes are organized, the material resources (such as equipment), and the human resources (such as staffing, education). This focus is the least well-known of the triad. It examines how the system evokes people to make medication errors and ultimately cause patient harm. In most cases a person never intended to make an error, the system made it possible for this person to make the mistake. The paradigm shift of looking at the system in stead of the individual (systems approach versus persons approach) has been introduced in health-care in the last decade, taking the petrochemical and aviation industry as examples and learning from their experience in creating a safety management system. Incident reporting and analysis, an example of a systems focus and a fundamental part of a safety management system, has already been widely spread in healthcare. The experience with prospective risk analysis, generally a structured method combined with implicit experience-based input, as an adequate method to measure medication-related problems and risks is however more limited.

When considering a process focus, the ‘process’ is the actual conduction of care activities, such as prescribing medication and diagnosing disease. Most medication safety literature has a process focus. Medication errors, as errors of commission or
omission in the conduction of tasks as prescribing and administering medication, are mostly reported. Medication errors can be relatively easily detected and measured using explicit criteria and have therefore been frequently used as a measure in studies. However, medication errors have the disadvantage of the difficulty to estimate their (potential) severity. The question which part of the detected errors would ultimately have led to patient harm is not an easy one to answer.

Finally, outcome denotes the effects of the care activities on the patient’s health. Besides medication errors, many medication safety studies focus on ADEs. ADEs are a measure of outcome: actual patient harm caused by medication. Although ADEs are the most relevant measure and the best option to measure what has actually happened to the patient (did he/she benefit or did he/she suffer harm), the golden standard of ADE measurement demands a laborious review of patient record combined with implicit expert judgment. Expert panel ADE judgment is known for its reliability issues\[25,26\].

In addition, one can characterize measuring methods as implicit, explicit or as a combination thereof. Explicit criteria are generally applied as rigid, objective ‘black and white’ standards. Explicit methods allow little to no room for subjective interpretation and exceptions. Therefore it can be possible that specific cases are judged unjustly as incorrect. However, explicit methods can achieve very good reliability and can be implemented at low costs. Pure implicit measurement methods rely on clinical judgment, are time-consuming and costly. They generally lack a consensus-based structure. It is more difficult to obtain reliable and valid results using pure implicit criteria, however it allows individualized assessment in exceptional patient cases. The combination of both explicit and implicit criteria could result in a method that has the advantages of both strategies: a method that is objective and structured where possible, but at the same time provides the reviewer the opportunity to apply clinical judgment if necessary\[24-26\].

Hence, the three foci of measuring medication-related problems (system/process/outcome) have their own characteristics and their advantages and disadvantages.

Objectives of this thesis

The aim of this thesis is to describe the development of three measurement methods, each with a distinct focus (system, process and outcome), for medication related problems in elderly hospitalised patients and to compare the results achieved in their application.
Outline of this thesis

This thesis contains seven chapters. In this introductory chapter (Chapter 1) the general introduction, the objective and outline are described.

Chapter 2 details the elderly patient population and addresses the issues of acute admissions, medication related problems, and geriatric syndromes as a preceding chapter of the thesis. It describes a prospective cohort study aimed to investigate whether geriatric syndromes (atypical symptoms like falls or delirium) presented just before or at hospitalisation are associated with ADEs in acutely admitted elderly medical patients.

Chapter 3 focuses on one of the three foci of measurement of medication related problems in elderly: measuring at systems level. In this chapter we describe the development and application of prospective risk analysis method for medication safety.

Chapter 4 describes measurement of medication related problems at process level using explicit quality indicators (QIs). The Assessing Care of Vulnerable Elderly (ACOVE) [27] quality indicators were developed in 2001 and were the first very comprehensive set of explicitly phrased quality indicators meant to measure the quality of care of various relevant conditions and processes of the care for elderly. The ACOVE QIs are unique among other methods for measurement of medication related problems in elderly because of their comprehensibility, their explicit phrasing, their reliability, their attention for undertreatment, and in that they reflect the minimal level of expected care.

Chapter 4.1 describes a systematic review in which we reviewed literature to examine and analyze the various ways the ACOVE QIs have been applied in medical science since their introduction over a decade ago. The studies found were categorized within a comprehensive thematic model.

In Chapter 4.2 we describe a study in which we developed a new QI set to assess the quality of pharmaceutical care of hospitalised elderly in the Netherlands based on the original ACOVE QIs.

Chapter 4.3 is a systematic review in which we aimed to summarize and analyze all studies that assessed the quality of care using QIs from or based upon the ACOVE in order to evaluate the state of the quality of care for the reported conditions.

In Chapter 4.4 we describe a study in which the quality of pharmaceutical care of 200
hospitalised Dutch elderly was assessed using the QI set described in Chapter 4.2. Furthermore, in this chapter we also assess whether an association exists between measured quality of care and the QIs, mortality, and readmissions.

Chapter 5 focuses on measurement of medication related problems at outcome level (ADEs).

In Chapter 5.1 we describe the research protocol of the WINGS study, a multicentre study to assess reduction of ADE incidence in elderly internal medicine patients by on-ward pharmacy services.

In Chapter 5.2 the results of the baseline measurement of the WINGS study are described.

In Chapter 6 the results presented in this thesis are discussed in a broader context. Implications for clinical practice and recommendations for future research are provided.

In Chapter 7 the summary is provided.

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Association between acute geriatric syndromes and medication related hospital admissions

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Drugs Aging. 2012 Aug 1; 29(8): 691-9
Abstract

Background: Elderly patients are at a 4-fold higher risk of adverse drug events (ADEs) and drug-related hospitalisation. Hospitalisation of an elderly patient is often preceded by geriatric syndromes, like falls or delirium.

Objectives: The primary aim of this study was to investigate whether geriatric syndromes were associated with ADEs in acutely admitted elderly patients.

Methods: Consecutive medical patients, aged 65 years or more, who were acutely admitted, were enrolled. An initial multidisciplinary evaluation was completed and baseline characteristics were collected. A fall before admission was retrieved from medical charts. Delirium was determined by the Confusion Assessment Method.

Results: A total of 641 patients were included. Over 25% had an ADE present at admission, 26% presented with delirium and 12% with a fall. Delirium was associated with the use of antidepressants, antipsychotics and antiepileptics. In all ADEs (n=167), ADEs were associated with a fall, with non-steroidal anti-inflammatory drugs or diuretics, but not with pre-existing functioning, delirium or older age. For ADEs involving psychoactive medication (n=35), an association was found between delirium, falls, opioids and antipsychotics in bivariate analyses. A fall just before hospitalisation (odds ratio [OR] 3.69 [95% CI 1.41, 9.67]), antipsychotics (OR 3.70 [95% CI 1.19, 11.60]) and opioids (OR 14.57 [95% CI 2.02, 105.30]) remained independently associated with an ADE involving psychoactive medication.

Conclusion: This prospective study demonstrated that, in a cohort of elderly hospital patients, a fall before admission and prevalent delirium are associated with several pharmacological groups and/or with ADE-related hospital admission.

Background

Pharmacotherapy is an important component of medical treatment but is often a cause of adverse drug events (ADEs). ADEs are the most frequent type of adverse events occurring in medical in-patients and a considerable part of hospital admissions are related to ADEs. ADEs have also been associated with unnecessary hospital admission[1]. Compared with younger patients, patients aged 65 years or older are at a 4-fold higher risk for ADEs[2]. This can be ascribed to their co-morbidities, complex care, presence of cognitive, social and functional limitations, use of multiple drugs, and altered phar-
macokinetics and pharmacodynamics\textsuperscript{[3,4]} . A recent systematic review showed that the odds of being hospitalised by ADE-related problems is four times higher for elderly persons (16.6\% vs 4.1\%)\textsuperscript{[5]} . Approximately 50\% of ADEs are preventable\textsuperscript{[4,5]} , and can be resolved if detected in time. In the traditional model of medical diagnosis, there is a clear relationship between typical clinical signs and symptoms prior to or present at hospital admission. However, it is believed that this model does not accurately define illness presentations in older, vulnerable, hospital patients\textsuperscript{[6,7]} . As observed commonly in geriatric medicine, many of these patients present atypically, such as pneumonia without fever, or with unintentional fall or delirium. The term ‘geriatric syndrome’ is used to capture these atypical presentations that do not fit into discrete illness categories. Geriatric syndromes are understood to have the following features: they occur in older, often vulnerable persons; although precipitated by one or more acute triggers, they are multifactorial in aetiology; they seldom follow a typically episodic course; and they frequently lead to persistent functional impairment\textsuperscript{[8,9]} . An acute illness leading to hospitalisation is often accompanied by one or more geriatric syndromes, especially falls and delirium (15–30\% and 10\%, respectively)\textsuperscript{[10–13]} . These geriatric syndromes are associated with substantially poorer discharge outcomes such as functional decline, institutionalisation and mortality\textsuperscript{[14]} . Many ADEs present typically, for example, with gastrointestinal bleeding, nausea, or rash. However, it is also common in elderly hospitalised patient that many ADEs present with atypical symptoms, and can be readily overlooked at admission. Since both geriatric syndromes (like delirium and falls) and ADEs are frequently found in acutely hospitalised elderly patients, a possible association or sequential time course may exist. For instance, ADEs may reveal themselves first as geriatric syndromes like delirium or falls before they lead to hospital admission. If this hypothesized association is recognized in a timely manner, early intervention aimed at the underlying cause of the ADE may prevent an unnecessary hospital admission and its attendant complications, such as functional decline\textsuperscript{[14]} . The overall aim of this study was to investigate whether a fall before admission and prevalent delirium are associated with specific pharmacological groups and ADE-related hospital admission in a cohort of acutely admitted medical patients aged 65 years and older.

Methods

Design and Participants

This prospective cohort study was conducted between 1 December 2002 and 1 April 2006, at the Academic Medical Center, Amsterdam, a tertiary university teaching hospital. All consecutive patients aged 65 years or older who were acutely admitted to the Department of Internal Medicine were enrolled. Patients were excluded if they
were unable to speak or understand Dutch or English, if they or their relatives did not give permission for the study, if they came under intensive care or cardiac monitoring, or if they were transferred to a ward other than Internal Medicine. The study was approved by the hospital’s Medical Ethics Committee.

Measurements

The research team was composed of two attending physicians in geriatric medicine, a clinical nurse specialist and two research nurses, all trained in geriatrics, and a clinical pharmacist. Patients and medical and nursing staff were interviewed by the nurses to determine study eligibility of patients within 48 hours of admission. An initial, multidisciplinary evaluation was completed for all participants by members of the study team to identify prevalent delirium, present at the time of hospital admission. Delirium was scored within 24 hours after admission by research physicians using the Confusion Assessment Method (CAM) [15]. Information for diagnosing prevalent delirium was based on a psychiatric examination of the patient including cognitive testing (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM IV] criteria), medical and nursing records, including the Delirium Observation Screening Scale (DOS) [16], and information given by relatives concerning the 24 hours prior to admission. The occurrence of one or more unintentional falls within 1 week before hospital admission was abstracted from the physician’s notes in the medical record and/or from the discharge summary. The research physicians also completed a Charlson Comorbidity Index and the main diagnosis International Classification of Diseases, 9th Revision (ICD 9) code, both based on information at discharge [17].

The research nurses collected demographic and clinical data from all study participants. They also screened for global cognitive impairment using the Mini-Mental State Examination (MMSE). Cognitive functioning before hospital admission was scored by medical history and the Informant Questionnaire on Cognitive Decline – short form (IQCODE-SF). The IQCODE-SF assesses global cognitive impairment based on the response of an informant who has known the patient for at least 10 years [18]. The informant was asked to recollect the patients’ functioning 2 weeks prior to hospital admission and to compare it with his or her functioning 10 years before. Patients with a mean score of 3.9 or more on the IQCODE-SF have serious cognitive impairment [18,19]. To measure functionality, patients’ relatives were asked to complete the modified 15-item Katz Activities of Daily Living (ADL) Index score, also based on the patient’s condition 2 weeks before admission [20]. This is a validated 15-item scale measure to rate instrumental ADL (IADL), modified from the original ADL index questionnaire developed by Katz et al [21]. Performance is graded according to the number of disabilities (i.e. a higher score indicates a worse functional status).
Outcomes

The primary outcome was an ADE. An ADE was defined as an undesirable clinical manifestation consequent to and caused by the administration or omission of a particular drug or interacting drugs. To determine whether an ADE was associated with the cause leading to hospital admission, the discharge summary and medical record abstraction were separately reviewed by a clinical pharmacist and a geriatrician.

Our study was limited to drug-related incidents occurring prior to hospitalisation that led directly to a hospital admission. Drug-related incidents occurring during the course of a hospitalisation were not considered in the context of this study. Drug-related incidents were detected by (i) review of hospital discharge summaries and (ii) review of emergency department notes. All available discharge summaries relating to hospitalisations for the study population during the study were obtained for review. The information contained in these discharge summaries was reviewed for evidence of a drug-related incident that led to an admission. Reviews of discharge summaries and medical record abstractions were performed by trained clinical pharmacist and geriatrician investigators, who also classified the involved drugs. Admissions were classified as drug-related if both reviewers judged the drug to have made a dominant or partial contribution to the admission. When raters disagreed, consensus was reached. Drugs that were present at admission and are often associated with ADEs were divided into pharmacological groups (table I).

Statistical Analysis

Descriptive statistics were applied to describe baseline characteristics and results about ADEs and pharmacological groups. To identify potential associations between patients and/or ADEs and atypical illness presentations (fall or delirium) present on admission, a multivariate logistic regression analysis with backward selection was conducted, using variables with a p-value ≤ 0.2 for selection. A p-value < 0.05 was considered statistically significant. We hypothesized that there would be associations between falls and delirium, and between prior functional and cognitive status and delirium as well. Therefore, these were tested separately before the multivariate logistic regression analysis took place. Associations were analysed for all ADEs in general and also specifically for the ADEs involving psychoactive drugs as these drugs are known to contribute to delirium. All statistical analyses were performed using SPSS software (version 16.0; SPSS Inc., Chicago, IL, USA).
Results

Study Population

In total, 1092 consecutive patients were screened. A total number of 240 patients (22%) did not give informed consent or withdrew consent from the original study, 36 patients (3.3%) were too ill, 44 patients (4%) were not able to speak or understand Dutch and 131 patients (12%) could not be included within the predefined time frame. A total of 641 patients were included in this study. Of these, 48 patients (10%) died in hospital. Table II shows the baseline characteristics of our study population. Mean age was 77.8 years (SD 7.9 years), 46.6% were male, 67.6% of the patients lived at home and 28.6% had pre-existing cognitive impairment. The prevalence of delirium at admission and a fall prior to admission was 25.9% and 12%, respectively, and 5.4% of the patients had both a fall and delirium. Prevalent delirium and a prior fall were highly correlated (p=0.0046). We previously demonstrated a strong independent association between prior cognitive and functional impairment with prevalent delirium in a population of acutely admitted medical patients\[^{22}\].

Adverse Drug Events (ADEs)

Table I contains the associations of fall and delirium with drug groups that are commonly associated with ADEs. The use of antidepressants, antipsychotics and antiepileptics were associated with delirium; none of these were related with a prior fall. Table III shows the distribution of ADEs over pharmacological groups and the percentage of ADEs due to a drug group coinciding with a fall or delirium. A total of 167 ADEs contributed to an acute admission. Diuretics were most frequently associated with an ADE, followed by coumarins, immunosuppressants and non-steroidal anti-inflammatory drugs (NSAIDs). ADEs involving antidiabetics, antidepressants, antihypertensives and antipsychotics were related to more than half of the cases with a fall. ADEs involving diuretics, theophylline, antipsychotics, antidepressants, antihypertensives and lithium occurred in many cases in combination with delirium.
Correlates of ADEs

Table IV shows the analysis of variables associated with an ADE contributing to a hospital admission. According to the bivariate analysis, a confirmed ADE at admission was associated with a fall, and also with use of diuretics, NSAIDs and prednisolone. Delirium was not significantly associated with an ADE in this analysis. The multivariate logistic regression analysis showed that a fall just before acute hospitalisation and diuretics were independently associated with an ADE-related hospital admission.

Table V shows the results of a similar analysis including only ADEs involving psychoactive medication (n = 35). In this group, both delirium and falls were associated with ADEs, as was the use of antipsychotics and opioids. These associations remained similar after adjustment except the odds ratio for delirium (OR=1.93) did not remain significant. Post hoc power calculations revealed that our study did not have adequate power to detect a delirium effect.

Table I. Pharmacological groups associated with delirium and falls (n = 647)

| Pharmacological group (n) | Falls [n (%)] | p-Value | Delirium [n (%)] | p-Value |
|--------------------------|---------------|---------|------------------|---------|
| Antidepressants (38)     | 6 (15.8)      | 0.77    | 15 (39.5)        | 0.05    |
| Antipsychotics (37)      | 8 (21.6)      | 0.15    | 23 (62.2)        | <0.001  |
| Opioids (15)             | 1 (6.7)       | 0.38    | 5 (33.1)         | 0.52    |
| Diuretics (265)          | 29 (10.9)     | 0.23    | 70 (26.4)        | 0.80    |
| Antiepileptics (9)       | 0 (0)         | 0.21    | 7 (77.8)         | <0.001  |
| Prednisolone (69)        | 6 (8.7)       | 0.33    | 12 (17.4)        | 0.09    |
| NSAIDs (65)              | 9 (13.8)      | 0.69    | 15 (23.1)        | 0.59    |

a Tested with Chi-squared (w2) test.
NSAID=non-steroidal anti-inflammatory drug.
Table 2. Patient characteristics at admission

| Variable                                           | Patients (n = 641) |
|---------------------------------------------------|--------------------|
| **Demographic**                                   |                    |
| Age [years, mean (SD)]                           | 77.8 (7.9)         |
| Male (%)                                          | 45.6               |
| Years of education [mean (SD)]                   | 9.3 (3.5)          |
| Ethnic background (% Caucasian)                  | 88.5               |
| **Social status (%)**                            |                    |
| Single/widowed/divorced                          | 53.7               |
| Married/living with partner                      | 46.3               |
| **Living arrangement (%)**                       |                    |
| Independent                                      | 67.6               |
| Senior residence                                 | 16.8               |
| Home for the elderly                             | 10.7               |
| Nursing home                                     | 3.9                |
| Intermediate care                                | 1.0                |
| **Medical history**                              |                    |
| Charlson Comorbidity Index score [mean (SD)]     | 3.4 (2.3)          |
| Pre-existing functional impairment [Katz ADL Index score, mean (SD)] | 5.1 (3.8) |
| Pre-existing cognitive impairment (%)             | 28.6               |
| **Situation at admission**                       |                    |
| MMSE score [mean (SD)]                           | 21.5 (6.9)         |
| ADE-associated hospital admission (%)            | 25.8               |
| Delirium prevalence on admission (%)             | 25.9               |
| Fall within 1 week before hospital admission (%) | 12.0               |
| **Diagnostic ICD category (%)**                  |                    |
| Neurological disease                             | 0.8                |
| Infectious disease                               | 53.3               |
| Endocrine disease                                | 6.5                |
| (Haematological) malignancy                      | 22.0               |
| Pulmonary disease                                | 8.2                |
| Cardiovascular diseases                          | 9.9                |
| Gastrointestinal disease                         | 33.5               |

* Inclusion in multiple categories possible.

ADE=adverse drug event; ADL=Activities of Daily Living; ICD=International Classification of Diseases
MMSE=Mini-Mental State Examination; SD=standard deviation.
Table 3. Pharmacological groups associated with all identified adverse drug events (n = 167) and prevalence of delirium and falls within that group

| Pharmacological group                                      | ADEs [n (%)] | Pharmacological group associated with ADE in those who sustained a fall (%)<sup>a</sup> | Pharmacological group associated with ADE in those with prevalent delirium (%)<sup>a</sup> |
|-----------------------------------------------------------|--------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| Diuretics                                                 | 49 (29.3)    | 22.4                                                                              | 46.9                                                                              |
| Coumarins                                                 | 20 (12.0)    | 15.0                                                                              | 25.0                                                                              |
| Immunosuppressants                                        | 20 (12.0)    | 10.0                                                                              | 5.0                                                                               |
| NSAIDs                                                    | 17 (10.2)    | 11.8                                                                              | 29.4                                                                              |
| Antidiabetics                                             | 13 (7.8)     | 53.8                                                                              | 38.5                                                                              |
| Platelet aggregation inhibitors (acetylsalicylic acid/carbasalate calcium) | 11 (6.6)  | 9.1                                                                               | 9.1                                                                               |
| Antibacterials                                            | 8 (4.8)      | 37.5                                                                              | 12.5                                                                              |
| Opioids                                                   | 8 (4.8)      | 12.5                                                                              | 28.6                                                                              |
| Prednisolone                                              | 4 (2.4)      | 25.0                                                                              | 25.0                                                                              |
| Antihypertensives                                         | 4 (2.4)      | 75.0                                                                              | 50.0                                                                              |
| Antidepressants                                           | 3 (1.8)      | 50.0                                                                              | 100.0                                                                             |
| Digoxin                                                   | 2 (1.2)      | 0.0                                                                               | 0.0                                                                               |
| Theophylline                                              | 2 (1.2)      | 0.0                                                                               | 100.0                                                                             |
| Antipsychotics                                            | 2 (1.2)      | 50.0                                                                              | 100.0                                                                             |
| Lithium                                                   | 1 (0.6)      | 0.0                                                                               | 100.0                                                                             |
| Calcium                                                   | 1 (0.6)      | 0.0                                                                               | 0.0                                                                               |
| Antihistamines                                            | 1 (0.6)      | 0.0                                                                               | 0.0                                                                               |
| Diagnostics                                               | 1 (0.6)      | 0.0                                                                               | 0.0                                                                               |
| Total                                                     | 167          | NA                                                                                | NA                                                                                |

<sup>a</sup> A patient could have both sustained a fall and presented with delirium at admission in combination with an ADE; percentages summed can therefore exceed 100%.

ADE=adverse drug event; NA=not applicable; NSAID=non-steroidal anti-inflammatory drug.
Table 4. Factors associated with an adverse drug event\(^a\) (n = 167) contributing to a hospital admission identified by bivariate and multivariate logistic regression analysis

| Variable                               | Bivariate analysis | Multivariate analysis |
|----------------------------------------|--------------------|-----------------------|
|                                       | OR                 | 95% CI                | OR                 | 95% CI                |
| **Demographic**                        |                    |                       |                    |                       |
| Age (continuous)                       | 1.01               | 0.99, 1.03            |                    |                       |
| Male (dichotomous)                     | 1.25               | 0.86, 1.81            |                    |                       |
| Years of education (continuous)        | 1.00               | 0.94, 1.06            |                    |                       |
| Living independently (dichotomous)     | 0.82               | 0.46, 1.46            |                    |                       |
| Social situation (dichotomous)         | 1.07               | 0.68, 1.70            |                    |                       |
| **Medical history**                    |                    |                       |                    |                       |
| Charlson Comorbidity Index             | 0.97               | 0.89, 1.05            |                    |                       |
| Pre-existing functional impairment     | 1.00               | 0.99, 1.01            |                    |                       |
| (Katz ADL Index score)                 |                    |                       |                    |                       |
| Pre-existing cognitive impairment      | 1.00               | 0.99, 1.01            |                    |                       |
| **Situation at admission**             |                    |                       |                    |                       |
| Prevalent delirium                     | 1.21               | 0.81, 1.80            |                    |                       |
| Fall within 1 week before admission    | 2.06               | 1.26, 3.36            | 2.27               | 1.16, 4.45            |
| **Pharmacological group**              |                    |                       |                    |                       |
| Antidepressants                        | 0.82               | 0.39, 1.74            |                    |                       |
| Antipsychotics                         | 1.18               | 0.57, 2.44            |                    |                       |
| Opioids                                | 1.53               | 0.54, 4.38            |                    |                       |
| Diuretics                              | 3.10               | 2.12, 4.53            | 3.87               | 2.33, 6.42            |
| Antiepileptics                         | 1.81               | 0.48, 6.84            |                    |                       |
| Prednisolone                           | 1.98               | 1.14, 3.44            | 1.90               | 0.58, 2.85            |
| NSAIDs                                 | 2.82               | 1.60, 4.97            | 5.87               | 2.70, 13.01           |

\(^a\) Significant results in bold.

ADL=Activities of Daily Living; CI=confidence interval; NSAID=non-steroidal anti-inflammatory drug; OR=odds ratio.
Table 5. Factors associated with a psychoactive medication-related adverse drug event\(^a\) (n = 35) contributing to a hospital admission identified by bivariate and multivariate logistic regression analysis

| Variable                          | Bivariate analysis | Multivariate analysis |
|-----------------------------------|--------------------|-----------------------|
|                                   | OR  | 95% CI   | OR    | 95% CI   |
| **Demographic**                   |     |          |       |          |
| Age (continuous)                  | 0.99 | 0.94, 1.05 | 0.99 | 0.94, 1.05 |
| Male (dichotomous)                | 1.78 | 0.72, 4.41 | 1.78 | 0.72, 4.41 |
| Living independently (dichotomous)| 0.76 | 0.27, 2.14 | 0.76 | 0.27, 2.14 |
| Social situation (dichotomous)    | 0.99 | 0.43, 2.28 | 0.99 | 0.43, 2.28 |
| **Medical history**               |     |          |       |          |
| Charlson Comorbidity Index        | 1.09 | 0.94, 1.26 | 1.09 | 0.94, 1.26 |
| Pre-existing functional impairment (Katz ADL Index score) | 1.07 | 0.96, 1.19 | 1.07 | 0.96, 1.19 |
| Pre-existing cognitive impairment | 1.58 | 0.65, 3.81 | 1.58 | 0.65, 3.81 |
| **Situation at admission**        |     |          |       |          |
| Prevalent delirium                | 2.05 | 1.01, 4.15 | 1.93 | 0.76, 4.94 |
| Fall within 1 week before admission | 3.00 | 1.40, 6.40 | 3.69 | 1.41, 9.67 |
| **Pharmacological group**         |     |          |       |          |
| Antidepressants                   | 1.83 | 0.61, 5.48 | 1.83 | 0.61, 5.48 |
| Antipsychotics                    | 3.36 | 1.29, 8.74 | 3.70 | 1.19, 11.60 |
| Opioids                           | 5.71 | 1.72, 18.90 | 14.57 | 2.02, 105.30 |
| Diuretics                         | 0.78 | 0.38, 1.58 | 0.78 | 0.38, 1.58 |
| Antiepileptics                    | 4.27 | 0.85, 21.37 | 4.27 | 0.85, 21.37 |
| Prednisolone                      | 1.41 | 0.52, 3.78 | 1.41 | 0.52, 3.78 |
| NSAIDs                            | 0.81 | 0.24, 2.73 | 0.81 | 0.24, 2.73 |

\(^a\) Significant results in bold.
ADL=Activities of Daily Living; CI=confidence interval; NSAID=non-steroidal anti-inflammatory drug; OR=odds ratio.
Discussion

This study demonstrated that, in a cohort of older hospitalised patients, a fall sustained 1 week before admission is associated with ADE-related hospital admissions and prevalent delirium is associated with specific pharmacological groupings. These findings have important clinical implications. From the perspectives of patient safety and healthcare costs, timely recognition of both geriatric conditions and their possible associations with an ADE might reduce unnecessary hospital admissions. Previous studies have investigated incidence and types of preventable adverse events, but, to our knowledge, our study is the first to study associations of geriatric syndromes and ADEs contributing to hospital admission. After adjustment for demographic and other variables, the association with falling as a geriatric syndrome contributing to hospital admission remained strong.

Over 25% of the elderly patients were hospitalised because of ADE-related admissions. Our results on the frequency of this number of ADEs are compatible with the literature. The prevalence rates of delirium in our study are consistent with those reported in the literature. Although delirium had a high prevalence in another ADE study in older medical patients, the association between ADEs and delirium or other geriatric syndromes was not investigated. The prevalence of prior falls in our study is lower than that reported by other studies, although the difference is small. We attribute this to a relatively younger population (65 years and above) and to an under-reported number of falls. The pharmacological groups most frequently causing an ADE in our study (diuretics, coumarins, NSAIDs and platelet aggregation inhibitors) correspond to findings in literature. Preventative measures should be focused on these high-risk groups. Our study showed that antidiabetics and antihypertensives were the most commonly prescribed drugs, and that antipsychotics and antidepressants coincided with a fall in more than half of the cases. Although a possible causative relationship was not studied, it can be hypothesized that uncontrolled blood glucose, low blood pressure and other failing physiological systems in older patients can facilitate falling and hospital admission. The strength of our research is that it is based on a large hospital study that provides prospectively collected data on geriatric syndromes and other characteristics in addition to the ADEs. This study investigated both community-dwelling elders and residents of homes for the elderly and nursing homes, giving a complete picture of the whole range of acutely hospitalised elderly persons. Because of the more detailed data available on the patients’ clinical presentation, it was possible to incorporate relevant additional measures to study ADE-related hospital admissions. In particular, complete assessment of geriatric syndromes, by means of a Comprehensive Geriatric Assessment (CGA), has not been systematically accounted for in other ADE
studies. The importance of these and perhaps also other geriatric conditions should not be underestimated because their presence reflects reduced physiological reserves and may throw a shadow on their functional trajectory after discharge.

Our study also has important limitations. Firstly, all ADEs were retrieved from discharge summaries, potentially resulting in a selection bias with only the most severe cases being detected. For instance, there might be a possibility that sedative medications, which are associated with impaired physical function and falls, are under-reported, although our incidence and prevalence rates coincide with the literature\[^{23,24}\]. Secondly, there might exist a potential diagnostic bias. If we were aware of the fact that the patient had a fall prior to admission, we may have been more likely to detect a hospital admission related to medication as well.

Thirdly, we did not study the severity or preventability of ADEs because this was outside the scope of our study. Fourthly, we expected to confirm an association between a prior vulnerable state, reflected in functional and cognitive impairment or in the prevalence of delirium and ADE-related admission, but in the bivariate analysis this could not be demonstrated for all three variables or for age per se. This obvious association could not be demonstrated in our population. Within a restricted population of acutely admitted older medical patients, higher age and other characteristics of frailty are the norm. This is consistent with other studies confined to the geriatric age group\[^{23}\]. Since the geriatric syndromes, delirium and falls, were only assessed after the ADEs had already occurred, temporal association and causality cannot be determined in our analyses and may have influenced the associations seen, such as for delirium. Although delirium is often ascribed to medications and ADEs, in our present analysis, delirium did not retain significance in the final model, and was only associated with psychoactive medication. In the post hoc analysis, our study did not have adequate power to examine a delirium effect. As we expected to find more evidence of a relationship between delirium and ADEs, we carefully examined literature on this subject. In our review of the literature, we could not identify any previous studies examining the independent relationship between ADEs and geriatric syndromes (delirium and falls). In a large ambulatory cohort, only 2.4% of all ADEs presented with neuropsychiatric symptoms, including delirium\[^{24}\]. Fifthly, some pharmacological groups show a strong association in the multivariate analysis. It is important to note that the geriatric syndromes and pharmacological groups might act as mediators of the effect between ADEs and hospitalisation; thus, their independence and causal relationships cannot be established in these analyses, which must be considered associational only. Sixthly, some of the geriatric syndromes may be discounted in a manual review of these ADE lists because they
were less clinically dramatic, less characteristic of drug effects in general or may have subtle pharmacological explanations. They may only become recognized when post hoc analyses are sought based on more refined pharmacological knowledge of illness presentations in vulnerable older patients. Additionally, geriatric syndromes presenting atypically often fall out of view because many preventative measures are single disease oriented and not complex problem oriented. Disease management is too often insufficiently equipped to address vulnerable patients whose healthcare utilisation is related to multiple interacting problems and diseases. This study therefore has relevance to the shared care of elderly persons and promotes hospital care management of both diseases and disabilities in vulnerable patients.

Conclusions

To prevent elderly patients from unnecessary admissions, more proactive, preventative initiatives should be undertaken, especially in primary care. This could lead to a timely identification of ADEs revealing themselves as an atypical illness presentation, namely with a fall or delirium as a geriatric syndrome, or even to prevention from an acute hospital admission. Additionally, geriatric syndromes presenting in hospital patients need a more systematic and holistic approach to recognize them in time as potential ‘atypical’ presentations of an ADE. Geriatric syndromes, especially falls, may indicate important warning signs and thus may require additional evaluations to understand potential underlying pathological processes like harmful medications.

Acknowledgments

This research was supported by an unrestricted grant from the Academic Medical Center, Amsterdam. SI’s contribution to this work was supported in part by grants #P01AG031720 from the National Institute on Aging, #IIRG-08-88738 from the Alzheimer’s Association, and by the Milton and Shirley F. Levy Family Chair.

The authors have no conflicts of interest that are directly relevant to the content of this article.

PW was responsible for data acquisition, data analysis and drafting of the manuscript. SdR was responsible for the concept and design of the study, data acquisition, data analysis and drafting of the manuscript. BB contributed to the concept and design of the study, interpretation of the data and critical review of the manuscript for methodological content and accuracy. SI contributed to the data analysis, interpretation of the
data and revision of the manuscript. JP, BvM and SS contributed to interpretation of the data and revision of the manuscript. All of the authors had access to the data and gave final approval of the version to be published.

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Application of the Bow-Tie model in medication safety risk analysis

Consecutive experience in two hospitals in the Netherlands

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*Drug Safety* 2009; 32 (8): 663-673
Abstract

Background: To improve medication safety effectively, one should systematically analyse and assess the risks for medication errors and determine the possible causes. So far, no risk-analysis instrument exists in healthcare that can be used to analyse and visualize risks, causes and consequences of potential adverse events in a prospective manner. In high-risk industries such as petrochemistry and aviation, the Bow-Tie model is frequently used. This model combines causes, errors, preventive and recovery measures, and consequences in one model and gives insight into the magnitude and causes of existing safety risks. The aim of our project was to study the usefulness of the Bow-Tie model in the hospital setting for prospective analysis of risks in the medication process in order to develop a practicable method.

Methods: The model was first adapted to the clinical setting. Thereafter, the risk-analysis model was applied in a large tertiary teaching hospital in multidisciplinary sessions. The sessions and risk-analysis method were evaluated on the following aspects: applicability, comprehensibility, creation of awareness in and motivation of participants, and the capability of the ‘system approach’ (the approach taken by the Bow-Tie model, which focuses on the conditions under which individuals work and tries to build defences to avert errors or mitigate their effects, in contrast to a ‘person approach’, which focuses on errors of individuals, blaming them for forgetfulness, inattention etc.). Based on this evaluation, the risk analysis method was adjusted and consecutively applied in a general teaching hospital. After evaluation of the sessions in the second hospital a recommended method for risk analysis with the Bow-Tie model was defined.

Results: The risk-analysis method with the Bow-Tie model in the first hospital gave insight into many medication safety-related risks. However, the method was insufficient on comprehensibility and on the creation of awareness and motivation owing to a great number of determined risks which made thorough analysis, drawing of Bow-Ties and prioritizing difficult. The adjusted method in the second hospital focused more on the in-depth analysis of a small number of important safety issues of a department with specific attention for underlying causes. This approach was considered better in applicability, comprehensibility and the creation of awareness. Furthermore, by analyzing underlying causes, more attention could be paid to latent conditions (which can translate into error-provoking conditions) within the system.

Conclusion: We found the Bow-Tie to be an appropriate model for prospective risk analysis of medication safety in a hospital. By applying the model in two hospitals consecutively we developed a feasible method for risk-analysis sessions. Key factors of
this recommended method are a focus on the prioritized selection of safety issues and specific attention to latent conditions within the system by analysing these safety issues in depth to the root causes with the help of the Bow-Tie model.

Background

Patient safety is an important issue in healthcare. Adverse drug events (ADEs) occur frequently\cite{1-7}. Whereas some ADEs cannot be prevented (unintended adverse drug reactions), many ADEs are due to systematic medication errors and organizational failure and are therefore preventable\cite{8}. Currently, many healthcare organizations are working to improve patient safety in general and medication safety in particular. In order to improve medication safety effectively, one should systematically analyse and assess the risks for medication errors, and determine the possible causes. However, experience with systematic risk analysis is still scarce in healthcare. So far, no risk-analysis instrument exists that can be used to analyse and visualize risks, causes and consequences of potential adverse events in a prospective manner. To develop useful methods for systematic risk analysis in healthcare, one can apply the knowledge of risk management in the petrochemical and other high-risk industries. In these industries, broad experience exists with the application of risk-analysis instruments within safety management systems.

One of the risk-analysis instruments frequently used in the petrochemical industry is the Bow-Tie model\cite{9-12} (figure 1). This model combines causes, errors, preventive and recovery measures, and consequences in one model, and gives insight into the magnitude and causes of existing safety risks. Thereby, it helps to prospectively prioritize potential risk-reducing interventions. With this model it is possible to depict the relationship between causes and consequences of a specific unwanted event in an understandable manner. Weaknesses in processes (ineffective or missing safeguards and barriers) can be visualized.

The aim of our project was to study the usefulness of the Bow-Tie model in the hospital setting for prospective analysis of risks in the medication process in order to develop a practicable method.
Figure 1. The Bow-Tie model. The model combines the concepts of fault and event trees used in risk assessment and resembles the shape of the men’s fashion accessory with the same name. It integrates the understanding of how accidents happen derived from Reason’s Swiss Cheese Model\([13,14]\). ‘Top events’ are placed centrally in the Bow-Tie. Top events present an unwanted situation or event that has the potential to cause damage. In other words, a hazard is released, but has not yet caused any harm. An example of a top event at an oil-drilling platform would be an oil pipeline leak. This oil pipe leak can have various causes and consequences, which can be analysed with the Bow-Tie model. The left-hand side of the Bow-Tie describes how causes (for example high pressure in the pipeline), either in isolation or in combination, can release a hazard and lead to the undesirable top event. The right-hand side represents the various scenarios that might develop from the undesired top event (for example a fire or an explosion), dependent upon the effectiveness of systems and activities to stop progression to lasting harm and damage\([9]\). Barriers on the left side normally prevent a cause from releasing a hazard and becoming a top event, whereas recovery barriers on the right side of the model prevent a top event from causing actual harm. An example of a preventative barrier (left side) would be a pressure-relief valve or strengthened pipes on the platform. An example of a recovery barrier (right side) would be a fire-extinguishing system.
Methods

Setting

The study was performed between January and December 2005 in a large tertiary teaching hospital (Academic Medical Center Amsterdam) and consecutively in a large general hospital (Diakonessenhuis Utrecht-Zeist-Doorn) between March and May 2006. The tertiary teaching hospital (hospital A, 1002 beds) consists of a general and a children’s hospital. There is a hospital-wide implemented Computerized Physician Order Entry (CPOE) system. The general teaching hospital (hospital B, 627 beds) started the implementation of a CPOE system in 2005–6. In both institutions, hospital pharmacists did not operate on the ward on a daily basis, but performed their tasks mainly in a centrally located hospital pharmacy department and could be consulted on demand by physicians and nurses.

Trajectory Overview

The application of the Bow-Tie model was conducted as follows: the model was first adapted to the clinical setting by determining medication safety ‘top events’ (see the next section for further details). Thereafter the model was used and tested in hospital A. The performed risk analysis was evaluated and alterations were made in the method to improve the application of the Bow-Tie model in hospital B. Based on the experiences in both hospitals a recommended method for risk analysis was determined.

Adaptation of the Bow-Tie Model for Medication Safety Risk Analysis

First the Bow-Tie model was translated to the medication use process by determining medication safety-specific ‘top events’ that would be placed centrally in the model. Top events in our model were described as an unwanted event or error that takes place (e.g. an incident, a hazardous situation), but at that moment has not yet caused any harm or has not yet had any consequences. Interviews were held by an external safety expert, experienced in risk analysis in the oil and aviation industries, with representatives of five key professions (an internal medicine physician, a surgeon, a paediatrician, two nurses, two hospital pharmacists and a pharmacy technician) in order to get insight into the medication use process and its risks. In our definition, the medication use process encompassed prescribing, transcribing, dispensing, administering and monitoring. Based on risk safety theories, themes from the interviews were grouped by the external expert and three basic top events were determined for the medication use process.
1. A patient receiving the wrong drug; this top event includes therapeutic omissions – a patient not receiving an indicated drug because a doctor forgot to prescribe it. This top event was named ‘wrong drug’.

2. A patient receiving a wrong dose, for example, because of an erroneous drug order. This top event was named ‘wrong dose’.

3. A patient being given the drug incorrectly in both timing and manner. This top event was named ‘wrong administration’. Choosing the incorrect route of administration is an example of a wrong manner of administration (e.g. intrathecally instead of intravenously). A patient receiving a drug 2 hours late is an example of incorrect timing. This top event also includes the omission of one or more administrations of a prescribed drug.

Application of the Bow-Tie Model

Following adaptation, the Bow-Tie model was applied in two hospitals successively. Multidisciplinary sessions were organized. In hospital A the risk analysis was performed at the departments of surgery, internal medicine and intensive care, and in the paediatric hospital. The teams consisted of physicians, nurses and pharmacists (partly vol-

Table 1. Frequency and severity scales

| Frequency | Details |
|-----------|---------|
| 0         | Has never happened |
| 1         | Has happened in a hospital somewhere in the world |
| 2         | Has happened in a hospital somewhere in the Netherlands |
| 3         | Has happened in this hospital (this year) |
| 4         | Has happened in this department (this year) |
| 5         | At least once per month in this department |
| 6         | Happens daily in this department |

| Severity of consequences | Details |
|--------------------------|---------|
| 0 | No effect |
| 1 | Minimal effect, no harm |
| 2 | Discomfort and minor harm, monitoring necessary |
| 3 | Harm and severe complaints, intervention and prolonged hospital stay |
| 4 | Fatal |
unteers and partly individuals suggested by the head of the department). The team members were individuals other than those representatives who were interviewed for the top event determination. Group size varied between five and ten persons. During every 2-hour session there were one or two facilitators and a note-taker. The overall number of sessions was nine. In hospital B, sessions were held at the departments of internal medicine and surgery (four sessions in total, two per department). Team composition and group size, as well as the duration of the sessions, were comparable to the sessions in hospital A. Participants attended all of the sessions. Two of the authors participated in the sessions in both hospitals, one author as facilitator (PW), the other as an observer (SS).

Bow-Tie risk analysis in hospital A consisted of the following three stages

Risk analysis (analysing the safety situation)

For each of the three top events, all possible causes that could lead to this event were determined. For all causes that could lead to one of the top events, existing preventive barriers on the left side of the model were discussed, but also barriers that could be implemented in the future to improve the safety of the process. Potential consequences were discussed if a top event would progress to eventually cause harm or damage. Recovery barriers, both existing and future, on the right site of the model that mitigate or prevent the consequences were determined. Finally, situations that could make a defensive or recovery barrier less effective (degrading factors) were discussed.

Figure 2. Risk matrix. The black area in the risk matrix corresponds with risks that are unacceptable, the medium-grey area with risks that should be reduced and managed, and the light grey area with risks that are acceptable.
Risk assessment

Risks were assessed in terms of (i) the existence of barriers; (ii) the number of barriers; and (iii) the existence and effect of barrier-degrading factors.

Prioritization: A risk-prioritization step was undertaken. In order to prioritize, estimations were made of the frequency of possible causes and the seriousness of possible consequences. Scales (table I) and a risk matrix (figure 2) were used for this purpose. In estimating the consequences team members had to consider the worst possible outcome.

Adjustments in the risk analysis strategy for hospital B involved the following. Instead of systematically working through the top events and determining as many risk factors as possible, team members first pointed out safety issues that were considered highly relevant problems at their department. Thereafter, before using the Bow-Tie, those safety issues were prioritized using the risk matrix to achieve a maximum of three top events. Top events were made department specific and were more specified: the type of (sub) process, type of drug (group) and type of patient were defined instead of only ‘wrong drug’ as in hospital A. The Bow-Tie analysis of these selected issues was conducted in greater depth. In-depth analysis would involve visualizing and analyzing all data in the Bow-Tie model and discussing the Bow-Tie diagrams until potential underlying causes were determined. The facilitators planned to create an open atmosphere for discussion and to motivate each member of the multidisciplinary team to speak up and give their point of view.

Evaluation Methodology

In both hospitals, the risk-analysis approach was tested qualitatively. Evaluation took place by participatory observation and in discussions with the multidisciplinary panel at the start and ending of sessions. In particular, the method was evaluated for the following aspects by asking the multidisciplinary team: whether the model is applicable in the healthcare setting for risk analysis in medication safety (applicability); whether the model is able to give insight into the present safety situation and risks in a comprehensible manner (comprehensibility); whether the application of the model increases the awareness in the participants of medication risks and creates a sense of urgency to address these problems (awareness and motivation); whether the application of the model helps to reveal the underlying causes (latent conditions), which can translate into error-provoking conditions of medication safety problems (the ‘system approach’, which focuses on the conditions under which individuals work and tries to build
defences to avert errors or mitigate their effects, in contrast to a ‘person approach’ which focuses on errors of individuals, blaming them for forgetfulness, inattention, etc.]^{[4]} Discussion notes were documented and evaluated with peers (MK, PB, PH). The findings were used to further improve the method.

Results

Applying the Model and Evaluation of the Approach

Hospital A

The chosen approach in the sessions of hospital A gave insight into many medication safety-related risks, but made in-depth discussion and analysis of specific risks difficult. In more detail, the four aspects were evaluated as follows.

Applicability

The systematic manner of discussing the three top events (wrong drug, wrong dose and wrong administration), and thinking of as many risk factors as possible during the sessions gave in-sight into a number of local medication-related problems at the participating departments, but, most of all, into many general hospital-wide risks. Some examples of hospital-wide risks are shown in table II. The nonspecific formulation of the three top events hampered the analysis. Sometimes it was impossible to determine specific barriers because some were drug-dependent (e.g. the antidote acetylcysteine for paracetamol [acetaminophen] as a recovery barrier). Furthermore, because of drug dependency, the determination of possible consequences was considered difficult.

Comprehensibility

Group members found it difficult to interpret the large amount of collected information during the sessions. Because of the nonspecific top events, drawing of Bow-Ties and prioritizing the necessary medication safety improvements were considered to be complicated.

'System Approach'

Analysis with the Bow-Tie was considered time consuming. Participants had no possibilities to go into an in-depth analysis of their local medication safety problems with specific attention to latent conditions in the system.
Table 2. Examples of hospital-wide risks, current barriers and proposed future barriers in hospital A

| Risk factors (causes)                                      | Current barriers                                                                 | Future barriers                                                                                           | Top event⁴ |
|------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|------------|
| Administration errors with injectable drugs                | Prevention: only check by second nurse at some wards; only second check with high-risk drugs (e.g. antineoplastics) | Prevention: general second check; barcode-assisted electronic administration check; handbook consisting of protocols with evidence-based information on drug administration | Wrong administration |
| Prescribing the wrong dose owing to: not taking co-morbidities into account; insufficient drug knowledge | Prevention: dosage check during drug ordering by CPOE Recovery and mitigation: pharmacist checks overruled dosage alerts generated by CPOE within 48 h | Prevention and recovery: decision support and a more intelligent CPOE (using laboratory values in dosage advising); reactive pharmacist participation in direct patient care, medication review Recovery: therapeutic drug monitoring | Wrong dose |
| Transfers and medication information exchange: between wards; between hospitals; at admission and discharge | Prevention: pharmacy service point: responsible for correct medication history information at admission by contacting patient’s pharmacist and responsible for checking and faxing discharge prescriptions to patient’s pharmacist | Prevention: electronic data exchange between healthcare professionals; a national medication or medical record | Wrong drug
Wrong dose Wrong administration |
| Drug order stickers attached in paper medication record of the wrong patient | No structural barriers; coincidental discovery by nurse | Prevention: barcode-assisted electronic administration check; electronic patient record, abandoning paper records | Wrong drug |

⁴ Top events are an unwanted situation or event that has the potential to cause damage.

CPOE=Computerized Physician Order Entry.
Creation of Awareness and Motivation

Session leaders pointed out that participants felt little ownership of the analysed risks as a result of too much information and the impossibility of thoroughly analysing ward-specific risks, which participants often considered to be most urgent.

Hospital B

The altered strategy in hospital B made in-depth discussion and analysis of ward-specific risks possible and increased the safety awareness of participants. In more detail, the four aspects were evaluated as follows.

Applicability

Session leaders pointed out that the approach was effective and created motivation in the teams. Letting participants select and prioritize specific safety issues before drawing Bow-Ties allowed a more efficient risk-analysis process. In-depth analysis of the safety

![Image of Bow-Tie diagram for hospital B](image-url)

**Figure 3.** Visualisation of a Bow-Tie diagram for hospital B.
issues with the Bow-Tie diagram and the systematic determination of the underlying causes made it easier to define possible improvements.

Comprehensibility

Drawing a Bow-Tie was considered easier if a more specific top event was being analysed more thoroughly. Furthermore, it stimulated the discussion during the sessions.

'System Approach'

Ward-specific safety issues were analysed with regard to the underlying causes. Determining these causes gave insight into the latent conditions and directed the participants to the most suitable and possibly effective improvements.

Creation of Awareness and Motivation

The fact that participants prioritized and selected a set of local safety issues that they considered most urgent stimulated them to analyse these issues and to think of possible improvement projects. Moreover, the analysis process was an eye-opener for the team members. Many aspects that were discussed created understanding for the difficulties of one another’s professions.

Table 3. Recommended method for risk analysis with the Bow-Tie model

| 1. Select multidisciplinary groups and inform participants about the principles of the method |
| 2. Arrange a brainstorm session leader and one to two note-takers for each session |
| 3. During the session explain the principle of the model by using simple examples |
| 4. Brainstorm over possible (local) top events and safety issues |
| 5. Prioritize safety issues |
| 6. Specify the top events and analyse the highest priority risk in depth with the Bow-Tie model |
| 7. Brainstorm about root causes, initial errors, present barriers (preventive and recovery) and consequences. Draw Bow-Ties |
| 8. Brainstorm about risk factors that negatively influence barriers |
| 9. Assess if safety is sufficiently managed |
| 10. Brainstorm about new or improved barriers. Draw these in a Bow-Tie for the new situation |
| 11. Categorize all the data in tables |
| 12. Draw up an improvement plan with follow-up actions (multidisciplinary) |
Figure 4. Basic Bow-Tie model for medication safety-risk analysis with an example of a specified top event to illustrate the principle.
Figure 3 gives a visualisation of one of the specific top events and causes that were analysed in-depth with the Bow-Tie (lack of and delay in drug orders at the surgery department).

**Recommended Method for Risk Analysis with the Bow-Tie Model**

Based on the experiences in both hospitals, a recommended method for risk-analysis sessions with the Bow-Tie model in healthcare was made (table III). The basic structure of the Bow-Tie model for medication safety risk analysis should have the feature to depict underlying causes and is shown in figure 4. Errors that directly lead to a top event can be defined as ‘initial errors’ (e.g. errors that can be directly linked in a causal relationship to the top event, for example a nurse selecting the wrong drug in the storage room), which themselves can have multiple underlying, less obvious causes that can also be analysed during the risk-analysis process (e.g. a disorganized drug storage room). These ‘root causes’ or latent conditions are drawn in the event trees preceding the initial errors.

**Discussion**

We found the Bow-Tie to be an appropriate model for prospective risk analysis of medication safety in a hospital. By applying the method in two hospitals consecutively we developed a feasible method for risk-analysis sessions.

For this study we chose the Bow-Tie model, frequently used by the petrochemical industry, and applied it in two hospitals for prospective risk analysis on medication safety. The initial strategy followed during the risk-analysis sessions in the first hospital gave insight into many risks but was time consuming and unsatisfactory on aspects of creating awareness, the system approach and comprehensibility. The strategy resulted in too much information about general risks throughout the hospital, which made the risk analysis confusing and difficult to manage. The nonspecific formulation of the three basic top events made the determination of some barriers and consequences impossible because many are drug dependent. Focus on and thorough analysis of ward-specific risks was impossible, hampering the feeling of ownership in the participants. Therefore adjustments were made to the risk-analysis method before application in the second hospital. This adjusted method encompassed a prioritizing step before drawing Bow-Ties, a focus on the most important (local) risks, specifying the top events, and a thorough analysis of the risks with attention to underlying causes in the specific department. This adjusted method was found to be easily applicable.
Although participants had little experience with safety management, they understood the concept of the system approach (identifying latent conditions in contrast to focusing on the person making the error) and were able to determine root causes of specific top events with help of the facilitators. Furthermore, the sessions increased safety awareness and motivated the participants to brainstorm about and prioritize potential safety improvements. Hence, the Bow-Tie was shown to be an appropriate method to start medication safety initiatives, even in departments without specific expertise in this field.

In recent years, some other risk-analysis methods have been translated to the healthcare setting. Examples of methods that are used for analyses of adverse events or incidents are Root Cause Analysis (RCA)\cite{15-17} and incident report classification with the Eindhoven Classification Model (PRISMA)\cite{18,19}. Because of the important information that root causes can give, we incorporated this principle into the Bow-Tie model for medication safety-risk analysis (figure 4). Thus, without the need for incident reports, aspects of RCA can be used prospectively in our Bow-Tie model. Several other studies have described the application of Failure Mode and Effect Analysis (FMEA) as a prospective risk-analysis instrument in healthcare\cite{20-23}. In contrast to FMEA, where a specific process is the subject of analysis, the Bow-Tie method centralizes top events of a specific safety item (in our study ‘the hazard’ medication) and helps to analyse their causes and consequences. It can depict the relationship between causes, top events, barriers and consequences in a comprehensible manner for every discipline. Therefore, the Bow-Tie model is primarily useful for an initial multidisciplinary risk analysis of a broader safety topic, whereas the FMEA seems more suitable to analyse a specific high-risk process in more detail\cite{24-28}. Because of these different purposes, both risk-analysis instruments are complementary rather than competitive.

This study has some limitations. It was set up as an explorative study on the application of the Bow-Tie model in clinical practice. The focus was on the determination of a recommended method for using the Bow-Tie. We did not study the possible post-analysis effects of our risk analysis on front-line staff and daily practice. Therefore, no conclusions can be drawn on induced change. The risk-analysis approach was qualitatively evaluated by participatory evaluation and by asking participants about specific aspects of the method. Thereafter the findings were discussed with peers. Therefore some bias in the evaluation could have been introduced owing to the specific experience of or professional relationships between the participants. As for participatory evaluation, the problem applies that the results could be biased in their favour by participating stakeholders, but we tried to manage this by selecting several different medical professions in the study team. Moreover, we tested the model in only two Dutch hospitals. Consequently, our findings could have limited generalizability. First and foremost, however,
we think that the safety culture in a specific hospital, the motivation and attitude of the participants and the question of whether the risk analysis is part of a well supported improvement plan with follow-up actions, will influence the success of the method and its results. If a hospital has no intention to take action upon the findings of the risk analysis, the effort will be in vain.

In future research, we will further expand the use of the Bow-Tie model for risk analyses in other fields of patient safety than medication. Although not examined in this study, the structure of the Bow-Tie model makes it possible to define standard practices of safety management\(^\text{[11]}\). Responsibilities and tasks can be appointed to every barrier, making the Bow-Tie model also a management tool. In that way, auditing with aid of the model can take place, as opposed to unstructured investigations or mere counting. This aspect of the model will be explored in future research.

**Conclusion**

The structure of the Bow-Tie model allows professionals in the clinical setting to identify the routes to and from medication safety top events. Barriers can be identified that either aim to prevent top events from occurring or aim to mitigate consequences. The structure of the model allows risks to be assessed by the identification of strong and weak points and these relationships can be visualized comprehensibly. Because the model can give an impression of the manner in which the medication and patient safety is managed (sufficiently or insufficiently), a risk analysis with the Bow-Tie model can be a suitable starting project in a larger safety improvement plan.

**Acknowledgements**

The authors express their gratitude to Prof. dr. P.T. Hudson (Department of Social Sciences, Leiden University, the Netherlands), M.D. Kalmeijer, PharmD, and P.N. Bakker, MD, PhD (Academic Medical Center, Amsterdam, the Netherlands) for their support in executing this study. Furthermore the authors would like to thank all participants in both study hospitals for their cooperation and input.

This study was partly funded by a governmental healthcare research grant (no 8120.0005, Patient Safety Program) of the Netherlands Organisation for Health Research and Development (ZonMw). The authors have no conflicts of interest to declare.
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4.1 Studies pertaining to the ACOVE quality criteria: a systematic review

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Int J Qual Health Care. 2012 Feb; 24(l): 80-7
Abstract

Purpose: To identify and uniformly describe studies employing the Assessing Care Of Vulnerable Elders (ACOVE) quality indicators within a comprehensive thematic model that reflects how the indicators were used.

Data sources: A systematic search of MEDLINE, EMBASE and CINAHL was conducted.

Study selection: English-language studies meeting our criteria published prior to January 2010.

Data extraction: Included studies were analyzed and described by two independent researchers.

Results of data synthesis: A total of 41 articles met our selection criteria. Studies were classified into the themes ‘Application of indicators’ (32 studies) and ‘Analysis and development of indicators’ (13 studies). ‘Application’ studies included assessing quality of care, influencing behavior of health professionals and examining the association of quality of care with other factors. ‘Analysis and development’ included studies developing new indicator sets, and those adapting and validating the original quality indicators to new settings.

Conclusions: The indicators were used in a wide range of applications with two main foci: the assessment of quality of care for elderly patients, and investigating the feasibility of similar indicators and their adaptation to new settings. Very few of the studies published to date have addressed the goal of care improvement. We foresee an important role for application of indicators that proactively help healthcare professionals to deliver the right care at the right time, for example by resorting to decision support systems.

Purpose

In recent years many studies have been dedicated to the care of elderly patients. The effects of multimorbidity, polypharmacy and the overall quality of care have been investigated[1-5]. Care for elderly patients is complex and not yet well understood[6]. Not only are elderly patients often excluded from clinical trials, but also due to their multimorbidity a multitude of possibly conflicting guidelines are contemporaneously applicable to them[7]. Studies have shown that elderly patients often do not receive
care appropriate to their age and conditions\cite{5,8}. The vulnerable elders, defined as the group of persons 65 years of age or older who are at high risk of death or functional decline, form an important subgroup for investigation\cite{9}. To improve care for elderly patients there is a need to know where, when and for which conditions deficits exist, calling for reliable and comprehensive methods for the assessment of quality of care that considers both medical and geriatric conditions\cite{10-12}. Many of the current methods are not intended to be comprehensive, but focus on a specific process of care or on the assessment of the quality of a treatment for one condition\cite{11,13-15}. In addition, many methods tend to be subjective, meaning that they depend to a large extent on the implicit knowledge and experience of the assessor, thus jeopardizing inter-rater reliability. Unlike subjective methods, objective methods consist of explicitly specified assessment instruments and are often based on literature review and expert consensus, and are therefore more reliable\cite{12}. However, most explicit methods for the assessment of the quality of care of elderly people are not comprehensive. In 2000, researchers at research and development (RAND) and university of California, Los Angeles (UCLA) developed the Assessing Care Of Vulnerable Elders (ACOVE) quality indicator set\cite{9,16}. This set consists of explicitly phrased IF – THEN clinical rules with comprehensive coverage of general medical and geriatric conditions. They are intended to evaluate, by means of gauging adherence to the rules, whether the care being delivered at the level of the health-care system meets pre-specified standards of quality. Assessment is meant to inform and, in consequence, to facilitate quality improvement efforts\cite{9,16}. The rules are based on evidence and expert opinion, and describe process rather than outcome measures. The rules also specifically address undertreatment that is often overlooked in the elderly patient population. Due to these properties, the ACOVE quality indicator set has a unique place amidst screening and assessment methods for measuring the quality of care of elders, especially the vulnerable ones.

This paper reviews the decade of research pertaining to the ACOVE quality indicators. The objective was to identify and summarize all studies published after the introduction of the ACOVE quality indicator sets in the literature. The studies are described in a thematic conceptual model meant to understand the different ways in which the ACOVE quality indicators have been used and to expose areas of promising future research.
Methods

Data sources

Relevant English-language articles published between the presentation of the ACOVE-1 initiative in 2001 and the end of January 2010 were searched in multiple databases (MEDLINE (using Scopus and PubMed), Ebsco-CINAHL and Ovid-EMBASE) by using the query ‘ACOVE OR (‘assessing care’ AND (vulnerable OR frail*))’.

Study selection

Articles were included if they used the original ACOVE quality indicators or adaptations, updates or extensions thereof. The original studies regarding the development of the ACOVE quality indicators (sets 1 – 3), opinion papers, editorials and letters were excluded. Congress abstracts were also excluded because they often provide limited details. Two reviewers independently examined the collected studies in two rounds. The first round consisted of critically reading the title, keywords and abstract. In the second round both reviewers independently assessed the full text of the articles selected in the first round. One investigator screened citations to identify additional possible candidate articles. Disagreements in each round between the two reviewers were resolved by consensus. In the cases when the reviewers were unable to reach consensus a third reviewer was involved to make a final decision. Inter-rater agreement has been calculated using Cohen’s kappa.

Data extraction

From the selected studies, the two reviewers independently used a structured form for abstraction to obtain the study characteristics, objectives, methods, affiliation of the authors and research group, and the number and focus of the quality indicators. Based on the ACOVE project’s intended objectives, the studies were provisionally organized into two main themes: ‘Implementation’ (how and to what extent were quality indicators applied for assessment and improvement of care) and ‘Development’ (adaptation and extension of quality indicators). Based on a bottom-up analysis of the study objectives and quality indicator application, subcategories were identified. These sub-categories were then organized into larger categories and put into a thematic conceptual model.
Results of data synthesis

Figure 1 shows the article selection flow diagram. From the 47 papers, 50 were selected for full text screening. A total of 41 articles met our selection criteria. Inter-rater agreement was high (kappa: 0.73, only five papers necessitated the involvement of the third reviewer). Analyzing the studies' objectives, methods, contents and types of quality indicator application, we arrived at five categories within the main themes 'Application of quality indicators', and 'Analysis and development of quality indicators'. This is shown in the thematic conceptual model (Fig. 2). To get insight into the nature of these studies, we describe the most important findings per category.

Application of quality indicators

Assessing the quality of care.

Eighteen studies\[^{5,17-33}\] in this category assessed the quality of different types of care. Eight articles pertained to the assessment of care for a specific condition: management and detection of pain\[^{18,29}\], falls and instability\[^{20}\], congestive heart failure care\[^{21}\], osteoarthritis\[^{24}\], pressure ulcer care\[^{26}\] and urinary incontinence\[^{17,28}\]. Ten studies focused on specific domain(s) of care or overall quality: pharmacologic care\[^{27,30}\] and appropriateness of prescribing/underuse\[^{22}\], quality of hospital care\[^{31}\], geriatric care\[^{19,33}\] and overall quality of care\[^{5,23,25,32}\]. From these 18 studies, 4 studies focused on nursing home residents\[^{17,18,26,32}\], 5 on managed care plans\[^{5,19,28-30}\], 2 on hospitalised patients\[^{22,31}\] and 5 on primary care patients\[^{20,23,25,27,33}\]. Two studies had mixed settings\[^{21,24}\]. The patient population in these studies mainly consisted of patients aged 65 or older (defined by a threshold age range of minimal 50 to maximum 75 years). Only seven studies explicitly mentioned that the population consisted of vulnerable elderly patients, all of which used the Vulnerable Elders Survey (VES-13) to identify vulnerability.

Two studies in this category explicitly mentioned the inclusion of patients aged 50 years or older. Overall, between 3 and 207 quality indicators were used in the 18 studies. When viewed per condition, there were between 1 and 43 quality indicators used. While 8 studies used the original ACOVE quality indicators\[^{5,20,22,24,28-30,33}\], 10 studies used adapted ACOVE quality indicators or newly developed ACOVE-like quality indicators\[^{17-19,21,23,25-27,31,32}\].

The source of data used to evaluate the quality indicators was in most cases a combination of medical record data and interviews with caregivers and patients. One study
used a combination of medical records, direct observation and electronic measurement\textsuperscript{[26]}. Two studies assessed the quality of care with interviews only\textsuperscript{[24,25]}, two studies by medical records only\textsuperscript{[21,31]} and three studies utilized administrative data\textsuperscript{[23,27,32]}. The majority of the studies did not assess the reliability of the medical record review; however, most of them reported the inter-rater reliability of assessing the pass rates of quality indicators.

In Supplementary material, Appendix B, all studies and their main findings are summarized and in Table 1 a brief summary of characteristics of the included studies is provided.

Association between quality of care and other factors.

Twelve studies fell into this category\textsuperscript{[34–45]}. The association between quality of care and the following factors were studied: multimorbidity\textsuperscript{[39,41]}, survival\textsuperscript{[34]}, functional decline

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{article_selection_flow_diagram.png}
\caption{Article selection flow diagram.}
\end{figure}
after discharge\cite{35}, time consumption of care processes\cite{40}, osteoarthritis severity\cite{38} and race\cite{36,37}.

Four studies had a more indirect approach to examine an association with the quality of care: three studies assessed whether care improvement on a specific care type targeted by the quality indicators also influenced the quality of non-targeted types of care\cite{42–44} and the fourth study examined the effect of an intervention that improved care for falls, incontinence and cognitive impairment in community-dwelling patients.

Figure 2. Thematic conceptual model of studies pertaining to the ACOVE quality indicators. There are five categories in the conceptual model pertaining to the ACOVE quality indicators (QIs): Cat A, studies that develop a new set of quality indicators; Cat B, studies that adapt the original ACOVE quality indicator set to a new setting; Cat C, studies that assess the quality of care; Cat D, studies that examine the association between the quality of care and other factors (such as health-care outcomes, patient opinion and patient characteristics); and Cat E, studies that aim to influence the behavior of or educate health-care professionals. Note: Some studies had two or more goals, and could therefore be assigned to more than one category. There were 41 distinct studies, 13 ‘Analysis and development’ studies and 28 studies that applied the quality indicators. *Outcome measures: quality indicator pass rates. **Examples of investigated associations or used outcome measures: patient's observed vs. expected overall quality score; effect of quality of care on survival; effect of number of morbidities on pass rates. ***Outcome measures: scores of knowledge before and after receiving the interventions, quality indicator pass rates.
on nine non-targeted conditions\cite{45}. In the 12 above-mentioned studies between 9 and 236 quality indicators were used. Four studies used adapted ACOVE quality indicators\cite{35,38,43,44}, five studies analyzed existing data collected with the original ACOVE quality indicators in the Wenger et al. study\cite{34,39–42}, and three studies utilized ACOVE-2 indicators\cite{36,37,45}. In most cases, the combination of medical record data and interviews with caregivers and patients was necessary for scoring the quality indicators\cite{34–36,39–42}. Two studies used a combination of medical records, direct observation, interviews and electronic measurement\cite{43,44}. Three studies assessed the quality of care using only medical records\cite{37,38,45}. The patient population in eight studies consisted of patients aged 65 or older\cite{34,35,39–44} of which six focused on vulnerable elderly\cite{34,35,39–42}, one on patients of 75 years and older\cite{45}, two on 60 years and older\cite{36,37} and one on 55 years and older\cite{38} (see also Table 1). Two studies focused on nursing home residents, seven on community-dwelling patients\cite{34,36,37,39–42}, one on hospitalised patients\cite{35} and two studies focused on patients in primary care\cite{38,45}. All study characteristics are shown in Supplementary material, Appendix B.

Influence the behavior of or educate health-care professionals.

This category contains two studies. The first study implemented a pharmacotherapist-led educational intervention that consisted of a theoretical presentation and a knowledge test, both based on 30 pharmacology-related quality indicators\cite{46}. The second study used a practice-based intervention based on ACOVE quality indicators in primary care that included case finding, physician education and practice efforts to improve the quality of care for falls and urinary incontinence\cite{33}. In this study 18 quality indicators were used for the assessment of the quality of care.

Analysis and development of quality indicators

Developing new ACOVE quality indicators.

One study by McGory et al.\cite{47} described the development of a completely new set of 76 quality indicators for vulnerable older patients undergoing abdominal operations. An expert panel rated and discussed the indicators using a modification of the RAND/UCLA method, which was used to develop the original ACOVE quality indicators.

Adaptation of quality indicators to a new setting and validation.

Twelve studies were classified into this category\cite{19,26,31,48–56}. Three studies reported on the translation of ACOVE quality indicators to another country. Steel et al.\cite{49} success-
fully translated ACOVE quality indicators to the UK in order to assess the quality of primary and secondary care for elders using patient surveys. Kroger et al.\cite{54} adapted a selection of 82 quality indicators for use in Canada to assess the quality of care of elderly people with cognitive impairment or dementia. Van der Ploeg et al.\cite{55} reported on the adaptation and validation of ACOVE-3 quality indicators in the Netherlands for use in general practice care quality assessment for vulnerable elders. The remaining studies adapted and validated quality indicators within the same country to another health-care setting, to other patient populations or to other conditions. Eight studies adapted the ACOVE quality indicators for the following purposes: assessment of quality of care for geriatric conditions\cite{56}, residential care\cite{57}, general medical conditions\cite{58} and pressure ulcer care\cite{26} in nursing homes, for home-based primary care\cite{48}, for geriatric and general hospital care\cite{31}, for care for osteoarthritis, rheumatoid arthritis and analgesics use\cite{52} and for community-dwelling patients with advanced dementia and poor prognosis\cite{19}. The final study classified into this category reported the validation, and not the adaptation of a quality indicator set. The quality indicator set, which had already been adapted to the nursing home setting, was validated in terms of measurement feasibility utilizing two data sources (medical record data and administrative data)\cite{56}.

Of the 11 studies that adapted a quality indicator set, 9 studies used the modified

\begin{table}
\centering
\begin{tabular}{|l|c|}
\hline
Characteristics & Number of studies (percentage) \\
\hline
Settings (or intended setting) & \\
Primary care & 14 (34) \\
Nursing home & 9 (22) \\
Hospitals & 4 (10) \\
Managed care & 5 (12) \\
Others & 9 (22) \\
\hline
Population & \\
VE & 11 (27) \\
\geq 75 & 4 (10) \\
\geq 65 & 18 (44) \\
\geq 55 & 3 (7) \\
Others & 5 (12) \\
\hline
Condition focus & \\
Single condition & 28 (68) \\
Multiple condition & 13 (32) \\
\hline
\end{tabular}
\caption{Brief summary of characteristics of the included studies}
\end{table}

We only categorized populations as VE, if the article explicitly mentioned the term ‘vulnerable elderly/elders’ in the text. VE: vulnerable elderly.
Studies pertaining to ACOVE quality indicators

RAND/UCLA (Delphi) method with the help of content experts\textsuperscript{[19,48–51,53–56]}. Two studies used a different approach: one used an expert panel to select quality indicators but did not mention how this selection process was conducted (e.g. whether it was based on Delphi rounds or not)\textsuperscript{[31]}, and the other study was not explicit on the quality indicator adaptation method or the professionals concerned\textsuperscript{[26]}.

The reasons for discarding or adapting the quality indicators for use in a new setting or country were varied, for example being inapplicable to that country or setting due to other guidelines, disagreement in the reported evidence, shortening or extending the follow up period or continuity of care, difference in recommended treatment and changing the medication options.

Involvement of ACOVE study group members.

Thirty-one studies (76%) of the included 41 were conducted in collaboration with one or more representatives of the original ACOVE study group. Ten studies (24%) were performed without (mentioned) support of the ACOVE group.

Discussion

A strong increase in the number of ACOVE-related studies was exhibited in recent years. In this systematic review we identified and summarized 41 relevant research papers pertaining to the ACOVE quality indicators. The studies were organized in a conceptual model containing five main categories providing a better understanding of where and how ACOVE quality indicators have been applied since 2001. Most research originated from the ACOVE group itself but there are some translational efforts to other countries. The efforts to collect data in order to assess care are substantial and there is paucity, in studies addressing quality-of-care improvement.

Our systematic literature search was designed to give a complete overview of the studies pertaining to the ACOVE quality indicators. Although our conceptual model for categorizing studies was based on the original goals of the ACOVE initiative and on a bottom-up analysis of the articles that were found, it is possible that other researchers in a comparable process would define other categories. We hope that the organisation chosen will prove useful for researchers to identify studies relevant to them and to put them in perspective. A future study is needed to report on the formal quality of the included studies, and the overall quality of care as assessed using the ACOVE quality indicators. The ACOVE quality indicators were used in several care settings (ranging from primary care to hospital care, from pharmacologic care to residential
care), for multiple conditions (from all ACOVE conditions to specific conditions like osteoarthritis or focusing on general medication use), and in several different elderly patient populations (from community-dwelling patients to nursing home residents). Our results showed that the concept of using ACOVE-like quality indicator has been extrapolated only to a limited extent to other patient populations than the elderly. Although the ACOVE set was developed for vulnerable elderly patients, the majority of the studies did not distinguish between the vulnerable elders and the general elderly population. This could be due to the difficulty of identifying who is vulnerable (the VES-13 considers age, self-rated health, limitations in physical function and functional disabilities).

In most studies, the combination of patient record review and interviews was used to extract the data. Only few studies used automated data extraction methods, because the required data are often unavailable, hard to access or difficult to standardize. Therefore, electronic capture of ACOVE-related data elements and facilitating their extraction forms important future work. Since evaluating the quality indicators imply laborious data collection activities, future work for care assessment and improvement will be considerably facilitated once the measurement systems are in place.

The distribution of studies over the model’s categories showed that quality indicators were mainly used in two categories: (i) those that applied the quality indicators for the assessment of the quality of care and (ii) those that examined whether an association existed between the quality of care and other factors (such as health-care outcomes, patient opinion and patient characteristics). Only one study in our review addressed the (positive) association between quality indicator performance and survival among community-dwelling vulnerable older adults. This association has also been addressed in a very recent study, not reviewed here, in which better quality indicator performance was associated with lower likelihood of death 1 year after discharge in hospitalised seniors[57]. Furthermore, our model showed that various studies were aimed at adapting the original ACOVE quality indicator set to a new setting.

Our results suggest two opportunities for additional work on quality indicator application. First, only one study developed a completely original indicator set that consisted of quality indicators with content not based on ACOVE indicators. This may be related to the difficulty of developing a new quality indicator set. Simply translating and adapting the comprehensive ACOVE quality indicators may prove sufficient in the same patient group. Translation between the USA and other countries has been shown to be possible, which theoretically facilitates the comparison of results between different countries[49,54,55]. Second, in contrast to the abundance of studies that used the quality indicators for retrospective quality assessment by screening medical records, only two
studies applied the quality indicators in a proactive manner to directly improve the delivered care\cite{33,46}. Our results suggest that the ACOVE framework has mainly been used to assess care, rather than to achieve the ultimate goal of the quality indicators, that of improving the quality of care, although it is possible that such initiatives are not always published. This assessment takes place after care has been delivered and often forms a painstaking, costly process typically requiring the examination of patient charts and interviewing patients or health-care workers. We believe that by decoupling assessment from improvement, crucial opportunities to improve care at the right time and the right place may be missed. Important future work consists of attempting to switch from using quality indicators solely as an assessment instrument, to using quality indicators as the basis for change of care delivery by providing timely and proactive feedback to the care givers. Computerized clinical decision support systems may play an important role in this vision.

Until now most research originated from the ACOVE group itself and specifically from the USA. We found six studies (five in Europe and one in Canada) that used the ACOVE indicators suggesting that they may be increasingly used outside of the USA. In sum, the ACOVE quality indicator set has formed the basis for many studies inspiring various applications and it holds promise of forming a common ground for aligning diverse research efforts. However, the gap between published studies on measuring and improving quality of care is still large.

Acknowledgements

A.A.-H., M.A. and S.d.R. conceived the preliminary study design. A.A.-H. supervised and integrated the whole work. M.A. and P.W. carried out the literature search, and performed acquisition, examination and analysis of the data. S.d.R. and A.A.-H. validated the data acquisition. M.A. and P.W. drafted the manuscript. All authors participated in the design of the paper, the regular discussions, and read and approved the final manuscript. No other persons contributed to this project. The authors declare that they have no conflicts of interest.

Funding

This work was supported by ZonMw (The Netherlands Organization for Health Research and Development) by grants for the PROFIT (#300020010) and ICOVE (#311020302) projects.
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Appendix A: ACOVE set evolution

In the first phase of the ACOVE initiative evolution, QIs were used for assessing the care of elderly people in several large care systems in the United States. Several articles related to the development of the ACOVE-1 QIs and the results obtained during their application were published in a special edition of the Annals of Internal Medicine in 2001[1-15]. The original ACOVE set (ACOVE-1) consisted of 236 QIs focusing on 22 conditions relevant for elderly patients (Continuity of care, Dementia, Depression, Diabetes mellitus, End-of-life care, Falls and Mobility disorders, Hearing impairment, Heart failure, Hospital care, Hypertension, Ischemic heart disease, Malnutrition, Medication management, Osteoarthritis, Osteoporosis, Pain management, Pneumonia and influenza, Pressure ulcers, Screening and prevention, Stroke and Atrial fibrillation, Urinary incontinence, Vision impairment). The QIs had comprehensive coverage including the domains of prevention, screening, treatment and follow-up.

After ACOVE-1, the ACOVE group carried out two consecutive projects. In phase 2 of the ACOVE project (ACOVE-2), the researchers used the results of ACOVE-1 and the QIs themselves, to evaluate several practical interventions in primary care practices aimed at improving performance of some of the most underperformed health care procedures as identified in ACOVE-1: care for falls and mobility impairment, urinary incontinence and cognitive impairment[16, 17]. ACOVE-3 was aimed to update and increase the coherence of the ACOVE-1 QI set for the medical care provided to vulnerable elders. The QIs were revised and expanded to keep up with the ever changing canon of medical literature[18]. The ACOVE-3 set includes 392 QIs covering 14 conditions.

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### Appendix B: table of extracted data

| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|-----------------------------|------------|
| Jellinek et al. (2008) CAT E         | 54 medical students and house staff | Before and after study (Aug 2004-May 2005) 29-bed acute care for elderly unit, teaching hospital, 705 bed (US) | Quantify the pretest and posttest results of medical students and house staff participating in a pharmacotherapist-led educational intervention |
| Schnelle* et al. (2003) CAT C        | 426 incontinent residents | Descriptive 18 NHs, 50-200 beds each (US) | Demonstrate reliability and feasibility of a protocol to assess urinary incontinence in NHs |
| Cadogan* et al. (2005) CAT C         | 542 NH residents      | Descriptive 38 NHs (50-200 beds each) (US) | Demonstrate reliability and feasibility of a protocol to assess pain management in NHs and assess pain management quality |
| Solomon* et al. (2003) CAT C CAT B3  | 372 VEs               | Content analysis (13-month period) Two senior managed care plans (US) | Evaluate applicability of QIs for AdvDem and PrProg |
| Smith et al. (2007) CAT B2           | ACOVE QIs             | Analysis and synthesis Mount Sinai medical Center (US) | To identify process QIs that are essential to high-quality, home-based primary care |
| MacLean* et al.[56] (2006) CAT B3    | ACOVE QIs, 399 Community dwelling VEs | Observational comparative (13-months) 2 senior health care plans with more than 20000 enrollees (US) | Comparing applicability, eligibility, and performance on 182 measures of health care quality indicators, between medical records and administrative data |
| Methods                                                                 | #1 QIs used | Conditions                  | Source of information                         | Assessor                                                                 |
|-----------------------------------------------------------------------|-------------|----------------------------|-----------------------------------------------|--------------------------------------------------------------------------|
| Baseline knowledge test → pharmaconavist-led 1-hour learning sessions → education during daily work rounds and consultations → post-test using a 15 item Questionnaire | 30          | All 22 ACOVE conditions    | Interview data, Medical record data. 15 item Multiple-choice test          | NA                                                                       |
| Protocol containing instructions to score                              | 9           | Urinary Incontinence care  | Medical records and interviews                | 1 physician and 3 nurses (People with prior experience in developing and scoring the rules.)|
| 6 QIs through medical record reviews and to score 3 QIs through interviews with patients |             |                            |                                               | Trained research physician or gerontological nurse practitioner          |
| Medical records review and interviews (to detect undocumented pain). Testing inter-rater reliability | 12          | Pain management and osteoarthritis | Medical records and interviews                  |                                                                                     |
| Formal analytic process using content analysis based on a 12-expert committee for scrutinizing AdvDem or PrProg (Modified UCLA/RAND method(delphi)) | 203         | All ACOVE conditions      | ACOVE QIs, interviews, medical records         | Expert committee for voting (10 physicians, 1 nurse, 1 social worker), 2 investigators (MD) for unification of domain set |
| Modified Delphi process with expert panel to rate validity and importance of QIs (Modified UCLA/RAND method(delphi)) | 260 (200 accepted) | All ACOVE conditions + Constipation and Insomnia | ACOVE QIs, Expert knowledge and literature (approach: 2 rounds of mailed survey) | Clinicians of national (US) panels with different practice, location and setting |
| Abstraction of medical records and administrative data and comparison in applicability, eligibility and performance. | 182         | All ACOVE conditions      | ACOVE QIs, Medical records from in- and outpatients (including administrative data) | Trained nurse abstractors                                                |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|----------------------------|------------|
| Rubenstein* et al. (2004) CAT C     | 372 VE              | Retrospective observational cohort study (13-month) 2 senior health care plans each with more than 20,000 enrollees (US) | Investigate quality of care for falls and instability |
| MacGory* et al. (2005) CAT A       | QIs for abdominal operations | Descriptive NA (US) | Developing process-based QIs for elderly patients undergoing abdominal operations |
| Steel* et al.[49] (2004) CAT B1    | ACOVE QIs           | Descriptive National project, collaboration of several professional networks (UK) | Adaptation of ACOVE QIs for use in patient review in England, to measure the extent to which older patients receive effective healthcare intervention in primary and secondary care |
| Asch et al. (2005) CAT C           | 489 patients        | Retrospective quasi experimental study 4 organizations participating in IHI BTS for CHF and 4 compatible comparison organizations (US) | Compare differences in indicator performance between baseline and post intervention periods for participating and nonparticipating organizations to evaluate the effects of the IHI BTS on QoC for chronic heart failure (CHF) |
| Spinewine et al. (2007) CAT C      | 203 patients aged >70 | RCT with patients as unit of randomization 27 Acute GEM unit (Belgium) | To evaluate the effect of pharmaceutical care provided in addition to acute GEM care on the appropriateness of prescribing, using a protocol |
| Authors/Category of concept model | Study population (n) | Study design/Period/Setting | Objectives | Methods | #1 QIs used | Conditions | Source of information | Assessor |
|----------------------------------|----------------------|----------------------------|------------|---------|-------------|-----------|----------------------|----------|
| Rubenstein* et al. (2004)         | CAT C                | 372 VEs Retrospective observational cohort study (13-month) | Investigate quality of care for falls and instability | Determination of the percentage of QIs satisfied concerning falls or mobility disorders through using Medical record abstractions and patient interviews | 8 Falls and instability | Medical records (including administrative data) and patient interview by telephone. Administrative data | Trained nurses for medical record abstraction, Physicians reviewed aspect of QIs |
| MacGory* et al. (2005)           | CAT A                | QIs for abdominal operations Descriptive NA (US) | Developing process-based QIs for elderly patients undergoing abdominal operations | Structured interviews and systematic reviews. RAND/UCLA Appropriate Methodology with expert panel | 89 (created) 76 (valid) Abdominal operations | Interviews, literature review and panel knowledge | 12-member expert panel |
| Steel* et al. (2004)              | CAT B1               | ACOVE QIs Descriptive National project, collaboration of several professional networks (UK) | Adaptation of ACOVE QIs for use in patient review in England, to measure the extent to which older patients receive effective healthcare intervention in primary and secondary care | 119 QIs, covering 16 clinical areas were reviewed by a panel of 10 clinical experts in England using a modified version of the RAND/UCLA method (delphi) for each QI | 119 (102 identified as valid) 16 clinical areas; Continuity of care, Dementia, Depression, Diabetes mellitus, falls, hearing, Hypertension, Ischaemic heart disease, medication use, Osteoarthritis, Pain, screening and prevention, Stroke, Urinary incontinence, Vision | Original ACOVE QIs and literature | 10 clinical experts |
| Asch et al. (2005)                | CAT C                | 489 patients Retrospective quasi experimental study 4 organizations participating in IHI BTS for CHF and 4 compatible comparison organizations (US) | Compare differences in indicator performance between baseline and post intervention periods for participating and nonparticipating organizations to evaluate the effects of the IHI BTS on QoC for chronic heart failure (CHF) | Measuring appropriateness of prescribing at on admission, at discharge and 3 months after discharge, using ACOVE/MAI and Beers criteria using medical records review, interviews | 23 Congestive heart failure | Medical records | Computerized tool, trained abstractors, nurses and medical record technicians |
| Spinewine et al. (2007)           | CAT C                | 203 patients aged >70 RCT with patients as unit of randomization 27 Acute GEM unit (Belgium) | To evaluate the effect of pharmaceutical care provided in addition to acute GEM care on the appropriateness of prescribing, using a protocol measuring appropriateness of prescribing at on admission, at discharge and 3 months after discharge, using ACOVE/MAI and Beers criteria using medical records review, interviews | 7 underuse criteria, focusing on osteoporosis/fracture, atrial fibrillation, ischemic heart disease, diabetes mellitus, heart failure, myocardial infarction | 7 | Medical records and interviews | Clinical pharmacist |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|-----------------------------|------------|
| Saliba* et al.[50] (2004) CAT B2,3 | 9 clinical experts in NH care | Descriptive National project (US) | To identify valid and feasible measures of specific care processes associated with improved outcomes for some conditions |
| Saliba* et al.[51] (2002) CAT B2 | 9 clinical experts in NH care, a content expert and a clinical oversight committee | Descriptive National project (US) | To identify QIs that can be used to measure NH residential care processes |
| MacLean* et al.[52] (2004) CAT B3 | 3 member clinical committee and a 9 member-multidisciplinary expert panel | Descriptive National project (US) | To develop a comprehensive set of explicit process measures to assess the quality of health care for osteoarthritis, rheumatoid arthritis, and analgesics use |
| Zingmond* et al.[23] (2007) CAT C | 100528 patients | Observational cohort study (2 year) Community-dwelling dual enrollees in Medicare and Medicaid, living in 19 California Counties (US) | To assess the applicability of process of care measures developed as part of ACOVE, that were adapted previously for use with administrative data. To measure the QoC in community — dwelling VE. |
| Min* et al.[41] (2007) CAT D | 372 community dwelling persons 65 years of age or older | Observational study, 2 managed care plans within 2 years (US) | Determination of whether combinations of 8 common comorbid chronic conditions are associated with overall QoC among vulnerable patients |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives | Methods | # QIs used | Conditions | Source of information | Assessor |
|-------------------------------------|----------------------|-----------------------------|------------|----------|------------|------------|----------------------|----------|
| Saliba* et al. [50] (2004)          | 9 clinical experts in NH care | Descriptive National project (US) | To identify valid and feasible measures of specific care processes associated with improved outcomes for some conditions | Formal analytic process using content analysis based on expert committee. The panel's median votes were used to identify a final set of QIs (subsequently reviewed by a clinical oversight committee) (Modified UCLA/RAND method(-delphi)) | 236 (68 identified as valid) | 6 geriatric conditions: Dementia, Falls & mobility disorders, Malnutrition, End-of-life care, Pressure ulcers; and Urinary incontinence | ACOVE QIs | Expert Committee (9 experts in NH care: 6 physicians, 2 registered nurses and 1 health system methodologists) |
| Saliba* et al. [51] (2002)          | 9 clinical experts in NH care, a content expert and a clinical oversight committee | Descriptive National project (US) | To identify QIs that can be used to measure NH residential care processes | Modified Delphi (9 clinical NH experts) panel process to rate potential QIs that were identified through reported interviews with residents and families and through a review of the scientific literature | 19 | General aspects of NH residential care | QIs, interview and reviews | Expert Committee (9 experts in NH care) |
| MacLean* et al. [52] (2004)         | 3 member clinical committee and a 9 member-multidisciplinary expert panel | Descriptive National project (US) | To develop a comprehensive set of explicit process measures to assess the quality of health care for osteoarthritis, rheumatoid arthritis, and analgesics use | A literature study was done for potential quality measures and a summary of existing data. A panel rated each proposed measure for its validity as a measure of health care quality. (modified RAND/UCLA) | 51 | 51 QIs to a specific situation, namely 14 QIs osteoarthritis, 27 QIs rheumatoid arthritis and 10 QIs analgesics use | QIs derived from literature | 9 member expert committee (expert in osteoarthritis, rheumatoid arthritis and community practitioners, academicians and people from geographically disperse regions) |
| Zingmond* et al. [23] (2007)        | 100528 patients | Observational cohort study (2 year) | Community-dwelling dual enrollees in Medicare and Medicaid, living in 19 California Counties (US) | To assess the applicability of process of care measures developed as part of ACOVE, that were adapted previously for use with administrative data. To measure the QoC in community-dwelling VE. | 43 | QIs that could be coded using administrative data by condition type or by intervention type from 22 conditions | Administrative data using linked Medicare and Medicaid | Computerized assessment |
| Min* et al. [41] (2007)             | 372 community dwelling persons 65 years of age or older | Observational study, 2 managed care plans within 2 years (US) | Determination of whether combinations of 8 common comorbid chronic conditions are associated with overall QoC among vulnerable patients | Measuring the care provided for 43 QIs by condition and by type and identification of care inaccessible to measurement by linked Medicine and Medicaid claims through using medical record. | 89 | QIs in 8 chronic conditions: hypertension(8), CAD(13), osteoarthritis (14), diabetes(10), CHF or AF(17), depression (17), osteoporosis (10) | Medical records, patient interviews | Trained nurses experienced in quality assessment, Physicians (were used for QIs that needed clinical expertise) and senior nurse reviewer |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|----------------------------|------------|
| Chang *et al.(2006) CAT D           | Random sample of 236 community-dwelling adults 65 years of older | Observational cohort study (13 months) 2 managed care organizations (US) | To investigate the relationship between patient-reported global ratings of health care and the quality of providers communication and technical QoC |
| Min* et al.[40] (2005) CAT D        | 372 community dwelling VE (July 98-July 99) | Observational cohort study 2 senior managed care plans (US) | Evaluation of influences of clinical conditions, types of care processes, and sociodemographic characteristics on the QoC |
| Saliba* et al.[50] (2004) CAT B2,3  | ACOVE QIs            | Descriptive study National project (US) | To develop a set of specific care process indicators associated with better outcomes for general medical conditions for VEs |
| Higashi* et al.[34] (2005) CAT D    | 372 community-dwelling VE, 65>= yrs, enrolled in managed care organizations | Observational cohort study. (July 98-July 99) 2 managed care organizations (US) | To examine the link between the QoC that patients received and their survival |
| Methods                                                                 | # QIs used | Conditions                  | Source of information                         | Assessor                                                                 |
|------------------------------------------------------------------------|------------|-----------------------------|-----------------------------------------------|--------------------------------------------------------------------------|
| ACOVE QIs were used to measure technical QoC. Survey questionnaires were sent to the patients to determine patients global ratings of health care | 236        | All 22 ACOVE conditions     | Medical records, patient interviews           | Trained nurses experienced in quality assessment, Physicians (were used for QIs that needed clinical expertise) and senior nurse reviewer |
| Analysis of data of the original ACOVE study of Wenger et al 2003 (see Wenger method). Studying associations between observed-minus-expected QoC and several factors (clinical (15 conditions), type of care process (15 processes), sociodemographic characteristics (age, sex, VES-13, education, income)) | 207        | All 22 ACOVE conditions     | Medical records, patient interviews           | Trained nurses experienced in quality assessment, Physicians (were used for QIs that needed clinical expertise) and senior nurse reviewer |
| Multistep process.  
1) translation of ACOVE QIs into potential NH QIs 2) identification of additional NH QIs 3) identification of NH care processes associated with improved outcomes by expert panel 4) external review by second expert panel 5) identification of QIs to be excluded for patients with AdvDem and PrProg by a separate panel and translation into corresponding in NH QIs(Modified UCLA/RAND method(delphi)). | 236 (114 finally identified as valid) | 11 medical conditions: Depression, DM, Hearing impairment, Heart failure, Hypertension, Ischemic heart disease. Osteoarthritis, Osteoporosis, Pneumonia and influenza, Stroke and atrial fibrillation, Vision impairment | Medical record Review | 9 experts panel: 6 physicians, 2 registered nurses and 1 health system methodologist |
| Statistical analysis of data on the QoC of the original ACOVE study of Wenger et al 2003 (see method Wenger for QoC measurement) and 3-years survival | 207        | All 22 ACOVE conditions     | Medical records (183 QIs), patient interviews (24 QIs) | Trained nurses experienced in quality assessment, Physicians (were used for QIs that needed clinical expertise) and senior nurse reviewer |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|----------------------------|------------|
| **Ganz et al. [24]** (2006) CAT C    | 339 elderly (>75 yrs) arthritis patients | Observational cohort study (13-months) Subgroup of 2 medical groups. One primary care group and one specialty group (US). | To describe the quality of osteoarthritis care provided to community-dwelling elderly patients and to characterize arthritis-related function in these patients |
| **Higashi et al. [39]** (2007) CAT D | 7680 patients (CQI study: 6712 patients, ACOVE study: 37265> = yrs, VHA project: 596) | Observational cohort study CQI: Oct 98-Aug 2000, ACOVE: Oct 99-Jan 2000 VHA: Oct97-Sep 1999 3 cohorts of community dwelling adult patients (US) | To study the relationship between the QoC and the number of medical conditions of a patient |
| **Kröger et al. (2007) CAT B1,3**   | 29 patients diagnosed with cognitive impairment dementia | Descriptive Integrated care system for VE (Canada) | To evaluate face and content validity, feasibility and reliability of QIs previously developed in the US and other countries to assess QoC of Canadian VE with cognitive impairment or dementia |
| **Steel et al. [25]** (2008) CAT C   | 8688 participants in the English longitudinal study of ageing, of whom 4417 reported diagnoses of one or more of 13 conditions | Observational cohort study Private households (UK) | To assess the receipt of effective healthcare interventions in England by adults aged 50 or more with serious health conditions |
| Methods | # QIs used | Conditions | Source of information | Assessor |
|---------|-----------|------------|----------------------|----------|
| Data was collected on demographics, functional status, and QoC via patient interviews and mailed questionnaires. 8 quality indicators were used to measure osteoarthritis care. (assessment using ACOVE-2 indicators, outpatient setting, >75 yrs) | 8 | Osteoarthritis care | Computer assisted telephone interview, Questionnaires | Research personnel |
| Analyzing the relationship between the QoC that patients received, defined as the percentage of QIs satisfied among those for which patients were eligible, and the number of chronic medical conditions each patient had | CQI: 439 VHA project: 348 QIs ACOVE: 236 | CQI: 30 clinical conditions and preventive care VHA: selection of CQI QIs covering 26 clinical areas ACOVE: see Wenger et al. 2003 | CQI and ACOVE: Medical records, patient interviews VHA: medical records | Trained research nurses |
| A modified RAND/UCLA, 2-round Delphi method was used to assess face and content validity (using a 33 person expert panel). Feasibility and reliability was assessed in a pilot study of 29 patients | 82 (72 identified as valid) | Cognitive impairment/dementia, Incontinence Pressure ulcers, Multiple medications, Malnutrition | QI set: ACOVE (57) AASW (1) NASW (1) AOTA (4) RAND (3) Shield et al (2) Scottish collegiate (2) NHS (2) IOM (1) Pilot: medical records + patients or caregivers interviews | Expert panel of 33 members (geriatric medicine n=9, nursing n=6, occupational therapy n=3, psychology n=3, neuropsychology n=2, pharmacy n=4, nutrition n=3 and social work n=3. Pilot: trained research nurses |
| A national structured survey questionnaire with face to face interviews using 32 QIs and 7 questions was performed to assess QoC for 13 conditions | 32 | Stroke Depression DM, Falls Hearing problems Hypertension Ischemic heart disease Osteoarthritis Osteoporosis Pain management Smoking cessation Urinary incontinence Vision | Patients (face to face interviews), expert panel | Not mentioned |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|------------------------------------|----------------------|----------------------------|------------|
| Bates-Jensen* et al.[26] (2003)    | 191 residents (elderly) | Observational study Eight NHs (US) | Reliability and feasibility of a standardized protocol to score QIs for pressure ulcer care; Assessment of Quality of PU care |
| Mikuls et al. (2005) CAT C         | 63105 gout patients   | Retrospective database analysis (between 1990-1999) All gout patients in a general practice research database (US) | To examine adherence to QIs concerning the quality of allopurinol use in the treatment of gout |
| Ganz* et al.[45] (2007) CAT D      | 357 intervention, 287 control patients >75 yrs | Controlled trial 1 primary care group and 1 multidisciplinary care group, consisting of patients having difficulty with falls, incontinence, or CI (US) | To determine whether an intervention that improved care for falls, incontinence, and CI by an absolute 15% change also affected QoC for masked conditions |
| Bates-Jensen* et al.[43] (2003) CAT D | 329 NH residents, 65>= yrs | Descriptive, Observational study (3 consecutive 12-hours days) 16 Nursing Homes (US) | To determine whether NHs that score in the extreme quartiles of pressure ulcer (PU) prevalence as reported on the MDS PU indicator provide different care |
| Simmons* et al. (2003) CAT D      | 400 long-term NH residents, 65>= | Cross-sectional observational study, 3 consecutive 12-hour days 16 NHs (11 lower quartile NHs, 5 upper quartile NHs) (US) | To determine whether NHs that score differently on prevalence of weight loss according to a MDS QI also provide different processes of care |
| Gnanadesigan* et al. (2004) CAT C | 372 community-dwelling VEs | Observational study, cohort 13-month 2 managed care plans (US) | To assess QoC provided to community-based VE with UI |
Studies pertaining to ACOVE quality indicators

| Methods | \# QIs used | Conditions | Source of information | Assessor |
|---------|-------------|------------|-----------------------|----------|
| ACOVE QIs for PU care were adapted. | 9 | Pressure Ulcer Care | Medical records, direct observations, wireless thigh monitor observation data | Trained physician and geriatric nurse practitioner; certified wound care nurse (3 QIs); thigh monitor |
| 3 QIs for allopurinol use in gout treatment were used | 3 | allopurinol use in treatment of gout and asymptomatic hyperuricaemia | National medical record database | Computer |
| For 9 masked conditions the QoC was assessed with QIs. | 68 | Falls or gait impairment, Urinary incontinence, Cognitive impairment | Medical records, administrative data using written guidelines | Experienced nurses aided by a senior nurse reviewer |
| The QoC for residents at risk for PU development was determined using 16 process QIs. | 16 | Pressure Ulcer Care (10), Urinary incontinence (1), Weight loss and Nutrition (5) | Medical records, direct human observation, Interviews, Data from a wireless thigh monitor | Research staff, a nurse certified in wound care (used standardized assessment system with specific data sources, assessment guidelines and scoring rules) |
| Quality of weight loss care was assessed using 16 QIs. | 16 | Weight loss care / Nutrition | Direct observation, patient, interviews, medical records | Medical record review by trained research physician or geriatric nurse practitioner |
| Quality of UI care was assessed using 10 QIs. | 7 | Urinary Incontinence care | Medical record (explicit abstraction guidelines were used), telephone interview | Trained nurses experienced in quality assessment |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|----------------------------|------------|
| Wenger * et al.[5] (2003) CAT C     | 372 community-dwelling vulnerable elderly | Observational cohort study, 13-month 2 managed care organizations (US) | To assess QoC provided to VE by evaluating the process of care using ACOVE QIs |
| Chodosh * et al. (2004) CAT C       | 372 community dwelling VEs (July 98-July 99) | Observational study 2 managed care plans (US) | Evaluation of QoC for chronic pain |
| Higashi* et al.[30] (2004) CAT C    | 372 community-dwelling VEs enrolled in managed care organizations (July 98-July 99) | Observational cohort study. 2 managed care organizations (US) | Evaluation of QoC (Pharmacological Care) |
| Arora et al. [35] (2007) CAT C CAT B2 | 328 VEs admitted at a general medicine ward | Prospective evaluation of QoC Academic medical center (US) | Adaptation of ACOVE QIs for QoC assessment of hospitalised elderly and use of QIs for QoC measurement |
| Broadbent et al. (2008) CAT D       | 320 randomly selected patients with osteoarthritis, >= 55 years | Retrospective observational study 18 general practices (UK) | To measure the recorded quality of primary care for osteoarthritis and assess variations by patient and/or practice characteristics |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives | Methods | #† QIs used | Conditions | Source of information | Assessor |
|-------------------------------------|----------------------|-----------------------------|------------|---------|-------------|------------|----------------------|----------|
| Wenger * et al. [5] (2003) CAT C   | 372 community-dwelling vulnerable elderly | Observational cohort study, 13-month | To assess QoC provided to VE by evaluating the process of care using ACOVE QIs | Quality of care was assessed using 207 QIs. (Overall QoC, QI for 22 conditions, Q for domain of care) | 207 | 22 ACOVE conditions | Medical Record (185 QIs), patient interview (22 QIs) (approach: Written abstraction guidelines and real-time consultation with a senior nurse reviewer) | Trained nurses experienced in quality assessment, Physicians (were used for QIs that needed clinical expertise) and senior nurse reviewer |
| Chodosh * et al. (2004) CAT C      | 372 community-dwelling VEs (July 98-July 99) | Observational study | Evaluation of QoC for chronic pain | QoC assessment using 11 QIs Analysis of data of the original ACOVE study of Wenger et al 2003 | 11 | Chronic Pain | Abstraction of administrative data & medical records on in- and outpatient, patient interviews. | Trained nurses in Quality assessment |
| Higashi * et al. [30] (2004) CAT C | 372 community-dwelling VEs enrolled in managed care organizations (July 98-July 99) | Observational cohort study. | Evaluation of QoC (Pharmacological Care) | QoC assessment using pharmacologic care related QIs (with more 5 eligible patients) by medical record abstracting (37 QIs) and patient telephone interviews (6 QIs) | 43 | NA | Chart abstraction and patient interview | Trained nurses in quality assessment (chart abstraction, interviews), physician (review for QI with clinical assessment) |
| Arora et al. [35] (2007) CAT C CAT B2 | 328 VEs admitted at a general medicine ward | Prospective evaluation of QoC Academic medical center (US) | Adaptation of ACOVE QIs for QoC assessment of hospitalised elderly and use of QIs for QoC measurement | Interviews for defining vulnerable elders (ADL), questionnaires (VES-13 and MMSE); QoC assessment with 16 QIs using a computerized chart abstraction tool that facilitated the manual chart abstraction | 16 | General medical delirium and Dementia Physical function Pressure ulcer | Chart abstraction (computerized tool were used) and patient interview | Trained research assistants |
| Broadbent et al. (2008) CAT D      | 320 randomly selected patients with osteoarthritis, >= 55 years | Retrospective observational study | To measure the recorded quality of primary care for osteoarthritis and assess variations by patient and/or practice characteristics | Data extracted from electronic & paper records of patients to assess recorded care using 9 QIs. QIs were selected from three sources (NICE, ACOVE, QIGP general practice QIs) and peer-reviewed by an independent expert panel including GPs QI score analyzed in relation to practice and patient characteristics | 9 (of which 8 were ACOVE based) | Osteoarthritis care | Chart and electronic record abstraction | Researcher (305 records) and assistant (15 records) |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|----------------------------|------------|
| Roth et al.[36] (2008) CAT D       | 200 community-dwelling older adults (100 white, 100 black; >= 60 years) | Prospective cohort study 2 senior housing complexes and a care program for elderly (US) | 1) To describe quality of medication use in older adults at baseline and differences between whites and blacks, 2) to examine the effect of race on medication-related problems, 3) to assess change in quality of medication use between whites and blacks over time |
| Zingmond* et al.[32] (2009) CAT C   | 21,657 NH registers, dually enrolled in Medicaid and Medicare. | Retrospective cohort study Nursing homes in 19 California counties (US) | Assessing which clinical conditions are inadequately measured and adaption of ACOVE for use with routinely collected data |
| Arora et al.[35] (2009) CAT D       | 898 hospitalised VEs aged 65 or older | Observational cohort study June 1, 2004 till June 1, 2007 University of Chicago med center (US) | To assess the relationship between QoC and functional decline |
| Van der Ploeg* et al. (2008) CAT B1 | ACOVE QIs | Descriptive (NL) Scientific institute | To adapt and validate the set of ACOVE QIs, oriented on GP care in the Netherlands |
| Methods | # QIs used | Conditions | Source of information | Assessor |
|---------|------------|------------|-----------------------|----------|
| Whites and blacks ≥ 60 yrs were interviewed 3 times over 1 year. Information on quality of medication use was collected using a clinical pharmacist and the ACOVE-2 QIs. Data on demographics, health literacy, functional status and participant-reported drug therapy concerns were collected. | 39 | 22 ACOVE conditions | Medical record abstraction | Clinical Pharmacist |
| Identification of care inaccessible to measurement by using Medicare and Medicaid claims linked to MDS. Assessment of quality of care | 50 | 16 conditions: Dementia, depression, diabetes, end-of-life care, falls, heart failure, hospital care, hypertension, ischemic heart disease, malnutrition, medication use, osteoarthritis, osteoporosis, stroke/AF, urinary incontinence, vision impairment | Administrative data | Computer |
| - | 16 | General medical, delirium and dementia, physical function, pressure ulcer | Medical chart abstraction (computer-based tool has been used) and patient interviews | Trained research assistants |
| 108 QIs were assessed by a panel of 9 experts. A modified version of the RAND/UCLA appropriateness method was used. | 108 (81 QIs identified as valid) | Dementia, depression, diabetes, end-of-life care, fall/morbidity, medication use, under nutrition, continuity and coordination of care | ACOVE QIs, reviews and expert knowledge | Panel of 9 experts: 5 GPs, 2 NH doctors, 2 clinical geriatricians |
| Authors/Category of conceptual model | Study population (n) | Study design/Period/Setting | Objectives |
|-------------------------------------|----------------------|----------------------------|------------|
| Roth et al.[37] (2009) CAT D        | 200 community-dwelling older adults (100 white, 100 black; >= 60 years) | Prospective cohort study 2 senior housing complexes and a care program for elderly (US) | To determine the prevalence and types of medication related problems in older adults and to examine the impact of race on quality of medication use |
| Wenger* et al.[33] (2009) CAT E CAT C | Community dwelling elderly >75 yrs (357 at intervention sites and 287 at control sites) | Controlled trial 2 community medical groups (US) | To determine effect of a practice-based ACOVE-2 intervention on care for falls, UI and cognitive impairment |

ACOVE: Assessing Care Of Vulnerable Elders; AdvDem: Advanced Dementia; PrProg: Poor Prognosis; VE: Vulnerable Elder; NH: Nursing Home; QoC: Quality Of Care; QI: Quality Indicators; EB: Evidence Based; IHI BTS: Institute of Healthcare Improvement’s Breakthrough Series; CHF: Chronic Heart Failure; GEM: Geriatric Evaluation and Management; MAI: Medication Appropriateness Index; DM: Diabetes Mellitus; CQA: Community Quality Index; VHA: Veterans Health Administration; PU: Pressure Ulcer; MDS: Minimum Data Set; CI: Cognitive Impairment; UI: Urinary Incontinence; NICE: National Institute for Health and Clinical Excellence; QIGP: Quality Indicators for General Practice; PIM: Prescribing Indicated Medication; AIM: Avoiding Inappropriate Medication; ECD: Education, Continuity, and Documentation; MM: Medication Monitoring; ADL: activities of daily living; GP: General Practitioner; QoL: Quality of Life; RA: Rheumatoid Arthritis; MD: Medical Doctor; CAD: Coronary Artery Disease; AF: Atrial Fibrillation; OA: Osteoarthritis; RA: Rheumatoid Arthritis; A-use: Analgesics use;

1:# = Number of quality indicators used.
| Methods                                                                 | #\(^1\) QIs used | Conditions                  | Source of information          | Assessor                           |
|------------------------------------------------------------------------|------------------|-----------------------------|---------------------------------|------------------------------------|
| Whites & blacks \(\geq 60\) yrs were interviewed 3 times over 1 year. Information on quality of medication use was collected using a clinical pharmacist and the ACOVE-2 QIs. Data on demographics, health literacy, functional status and participant-reported drug therapy concerns were collected | 39               | 22 ACOVE conditions         | Medical record abstraction        | Clinical Pharmacist                |
| Intervention: case-finding, physician education and a multicomponent practice-change effort. QoC assessment using QIs | 18               | Falls (5 QIs)               | Medical records, interviews, administrative data | Nurses with prior experience in quality assessment |
|                                                                        |                  | UI (6 QIs)                  |                                  |                                    |
|                                                                        |                  | Dementia (7 QIs)            |                                  |                                    |
4.2 Quality indicators for in-hospital pharmaceutical care of Dutch elderly patients

Development and validation of an ACOVE-based quality indicator set

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Drugs Aging. 2011 Apr 1; 28(4): 295-304
Abstract

Background: In 2001, the ACOVE (Assessing Care Of Vulnerable Elders) quality indicators (QIs) were developed in the US to measure the quality of care of vulnerable elderly patients. However, the ACOVE QI set was developed mainly to assess the overall quality of care of community-dwelling vulnerable elders (as opposed to hospitalised elderly). Therefore, they need to be adapted when used in a non-US hospital setting. In addition, the ACOVE QIs depend on patient and caretaker interviews to assess the quality of care.

Objective: The aim of this study was to develop and validate a set of explicitly phrased QIs to measure (without the need for interviews) the quality of pharmaceutical care of elderly hospitalised patients in the Netherlands.

Study Design: The QI set was developed based on the ACOVE QIs, Dutch national guidelines, evidence from the literature and expert opinion. The QI set focused on in-hospital pharmaceutical care and was evaluated in terms of whether the QIs were able to assess the quality of care using medical records and a hospital information system. In three review rounds, the QI set was adapted and judged on face and content validity. The feasibility of implementation of the QI set and inter-rater reliability were determined.

Setting: The study was conducted between September 2007 and August 2008 in a tertiary 1002-bed university hospital.

Research Team: Two pharmacists were responsible for the selection and adaptation of QIs. An internist-geriatrician, a physician with experience in quality assurance and internal medicine and a senior hospital pharmacist formed the expert panel responsible for reviewing the QIs.

Measurements: Fleiss’ k values and the intraclass correlation coefficient were calculated for inter-rater reliability.

Results: An 87-item QI set was accepted by the expert panel. Of this set, 49 QIs were based on ACOVE QIs and 38 QIs were newly added. The QI set demonstrated excellent inter-rater reliability and good feasibility.

Conclusions: We developed a valid and reliable set of QIs to efficiently assess the quality of the in-hospital pharmaceutical care provided to elderly Dutch patients.
Introduction

Pharmacotherapy is an essential component of medical care of elderly patients. However, older patients (aged >65 years) represent a vulnerable population and suffer more from medication related problems than younger adult patients, especially during hospital stays[1]. Older patients are at risk for several reasons: the coexistence of multiple morbidities and complex care needs; the presence of pre-existent cognitive, social and functional limitations; altered pharmacokinetics and pharmacodynamics; and the use of multiple drugs (polypharmacy) and, consequently, the risk of overtreatment and undertreatment[2-5]. Therefore, strategies are being developed to improve the quality of in-hospital pharmaceutical care of this population[6-8].

Adverse drug events (ADEs) are often used as an outcome measure for quality improvements in pharmaceutical care[9,10]. Many studies measure ADEs by manually studying medical records, often using so-called trigger tools[11-14]. These trigger tools help researchers to identify which medical records are suspect for an ADE. An expert panel subsequently reviews the suspected records and decides by consensus whether an ADE has actually occurred. This approach is considered the current gold standard in ADE incidence measurement. However, this approach is time consuming and relies heavily on the contributions of expensive experts. Another difficulty is posed by the fact that different practical conceptualizations of ADEs are used in studies. A recent review of several studies showed that ADE incidence in comparable populations varied between 2 and 52 ADEs per 100 admissions[15].

Another approach is to measure the quality of care using process indicators. Care processes can be assessed more efficiently and are more amendable than outcomes such as ADEs[16,17]. In 2001, the ACOVE (Assessing Care Of Vulnerable Elders) quality indicators (QIs) were developed to measure the quality of care of vulnerable elderly patients[18]. The ACOVE set consisted of 236 comprehensive indicators, focusing on 22 common elderly conditions and on important interventions such as prevention, diagnosis, treatment and follow-up. These QIs were developed based on literature review and on several levels of expert opinion, and have been applied successfully in several studies[19-23]. The ACOVE QIs are unique because they address, besides other healthcare issues, undertreatment, which is an issue often overlooked in other methods of quality-of-care assessment.

However, the ACOVE QI set was developed mainly to assess the overall quality of care of community-dwelling vulnerable elders[23]. Compared with these patients, hospitalised elderly are at greater risk of functional decline, delirium and polypharmacy, and conse-
Pharmaceutical care quality indicators for hospitalized elderly

Potentially greater morbidity, higher costs, longer length of stay and higher mortality [24]. Also, hospitals, the health inspectorate and health insurance companies are showing an increasing interest in QIs as a measure of quality. Therefore, it is important that hospital-specific QI sets are developed. In addition, the ACOVE set was developed in and for the US healthcare setting, which differs from its counterparts in other countries as a result of differences in healthcare policy, culture and therapy guidelines. To be able to use the ACOVE QIs in a European hospital care setting and with a focus on pharmaceutical care, they need to be adapted. As a consequence, indicators are changed, discarded and added on the basis of national guidelines, expert opinion and literature review [25]. Furthermore, according to the method reported by ACOVE researchers, patient and care-taker interviews are needed to assess the quality of care [18]. This, however, hampers convenient and routine application of the QIs because of the time investment involved. The original ACOVE approach would certainly impose a heavy burden on hospital resources. A QI method without the need for patient interviews would be more efficient.

The aim of this study was, therefore, to develop and validate a set of explicitly phrased QIs to measure efficiently (without the need for interviews) the quality of pharmaceutical care of elderly hospitalised patients in the Netherlands by selecting and adapting ACOVE criteria. Furthermore, we studied the feasibility and reliability of the QI set for prompt implementation in healthcare.

Methods

Setting

This study was conducted between September 2007 and August 2008 in a tertiary 1002-bed university hospital in the Netherlands (Academic Medical Center, Amsterdam).

Development of the Quality Indicator (QI) Set

The research team consisted of two pharmacists who were made responsible for selecting and proposing indicators (PW, JK) and an expert panel that included an experienced internist-geriatrician (SdR), a physician with experience in quality assurance and internal medicine (SS) and a senior hospital pharmacist (HvK). This panel reviewed the draft sets of QIs for face validity and content validity.

Our QIs had to meet the following criteria: (i) the content was related to pharmaceutical care; (ii) the content was applicable to a hospital setting; (iii) the content cor-
responded to national guidelines; and (iv) the assessment could be performed using medical records and a hospital information system.

The development process consisted of three review rounds. Each round consisted of a process of modification and formulation of QIs by the two designated pharmacists, followed by an expert panel review of content and face validity. Each individual panel member was asked to rate the selected QIs independently on a three-point Likert scale (‘yes’, ‘no’, ‘doubtful’) in terms of correspondence with the aim of the QI set in this study. Only when all panel members judged an indicator to be a ‘no’ or a ‘yes’ was the QI discarded or accepted, respectively. When a difference of opinion arose or when one or more members judged the QI as ‘doubtful’, a consensus view was reached through discussion in a consensus meeting.

In round 1, the two pharmacists selected QIs from the original ACOVE set that were related to pharmaceutical care. This first draft set was reviewed by the expert panel. In round 2, the two pharmacists subsequently modified these QIs based on the first-round comments of the panel to augment their validity. Textual changes to the selected QIs were made to make them suitable for assessment of the quality of in-hospital pharmaceutical care. In addition, Dutch national guidelines and evidence from international literature were used to help the pharmacists modify existing QIs and propose new QIs. Content experts (a neurologist, a vascular specialist and a cardiologist) were consulted for specific QIs for which the expert panel lacked knowledge. The second draft QI set was reviewed again by the panel. In round 3, the QIs were again modified to augment their validity based on the comments in round 2. The expert panel reviewed the adjusted third draft QI set to finalize the development process.

Improvement of the Applicability of the QI Set in Clinical Practice

To further improve the QIs, the set was tested after development on the medical records of ten preselected elderly patients who had experienced a long hospital stay, multiple co-morbidities and geriatric problems. We examined whether the QIs were explicit and comprehensive in their wording (sufficient to prevent differences in interpretation), mutually exclusive and able to assess the quality of in-hospital pharmaceutical care using only medical and nursing records and the hospital data information system. The phrasing of QIs was adjusted if necessary and reviewed again by the panel. To increase the efficiency of the medical record abstraction process, QIs were grouped by related condition and drug class.
Inter-Rater Reliability

The inter-rater agreement (reliability) was determined based on three pharmacists’ (YB, JK, MT) assessment of the quality of care of ten randomly selected patients (different to those used for the improvement of the QI phrasing). Fleiss’ k values were calculated to determine the agreement between the independent judgements of the three pharmacists on applicable disease conditions, applicable drugs (class) and the QI scoring results (passed or not passed). If QI scoring results were available from only (any) two of the three pharmacists, the intraclass correlation coefficient (ICC) based on a two-way random model was calculated. Values for k and ICC between 0.41 and 0.60 were considered to reflect moderate agreement, values between 0.61 and 0.80 to represent substantial agreement, and values >0.81 to represent almost perfect agreement[26].

Results

The development of the QI set is shown in figure 1.

Round 1

Identification of Relevant QIs

Of the 236 original ACOVE QIs, the two pharmacists selected a subset of 160 QIs that had been shown to be implementable and that had at least one eligible patient in a study by Higashi et al[21]. Of these 160 QIs, 80 were discarded because they were unrelated to pharmaceutical care. The expert panel subsequently discarded 15 more QIs because of non-correspondence with the criteria of the QI set, leaving 65 remaining QIs.

Round 2

Focus on In-Hospital Pharmaceutical Care

Of the 65 QIs selected during round 1, 48 were modified by the two pharmacists to make them applicable for in-hospital use, to make their phrasing more explicit and to adapt their content to Dutch national guidelines. Thereafter, in the expert panel meeting, nine of the 65 QIs were left unchanged, four were marked for adjustment in the next round and four were discarded because of a lack of clinical relevance or doubts about their applicability. This left 61 ACOVE-based QIs.
New QIs

In total, 38 QIs were newly added to the set. Of these, 21 were based on Dutch national guidelines, nine on expert opinion and eight on studies focusing on inappropriate medication for the elderly\(^{(27-29)}\). Six QIs concerning cardiovascular diseases were reviewed by content experts: four by a neurologist and two by a vascular expert and a cardiologist. Round 2 resulted in a total set of 99 QIs.

**Figure 1.** Development process of the quality indicator (QI) set. ACOVE=Assessing Care Of Vulnerable Elders.
Round 3

Nine QIs were modified based on the comments of the expert panel. Eleven QIs were discarded because of debate about their content validity and doubts about their applicability. A draft set of 88 QIs was completed after their face and content validity had been accepted by the expert panel.

### Table 1. Examples of quality indicators

| Prescribing indicated medication |  |
|----------------------------------|--|
| ALL diabetic elders with proven cardiovascular disease should be offered daily aspirin (acetylsalicylic acid) therapy (80–100 mg/day) OR ELSE an increased risk for cardiovascular complications exists |  |
| IF an elder has hypertension and has renal parenchymal disease with lowered glomerular filtration rate (creatinine >150 mmol/L) or microalbuminuria, THEN therapy with an ACE inhibitor or angiotensin II type I receptor antagonist should be offered |  |
| IF an elder had a transient ischaemic attack or non-invalidating stroke and no history of atrial fibrillation, THEN prophylaxis should be offered. The first choice treatment is aspirin 38–100 mg/day in combination with dipyridamole 200 mg twice daily (slow release). Both are to be given life long. If there is a contraindication for aspirin, THEN clopidogrel should be given |  |

| Avoiding inappropriate medication |  |
|----------------------------------|--|
| IF an elder requires analgesia, THEN meperidine (pethidine) should NOT be used OR ELSE there is risk for severe confusion |  |
| IF an elder has dementia, THEN a long half-life benzodiazepine such as diazepam, flurazepam, flunitrazepam, clorazepate or clordiazepoxide should NOT be used |  |

| Continuity and documentation of care |  |
|-------------------------------------|--|
| IF an elder is discharged from a hospital to a home or nursing home, THEN a discharge summary that includes information on medication at admission and discharge should be sent to the outpatient physician or nursing home within 14 days |  |
| IF a new drug is prescribed to an elder on an ongoing basis for a chronic medical condition, THEN the prescribed drug should have a clearly defined indication documented in the patient’s record |  |

| Monitoring of medication |  |
|--------------------------|--|
| IF an elder uses a maintenance dose of digoxin, THEN the maximal dosage per day is 0.125 mg UNLESS a lower dosage has previously been insufficiently effective for the patient and therapeutic drug monitoring has shown therapeutic blood levels at this high dosage |  |
| IF an elder is started on a new selective serotonin receptor inhibitor antidepressant treatment during the hospital stay, THEN evaluation of sodium levels should be performed by the prescribing physician (minimum once during hospital stay) or should be continued after discharge by a general practitioner (yearly) OR ELSE hyponatraemiae could occur |  |
Table 2. Quality indicators (QIs) per condition and drug/drug class

| Condition or drug/drug class | QI [total no. (new)] |
|------------------------------|----------------------|
| **Condition**                |                      |
| Hypertension                 | 3 (1)                |
| Diabetes mellitus            | 6 (3)                |
| Ischaemic heart disease      | 5                    |
| Delirium and cognitive dysfunction | 5 (5)              |
| Stroke                       | 7 (5)                |
| Arrhythmia                   | 1 (1)                |
| Heart failure                | 9 (1)                |
| Pneumonia                    | 1                    |
| Fall                         | 1 (1)                |
| Dementia                     | 4 (4)                |
| Depression                   | 8 (5)                |
| Osteoarthritis               | 2                    |
| Gout                         | 1 (1)                |
| Osteoporosis                 | 3                    |
| Parkinson’s disease          | 1 (1)                |
| Other                        | 9 (2)                |
| **Drugs or drug class**      |                      |
| Prophylaxis of VTE           | 1                    |
| Pain medication              | 4 (2)                |
| Sleep and anxiolytic drugs   | 1 (1)                |
| Opioids                      | 2                    |
| Coumarins                    | 4 (3)                |
| Corticosteroids              | 1                    |
| Diuretics                    | 1                    |
| Digoxin                      | 1 (1)                |
| NSAIDs                       | 2                    |
| Ophthalmics                  | 1                    |
| Anticholinergics             | 1 (1)                |
| ACE inhibitors               | 1                    |
| Endocarditis prophylaxis     | 1                    |
| **Total**                    | 87 (38)              |

VTE=venous thromboembolism.
Based on experiences during testing of the draft QI set on the ten test patients, 33 of the remaining 88 QIs were given more explicit phrasing. One QI was discarded because its content overlapped with other QIs. All textual adjustments and the removal of the QIs were agreed upon by the review panel. The average time required to apply the draft QI set to one medical chart (for one admission) was 45 minutes.

Composition of the Final 87-Item QI Set

The QIs were categorized in four domains based on the four important aspects of pharmaceutical care described by Higashi et al.;[21] prescribing indicated medication (39 QIs), avoiding inappropriate medication (14 QIs), continuity and documentation of care (26 QIs) and monitoring of medication (8 QIs). A selection of the QIs is shown in table I. The complete QI set is shown in Appendix S1. The final 87-item QI set consisted of 78 QIs focusing on 15 conditions and 13 specific drugs or drug classes and nine QIs focusing on condition-and drug-independent aspects of in-hospital pharmaceutical care (table II).

The final QI set consisted of 49 ACOVE-based QIs and 38 newly added QIs. Of the original ACOVE QIs, seven were added without adjustments and six with minor adjustments. Sixteen ACOVE QIs were adjusted based on expert opinion, 18 based on Dutch national guidelines, and two based on a combination of guidelines and expert opinion. Thirty-eight of the final 87 QIs were newly developed based on Dutch national guidelines (21 QIs), expert opinion (9 QIs) or literature on inappropriate medication for the elderly (8 QIs). Appendix S1 (Supplemental Digital Content) shows (per QI) whether QIs were based on an ACOVE QI or whether they were newly developed. Furthermore, the appendix shows the source used to justify changes to the content of all new QIs.

### Table 3. Inter-rater agreement expressed in Fleiss' k values (three raters) and intraclass correlation coefficient (ICC) [two raters]

| Parameter          | k (95% CI)          | ICC (95% CI)       |
|--------------------|---------------------|-------------------|
| Condition          | 0.87 (0.67, 1.00)   | NA                |
| Drug (class)       | 0.85 (0.70, 1.00)   | NA                |
| Quality indicator  | 0.88 (0.75, 1.00)   | 0.80 (0.63, 0.90) |

NA=not applicable.

Improvement of Applicability of the QI Set
Inter-rater reliability testing

A total of 150 unique patient-condition combinations, 120 unique patient-drug combinations, 89 unique patient-QI combinations for three raters and 31 unique patient-QI combinations for two raters could be obtained. The k values for the selection of applicable conditions, drug classes and QIs, and the ICC for QIs with only two raters are summarized in table III. The k and ICC values suggest almost perfect agreement in the application of the QI set.

Discussion

In this study, we developed a valid and reliable set of ACOVE-based QIs to assess the quality of in-hospital pharmaceutical care of elderly patients. Our QIs obviate the need to interview patients or their caretakers because they have been devised to be applied exclusively to unstructured medical records and nursing records as well as to structured diagnostic procedure results. Consequently, this approach reduces some of the labour associated with the original ACOVE assessment method and, therefore, facilitates its implementation in daily practice.

Several studies have reported on the use of QIs to measure overall quality of care, with most of the authors involved being related to the RAND institution, the organization responsible for the development of the ACOVE QIs. We conducted a study to develop a QI set specifically aimed at the measurement of the quality of in-hospital pharmaceutical care. Only one recent study by Spinewine et al.\textsuperscript{[30]} used seven pharmaceutical care-related ACOVE QIs to assess the appropriateness of prescribing for the hospitalised elderly in Belgium. However, these QIs were a selection sample from the subset of original ACOVE indicators used by Higashi et al.\textsuperscript{[21]} In addition, ours is only the second study that developed a QI set that can be assessed by abstracting only medical records and administrative data. Earlier, Arora et al.\textsuperscript{[31]} reported on the adaptation of ACOVE QIs to hospital care. In their study, 16 QIs were operationalized into a medical record abstraction tool for which interviews were unnecessary. However, these QIs did not focus on pharmaceutical care.

We have shown that a new QI set can be developed using an already existing set from another country and with a wider focus than that of pharmaceutical care. The subset of ACOVE QIs used in the study by Higashi et al.\textsuperscript{[21]} proved to be a good starting point for our set. These QIs, which have been proven to be feasible in multiple quality-assessment studies\textsuperscript{[19,20,32]}, made up 56% of our final set. Because these original ACOVE QIs...
focused on the domains of both primary and secondary care, they had to be adapted to the domain of hospital care. Furthermore, many of these ACOVE QIs were discarded because their content was not related to pharmaceutical care.

Three other studies mentioned the development of a QI set largely based on the ACOVE criteria. Steel et al.\[33\] adapted ACOVE QIs to the UK care setting for use in patient survey interviews in primary and secondary care. This process resulted in a 102-item QI set. These 102 QIs were all based on ACOVE QIs. Van der Ploeg et al.\[34\] adapted ACOVE QIs to the Dutch care setting for the quality assessment of general practice care. Of their final set of 81 QIs, 76 were ACOVE based and five QIs were newly added. Kroger et al.\[35\] developed a QI set for use in integrated care systems for elderly patients living in Canada. Of their final 72-item QI set, 79% were ACOVE indicators. These three studies confirmed that new and valid QI sets can be developed in other countries based on the US ACOVE indicators. However, before QIs can be used in a new setting, processes of adaptation and validation are necessary to take into account differences in care practice, guidelines and culture\[24\]. In our study, we also adopted comparable adaptation and validation measures using a multidisciplinary expert panel. Aside from the transfer of ACOVE indicators, this resulted in the addition of a number of new indicators (44% of the set) to our QI set based on Dutch national guidelines, the literature and expert opinion.

Before a QI set can be readily used for the assessment and improvement of care, its feasibility for measurement (in terms of comprehensibility and time consumption) and reliability of measurement in daily practice should be assessed\[35\]. Otherwise, it is possible that during the first application, chart abstractors will conclude that it is difficult or impossible to measure the QIs. Furthermore, reliability can be hampered by unclear phrasing of indicators. Thus, we first assessed the feasibility of our QIs on a random selection of patients and made appropriate changes to the phrasing of the indicators. We thereafter assessed the reliability of the QI set and found excellent reliability values (with a lowest k value of 0.85). Other studies reported lower reliability values for their QI sets (a range of 0.33–1.00)\[31,35-38\].

Our study had some limitations. Our expert panel, which was responsible for assessing the face and content validity of the QIs, was smaller than the expert panels of other ACOVE studies\[33-35\]. However, we selected a multidisciplinary panel that was sufficiently capable (experience, field of expertise) of reviewing a set of in-hospital pharmaceutical-care-related QIs and of suggesting adjustments based on evidence and expert opinion. Any content of specific QIs concerning areas of expertise that the panel did not cover were discussed additionally with specialists. Another limitation of our study was that no formal external validation process was conducted. Furthermore,
although other ACOVE studies used a nine-point scale based on the modified Delphi/RAND method, we used a simpler three-point Likert scale for the judgement of the QIs because this scale had sufficient discriminative ability for our approach\(^{39}\). Only when all experts completely agreed or disagreed (comparable to the top or bottom scores of a five-point or more Likert scale) was a QI accepted or discarded. For every case of disagreement or doubt, a consensus meeting was organized. In our approach, a five-, seven- or nine-point Likert scale would, therefore, not have had additional value. Also, because the QIs in our set had to be assessed by abstracting information from the medical and nursing records and hospital information system, it is possible that a registration bias may have been introduced in the reliability testing. If the necessary actions or a contraindication were not documented in the medical or nursing records, the QI was considered to be not passed.

Quality of care could have been underestimated when the correct care was delivered but not recorded\(^{40}\). Conducting a patient or caretaker interview may possibly have partly prevented this bias. This lack of patient or caretaker interviews could be a limitation of our QI method. However, these interviews would be labour intensive and would render the routine application of the QI set practically impossible. Our specific aim was to select and adapt QIs that could be assessed using only the medical record data. Furthermore, we are not familiar with any studies that have quantified the exact additive value of these interviews.

Compared with the original ACOVE QIs, some diseases were attributed fewer or no QIs in our set. This was due to the focus of our set (pharmaceutical in-hospital care). Some care processes related to the treatment or prevention of specific disease are mostly conducted outside the hospital, e.g. vaccination against pneumonia. Those QIs were discarded when adaptation of the QI to hospital care processes was impossible. In addition, one of the pharmacists responsible for the selection of the QIs also participated in the inter-rater reliability assessment. This could have influenced the results, but the other two raters were naive to the QIs, the record screening was performed independently and k values over three raters were excellent. Another possible limitation is that the average time needed to assess the QI set per patient in our study has limited external validity and may be different in other hospitals. However, if information in medical and nursing records is available in a more structured manner in another hospital, less time may be needed to assess a patient.
Conclusions

The QI set described in this study is valid (regarding face and content validity), feasible and leads to reproducible scores. It has been developed specifically for the Dutch setting and we therefore believe it should be generally applicable to hospital settings within the Netherlands. This QI set is, however, a starting point. Further validation is needed in one or more larger cohorts of elderly hospitalised patients. This will probably result in a further selection of indicators based on the eligibility of patients. The set could be further validated in these future studies by, for instance, examining the association between the quality of in-hospital pharmaceutical care assessed by the QIs and adverse outcomes such as unnecessary re-admissions and mortality. Another interesting approach might be the incorporation of QIs into clinical decision support systems that would apply these QIs automatically to structured patient and treatment data, provided that these are electronically available. Such an approach might greatly enhance the ability of healthcare professionals to make the right decisions at the right time to improve care for their most vulnerable patients.

Acknowledgements

No sources of funding were used to conduct this study or prepare this manuscript. The authors have no conflicts of interest that are directly relevant to the content of this study. The authors wish to thank Mila Tjoa, PharmD, at the Department of Clinical Pharmacy, Erasmus Medical Center, Rotterdam, the Netherlands, for her support in the assessment of the feasibility and reliability of the QI set. The authors also wish to thank Paul Kuks, PharmD, PhD, and Loraine Lie-A-Huen, PharmD, PhD, at the Department of Clinical Pharmacy Academic Medical Center, Amsterdam, the Netherlands, for revising the manuscript.

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## Domain 1. ‘Prescribing indicated medication’

| Indicator | ACOVE based (A) or New (N) |
|-----------|---------------------------|
| ALL diabetic elders with elevated blood pressure (SBP>140 mmHg) should be offered one of the following drugs (in order of choice) as an antihypertensive treatment: diuretic, calcium inhibitor, ACE inhibitor, AT2 receptor blocker or beta receptor blocker. | N* |
| IF an elder is diagnosed with delirium and a pharmacologic intervention is needed, THEN haloperidol (0.25-2.5 mg once or twice daily) should be the first-line treatment option UNLESS there is a known contraindication such as Parkinson’s disease or Lewy-bodies dementia. | N* |
| IF a hospitalised elder needs or already uses a NSAID and has one or more solitary risk factors such as age > 70 years or untreated H. pylori or previous ulcer, THEN the patient should receive prophylaxis with either a proton-pump inhibitor in combination with a NSAID or misoprostol in combination with a NSAID. | A* |
| IF an elder is presented with heart failure with AF without a sufficiently controlled ventricular response OR an elder is presented (or diagnosed in hospital) with heart failure without AF but with remaining complaints of heart failure despite treatment with ACE inhibitors, diuretics and beta blockers and/or spironolactone, THEN digoxin treatment should be initiated or given. | N* |
| ALL elders WITH a TIA and/or a cerebrovascular infarction in their history AND a plasma cholesterol > 5.0 mmol/l OR a LDL concentration > 2.5 mmol/l, THEN prophylaxis with cholesterol lowering medication should be considered. | N* |
| IF there are two or more cumulative risk factors present in an elder (age 65-70 years, use of acetylsalicylic acid/anticoagulants, serious rheumatoid arthritis, high dose NSAIDs (> DDD), use of corticosteroids, use of SSRIs, diabetes or heart failure), THEN the physician should consider giving the patient prophylaxis with either a proton-pump inhibitor in combination with a NSAID or misoprostol in combination with a NSAID. | A* |
| IF an elder had a recent TIA or a non-invalidating stroke due to AF, THEN a prophylaxis should be offered. The first-choice treatment is OA aiming at the INR range of 2.5-3.5. If there is a contraindication for OA, then aspirin 30-300 mg a day. | N* |
| Indicator                                                                 | ACOVE based (A) or New (N) |
|--------------------------------------------------------------------------|--------------------------|
| IF an elder has unstable angina or an acute MI, THEN he or she should be offered beta blocker therapy within 12 hours of presentation. | A                         |
| IF an elder admitted to a hospital has dementia complicated by a problematic behavior, THEN a pharmacologic treatment should be offered according to ‘flowchart problem behaviour’ if other non-pharmacologic interventions fail. | N'                        |
| IF an elder has established IHD AND his or her LDL cholesterol level > 2.5 mmol/l, THEN he or she should be offered cholesterol-lowering medication (statins). | A'                        |
| IF an elder has heart failure and atrial fibrillation, THEN OA should be offered to achieve an INR of 2.5 to 3.5. | A'                        |
| ALL diabetic elders with proven cardiovascular disease should be offered daily aspirin therapy (80-100 mg per day) OR ELSE an increased risk for cardiovascular complications will exist. | A'                        |
| IF a diabetic elder has an LDL level > 2.5 mmol/l, or a TC level > 4.5 mmol/l, THEN an intervention to lower cholesterol (statin) should be considered. This should be mentioned in the patient's record. | A'                        |
| IF an elder is started on or is already treated with an antidepressant medication, and an additional sleeping disorder or fear episodes are present and additional short treatment is started with benzodiazepines, THEN short t1/2 benzodiazepines should be used. Benzodiazepines with a long t1/2 (diazepam, flurazepam, flunitrazepam, clorazepate or chlordiazepoxide) should NOT be used OR ELSE there will be an increased risk of falls and fractures, respiratory depression, polyuria and incontinence (due to long half-life benzodiazepines). | N'                        |
| IF an elder has established ischemic heart disease (IHD) and is not receiving a coumarin, THEN he or she should be offered antiplatelet therapy consisting of aspirin and/or clopidogrel. | A' (+)                    |
| IF an elder has a newly reported chronic painful condition THEN treatment should be offered according to the pain scheme of the WHO pain ladder. | A' (+)                    |
| IF an elder has hypertension and has renal parenchymal disease with a lowered glomerular filtration rate (creatinine > 150 µmol/l) or microalbuminuria, THEN therapy with an ACE inhibitor or AT2 receptor blocker should be offered. | A' (-)                    |
| IF a hospitalised elder is at a very high risk for VTE (one of the following risk factors are present: heart failure, immobility, severe respiratory disease, severe acute infections, active malignancy, history of VTE, acute neurological diseases or inflammatory bowel diseases), THEN the patient should be offered venous thromboembolism prophylaxis with a LMWH UNLESS the patient is already taking coumarins or UNLESS it is contraindicated. | A' (-)                    |
| Indicator |
|-----------|
| IF an elder with chronic pain is treated with opioids, THEN he or she should be offered a laxative OR the medical record should document the potential for constipation or give an explanation why bowel treatment is not needed. |
| IF a diabetic elder has proteinuria, THEN he or she should be offered therapy with an ACE inhibitor or an AT2 receptor blocker. |
| ALL elders diagnosed with delirium and presumed vitamin B (B1 and/or B12) deficiency should be offered an adequate supplementation. |
| IF an elder has had a MI, THEN he or she should be offered a beta blocker. |
| IF an elder is admitted to the hospital with pneumonia, THEN the correct antibiotics should be administered within eight hours of hospital arrival. Check the kind of antibiotics against current local pneumonia antibiotic guidelines. |
| IF an elder is taking corticosteroids (≥ 7.5 mg prednisolone or equivalent) for more than one month, THEN the patient should be offered calcium and vitamin D AND a bisphosphonate. |
| ALL elders with repeating incidence of blood pressure > 185/95 mmHg in the chronic phase after stroke should be offered blood-pressure-lowering treatment consisting of beta blocker and thiazide diuretics as a secondary prevention. |
| IF an elder has heart failure AND left ventricular ejection fraction of 40% or less (or unknown), THEN he or she should be offered an ACE inhibitor or an AT2 receptor blocker in combination with a diuretic. |
| IF an elder had a TIA or non-invalidating stroke and no history of AF, THEN a prophylaxis should be offered. The first choice for treatment is aspirin 38-100 mg a day in combination with dipyridamole 200 mg twice daily (slow release). Both are to be given life-long. IF there is a contra-indication for aspirin, THEN clopidogrel should be given. |
| IF an elder has a new diagnosis of osteoporosis, THEN the use of calcium (when daily diet is insufficient) and vitamin D supplements (when exposure to sunlight is scarce) should be recommended. |
| IF an elder has a new diagnosis of osteoporosis, THEN the patient should be offered treatment with bisphosphonates. |
| IF an elder has heart failure and AF AND he or she has documented contra-indications to OA, THEN he or she should be offered aspirin. |
| IF a diabetic elder has proven cardiovascular disease AND a total cholesterol > 4.5 mmol/l or an LDL cholesterol > 2.5 mmol/l, THEN medical treatment (statins, aspirin, beta receptor blocker and ACE inhibitors) should be given unless contra-indicated. |
| Indicator                                                                                                                                           | ACOVE based (A) or New (N) |
|---------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| **Chapter 4.2**                                                                                                                                         |                           |
| IF an elder has an acute MI or unstable angina, THEN he or she should be given aspirin therapy within one hour of presentation (300 mg loading dose, 100 mg per day continuously). | A*                        |
| IF an elder is started on a new pharmacological antidepressant treatment during his or her hospital stay, THEN the first-line treatment should be a TCA (preferred are nortriptyline or clomipramine and NOT amitriptyline) or an SSRI (regular sodium concentration check) or venlafaxine or mirtazapine. | N*                        |
| IF an elder is diagnosed with delirium and a pharmacological intervention is needed but haloperidol is contra-indicated by Parkinson's disease or Lewy-bodies dementia or causes too many side-effects, THEN as a second-line treatment, an atypical antipsychotic (order of preference: 1) olanzapine or quetiapine, 2) risperidone, 3) clozapine or the cholinesterase inhibitor rivastigmine) can be considered UNLESS there is a known contraindication such as cardiovascular disease. | N*                        |
| IF an elder has stable heart failure AND a left ventricular ejection fraction of 40% or less, THEN a beta blocker should be offered (recommended beta blockers are carvedilol, bisoprolol and metoprolol) UNLESS the patient has a documented contra-indication (for example, uncompensated heart failure). | A*                        |
| IF an elder has valvular or congenital heart disease or an intracardiac valve prosthesis or hypertrophic cardiomyopathy or mitral valve prolapse with regurgitation or a previous episode of endocarditis AND a high-risk procedure is planned, THEN endocarditis prophylaxis should be given according to current local guidelines. | A†                        |
| IF an elder receives a diagnosis of acute ischaemic stroke during his or her hospital stay or at admission, THEN antiplatelet treatment with aspirin (loading dose of at least 160 mg aspirin) within 48 hours after the stroke should be offered and continued for at least 14 days. | A*                        |
| IF an elder receives a diagnosis of acute ischaemic stroke during hospital stay or at admission AND has blood pressure > 220-230/125-135 mmHg, THEN an intravenous treatment with blood-pressure-lowering drugs that can be titrated should be offered. | N*                        |
| IF oral pharmacological therapy is initiated to treat osteoarthritis in an elder, THEN paracetamol (acetaminophen) should be the first drug used, UNLESS there is a documented contra-indication. | A*                        |
**Domain 2. ‘Avoiding inappropriate medication’**

| Indicator                                                                 | ACOVE-based (A) or New (N) |
|---------------------------------------------------------------------------|----------------------------|
| IF an elder requires analgesia, THEN meperidine (pethidine) should not be used OR ELSE there is risk for severe confusion. | A†                        |
| IF an elder has hypertension and pharmacological antihypertensive treatment is initiated, THEN alpha-blocking agents such as doxazosin, prazosin and terazosin should not be used. | N§                        |
| IF an elder is treated for a chronic painful condition, THEN he or she should not be treated with indometacin OR ELSE there is a risk for gastropathy, neurological side effects and salt and water retention. | N*                        |
| IF an elder has cardiac arrhythmias AND therapy with an anti-arrhythmic is started, THEN disopyramide should not be used OR ELSE there could be a worsening of heart failure and fluid retention and strong anticholinergic effects. | N§                        |
| IF an elder has hypertension and asthma or COPD, THEN beta blocker therapy for hypertension should not be used UNLESS no other option remains. | A                         |
| IF an elder has dementia, THEN a long half-life benzodiazepine such as diazepam, flurazepam, flunitrazepam, clorazepate or chlordiazepoxide should not be used. | N§                        |
| IF an elder has a history of gout or an acute episode of gout, THEN a thiazide diuretic should not be prescribed to treat hypertension OR ELSE gout attacks could happen. | N§                        |
| IF an elder has a history of postural hypotension or heart block or glaucoma or urinary retention, THEN a tricyclic antidepressant should NOT be used because of the anticholinergic effects of TCAs. | N*                        |
| IF an elder has Parkinson’s disease, THEN a classical antipsychotic or metoclopramide should not be used UNLESS the patient is delirious, THEN clozapine is indicated. | N¶                        |
| An elder should not be prescribed a medication with strong anticholinergic effects IF alternatives are available OR ELSE there is a risk for acute glaucoma, urine retention, constipation and delirium. | N†                        |
| IF an elder has a cardiac, cardiovascular or cerebrovascular disease and a chronic painful condition, THEN he or she should NOT be treated with COX-2 selective NSAIDs because of an increased cardiovascular risk long-term. | N†                        |
IF an elder is admitted to a hospital for any acute or chronic illness OR for any surgical procedure, THEN the evaluation should include within one day: 1) diagnoses, 2) pre-hospital medications and 3) a current therapy plan.

IF a new drug is prescribed to an elder on an ongoing basis for a chronic medical condition, THEN the prescribed drug should have a clearly defined indication documented in the patient’s record.

IF an elder who has been prescribed an ocular therapeutic regimen becomes hospitalised, THEN the regimen should be administered in the hospital unless discontinued by an ophthalmological consultant.

IF an elder is hospitalised with heart failure or develops heart failure during hospital stay, THEN the following parameters should be measured within one day of hospitalisation or diagnosis: serum electrolytes (sodium and potassium), creatinine, blood urea, Hb, Hct, TSH and glucose.

IF an elder admitted to a hospital has dementia AND there is an acute decrease incognitive functions and worsening of behavior, THEN a diagnosis of delirium should be considered and a geriatrician should be consulted. This consultation should be noted in the patient’s record (clinical diagnosis or CAM score).

IF an elder is discharged from a hospital to his or her home or to a nursing home, THEN a discharge summary including information on medication at admission and discharge should be sent to the outpatient physician or nursing home within 14 days.
| Indicator                                                                 | ACOVE based (A) or New (N) |
|--------------------------------------------------------------------------|----------------------------|
| IF an elder is discharged from a hospital to his or her home OR to a nursing home AND he or she received a new drug (excluding temporary treatment during admission) OR a change in pre-hospital medication before discharge, THEN the GP or nursing home physician should be informed (including reasons for changes in medication and route of administration and information on dosing) by a discharge letter. | A† |
| IF an elder presents him- or herself with symptoms of cognitive dysfunction THEN the patient's medication possibly associated with these symptoms should be evaluated. Risky interactions should also be considered. This evaluation should be noted in the patient's record. | N† |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure THEN he or she should receive diagnostic screening for delirium (CAM score). This should be documented in the patient's record. | N† |
| IF an elder presents him- or herself with symptoms of delirium at admission or during his or her hospital stay, THEN the patient's medication possibly associated with these symptoms should be evaluated and risky interactions that could enhance the anticholinergic effects should also be considered. This evaluation should be noted in the patient's record. | N* |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure, THEN he or she should receive a cognitive function evaluation (MMSE score). This should be documented in the patient's record. | A† |
| IF a new drug is prescribed to an elder on an ongoing basis for a chronic medical condition, THEN the advice to evaluate the response to therapy within three months should be mentioned in the discharge letter. | A† |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure, THEN he or she should be examined for dementia AND this evaluation should be noted in the patient's record. | A† |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure, THEN he or she should be examined for depression (GDS score) AND this evaluation should be noted in the patient's record. | N† |
| ALL diabetic elders with proven cardiovascular disease should be examined for lipid metabolism disorders (TC, LDL, HDL and TG) and lab value evaluations should be noted in these patients' records. | N* |
| IF pain treatment is altered or newly begun in an elder, THEN he or she should be assessed for a response within six months AND this advice should be mentioned in his or her discharge letter. | A# |
| Indicator | ACOVE based (A) or New (N) |
|-----------|---------------------------|
| If an elder is admitted to a hospital after a fall incident or has a fall incident during his or her hospital stay, THEN the patient's medication should be screened for drugs that are associated with increased incidence of falling (hypoexcitants, tranquillizers, long acting benzodiazepines, antidepressants, sedatives and antipsychotics AND this evaluation should be noted in the patient's record. | N⁺ |
| If the attending physician suspects that an elder is depressed or has a depressive episode, THEN a geriatrician or psychiatrist should be consulted AND the medical record should document the symptoms and grade of severity and whether medication is started or not, and why. | A⁺ |
| If an elder has newly diagnosed heart failure, THEN left ventricular ejection fraction should be evaluated during his or her hospital stay. | A⁺ |
| If an elder admitted to a hospital receives a diagnosis of dementia OR has dementia diagnosed previously, THEN the patient's medication that possibly caused or worsened dementia-like symptoms should be evaluated (drugs with anticholinergic effects) AND this evaluation should be noted in the patient's record. | A⁺ N⁺ |
| If an elder has newly diagnosed heart failure, THEN left ventricular ejection fraction should be evaluated during his or her hospital stay. | A⁺ |
| If an elder admitted to a hospital receives a diagnosis of dementia OR has dementia diagnosed previously, THEN the patient's medication that possibly caused or worsened dementia-like symptoms should be evaluated (drugs with anticholinergic effects) AND this evaluation should be noted in the patient's record. | A⁺ N⁺ |
| If an elder has a new diagnosis of osteoporosis, THEN during the initial evaluation period, an underlying cause of osteoporosis should be sought by checking medication use and current alcohol use AND this should be noted in the patient's record. | A# |
| If an elder is started in-hospital on chronic coumarin treatment, THEN there should be an evaluation of the risk factors for bleeding during therapy before the patient is discharged AND the evaluation should be reported in the patient's record and at discharge to the GP. | N⁻ |
| If an elder is admitted to a hospital and after evaluation it is stated that there is no meaningful symptom response after four to six weeks of pharmacological antidepressant treatment begun in the outpatient setting, THEN one of the following should be initiated: the diagnosis should be reconsidered OR precipitating factors evaluated OR concordance should be evaluated OR the medication dosage should be optimized OR TDM should be performed (if applicable) OR the patient should be referred to a psychiatrist or psychotherapy should be offered. | A⁻ |
| If an elder with a history of cardiac disease is started on a TCA, THEN baseline electrocardiography should be performed before initiation of or within three months before treatment. | A |
| If an elder has a presumed stroke during his or her hospital stay or at admission, THEN a CT or an MRI of the head should be obtained before the initiation or continuation of thrombolytic treatment (r-TPA), OA, or antiplatelet therapy (aspirin, dipyridamole, clopidogrel). | A" |
| If oral pharmacological therapy for osteoarthritis in an elder is changed from paracetamol (acetaminophen) to a different oral agent, THEN there should be evidence that the patient has had a trial of maximum dose of paracetamol (suitable for age and co-morbid conditions. | A⁺ |
## Domain 4. ‘Monitoring of Medication’

| Indicator | ACOVE based (A) or New (N) |
|-----------|----------------------------|
| **IF an elder is newly started on a diuretic for chronic use, THEN during hospital admission, serum potassium and creatinine levels should be checked.** Within one month after discharge and yearly thereafter these parameters (potassium and creatinine) should be checked again. This advice should be mentioned in the discharge letter. | A* |
| **IF an elder begins receiving an ACE inhibitor, THEN serum potassium and creatinine levels should be checked within one month of initiation of therapy and thereafter yearly AND this advice should be mentioned in the discharge letter.** | A⁺ |
| **IF an elder uses a maintenance dose digoxin, THEN the maximal dosage per day is 0.125 mg UNLESS a lower dosage has previously been insufficiently effective for the patient AND TDM has shown therapeutic blood levels at this high dosage.** | N† |
| **IF an elder has an INR higher than the advised range (depending on the indication), THEN the possible causes of this elevation including interacting medications should be evaluated AND the coumarin dosage adjusted until the INR returns to within the therapeutic range.** | N⁺ |
| **IF an elder is newly prescribed a coumarin, THEN an INR should be determined by at least five to seven days after initiation, in-hospital or by the thrombosis service. The patient should be enrolled in the program of the thrombosis service AND this should be mentioned in the patient’s records.** | A‡ |
| **IF an elder is started on a new SSRI antidepressant treatment during his or her hospital stay, THEN evaluation of sodium levels should be performed by the prescribing physician (minimum once during hospital stay) OR should be continued after discharge by a GP (yearly) OR ELSE hyponatraemia could occur.** | N* |
| **IF an elder is started on a new pharmacological antidepressant treatment during hospital stay, THEN a frequent evaluation of effectiveness and side effects should be performed during the first four weeks of treatment (every week) by the prescribing physician OR IF the patient leaves hospital before this term, THEN this advice should be stated in the discharge letter.** | N* |
| **IF an elder uses an OA (acenocoumarol or fenprocoumon) AND also cotrimoxazole OR cefomandole OR metronidazole OR miconazole OR fluconazole OR itraconazole OR ketoconazole OR voriconazole, THEN INR should be monitored at least every week during concomitant use OR ELSE INR could rise and haemorrhagic events could result.** | N§ |
* : based on Dutch national guidelines. †: based on expert opinion. ‡: based on a combination of expert opinion and Dutch national guidelines. §: based on literature on inappropriate medication for elderly. ¶: based on a combination of literature on inappropriate medication for elderly and expert opinion. #: minor textual changes

AF=atrial fibrillation; AT2 antagonist=angiotensin II type 1 receptor antagonist; CAM=confusion assessment method; COPD=chronic obstructive pulmonary disease; COX-2=cyclooxygenase-2; CT=computed tomography; DDD=defined daily dose; GDS=Geriatric Depression Scale; GP=general practitioner; Hb=haemoglobin; Hct=haematocrit; IHD=ischaemic heart disease; HDL=high-density lipoprotein; INR=international normalized ratio; LDL=low-density lipoprotein; LMWH=low-molecular-weight heparin; MI=myocardial infarction; MMSE=Mini-Mental State Examination; MRI=magnetic resonance imaging; NSAID=nonsteroidal anti-inflammatory drug; OA=oral anticoagulation; SBP=systolic blood pressure; SSRI=selective serotonin reuptake inhibitor; t1/2=half life; TIA=transient ischaemic attack; TC=total cholesterol; TCA=tricyclic antidepressant; TDM=therapeutic drug monitoring; TG=triglyceride; TSH=thyroid stimulating hormone; VTE=venous thromboembolism.
4.3 Assessing quality of care of elderly patients using the ACOVE quality indicator set:

A systematic review

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PLoS One. 2011; 6(12): e28631
Abstract

Background: Care of the elderly is recognized as an increasingly important segment of health care. The Assessing Care Of Vulnerable Elderly (ACOVE) quality indicators (QIs) were developed to assess and improve the care of elderly patients.

Objectives: The purpose of this review is to summarize studies that assess the quality of care using QIs from or based on ACOVE, in order to evaluate the state of quality of care for the reported conditions.

Methods: We systematically searched MEDLINE, EMBASE and CINAHL for English-language studies indexed by February 2010. Articles were included if they used any ACOVE QIs, or adaptations thereof, for assessing the quality of care. Included studies were analyzed and relevant information was extracted. We summarized the results of these studies, and when possible generated an overall conclusion about the quality of care as measured by ACOVE for each condition, in various settings, and for each QI.

Results: Seventeen studies were included with 278 QIs (original, adapted or newly developed). The quality scores showed large variation between and within conditions. Only a few conditions showed a stable pass rate range over multiple studies. Overall, pass rates for dementia (interquartile range (IQR): 11%–35%), depression (IQR: 27%–41%), osteoporosis (IQR: 34%–43%) and osteoarthritis (IQR: 29–41%) were notably low. Medication management and use (range: 81%–90%), hearing loss (77%–79%) and continuity of care (76%–80%) scored higher than other conditions. Out of the 278 QIs, 141 (50%) had mean pass rates below 50% and 121 QIs (44%) had pass rates above 50%. Twenty-three percent of the QIs scored above 75%, and 16% scored below 25%.

Conclusions: Quality of care per condition varies markedly across studies. Although there has been much effort in improving the care for elderly patients in the last years, the reported quality of care according to the ACOVE indicators is still relatively low.
Introduction

The elderly population forms a precarious group characterized by multimorbidity, frailty and polypharmacy, leading to more complex care\cite{1,2}. Studies have shown that elderly patients do not receive the care that is known to be appropriate for them\cite{3,4}. It is postulated that there is much room for improvement of the quality of care for this group\cite{5}.

Efforts have been made to explore where, when and for which conditions quality deficiencies exist in order to know where improvements are needed. Measurement sets like HEDIS, with 75 measures across eight domains of care, have been developed to assist in assessing the quality of care. In addition criteria such as the Beers criteria were suggested to map the use of inappropriate medication for the elderly\cite{6,7}. The Assessing Care of Vulnerable Elders (ACOVE) quality indicator (QI) set was developed in the year 2000 by Rand Healthcare and the UCLA\cite{8,9} as a comprehensive method for assessing the quality of care of vulnerable elderly patients. Iterative expert panel meetings with review of the relevant evidence were used to generate a set of indicators to assess the quality of the process of care, rather than outcomes. RAND researchers postulate that these QIs represent minimal care rather than optimal care for the vulnerable elderly population, and are meant to assess and ultimately improve the quality of care\cite{8,9}. The resulting set consists of explicitly phrased IF-THEN clinical rules with comprehensive coverage of general medical and geriatric conditions, including comorbidities. These rules are intended to evaluate, by means of gauging adherence to the rules, the extent to which the care being delivered meets minimal standards of quality. The following is an example of an ACOVE indicator (or rule): “IF a vulnerable elder reports a history of two or more falls (or one fall with injury) in the previous year, THEN there should be documentation of a basic fall history (circumstances, medications, chronic conditions, mobility, alcohol intake) within three months of the report (or within four weeks of the report if the most recent fall occurred in the previous four weeks”). ACOVE-1 represents the first original set of QIs. The second phase of ACOVE (ACOVE-2) aimed at evaluating various interventions in primary care practices in order to improve care, but the QI set was not changed. The ACOVE-3 QI set is an updated and expanded set of QIs including five new conditions: COPD, colorectal cancer, breast cancer, sleep disorders, and benign prostatic hypertrophy.

Because ACOVE QIs or adaptations thereof have been used for over a decade for the assessment of quality of care, the opportunity now exists to synthesize the available evidence for the quality of care of a multitude of conditions in various settings. This paper reviews the studies that assessed the quality of care for elderly patients using
ACOVE (-based) QIs in order to evaluate the state of the quality of care for the reported conditions.

Methods

Data sources and searches

Studies were identified by searching MEDLINE (via Scopus and PubMed), CINAHL and EMBASE by using the following search query: ACOVE OR (“assessing care” AND (vulnerable OR frail*))

Study Selection and Data Extraction

Relevant articles were included which used ACOVE QIs or adaptations of ACOVE QIs to assess the quality of care, and were published in the English language after the introduction of the ACOVE-I set in 2001. Opinion papers, editorials, letters and congress abstracts were excluded. The last search was performed at the beginning of February 2010. Two reviewers (MA, PW) independently examined the collected studies in two rounds. The first round consisted of critically reading the title, abstract, and keywords. Studies selected in the first round had the full text reviewed in the second round. In the second round, we carefully checked the objectives of the studies and included those papers that used the ACOVE QIs (set 1, 2 or 3) or adaptations of those QIs to assess the quality of care of elderly patients. One investigator screened citations to identify additional candidate articles. In each round, disagreements between the two reviewers were resolved by consensus. If the two reviewers were unable to reach consensus a third reviewer was involved (AA) to make a final decision. Inter-rater agreement was measured by Cohen's kappa. Using a structured extraction form, the two reviewers independently extracted the following information from the included studies: study characteristics (e.g., author, type of study, year), objectives, results, conclusion, QIs used, and conditions assessed by the QIs (see appendix S1 and checklist S1).

Data Analysis and Synthesis

The results and conclusions of the included studies were evaluated to gain an overall picture of the quality of care for the elderly as measured by the ACOVE QIs. When possible, the results of the studies were combined, e.g. by extracting QI pass rates in each setting for each condition.

We analyzed the data at three levels: (1) conditions across studies, (2) conditions within
distinct settings in studies, and (3) QIs across studies. At level (1), we extracted for each condition the reported QI-pass rates from each study. We then reported the low- and high-scoring conditions irrespective of setting. Interquartile ranges were provided where it was possible to do so (when more than four numbers were available).

To identify the proportion of high-scoring QIs per condition we also calculated the number and proportion of unique QIs with a mean score above 50% for each condition among all studies addressing that condition. For similar QIs among studies, their pass rates were first averaged. For example, consider two studies, one applying four QIs and the other three QIs for the same specific condition, of which two QIs are identical. We first average the pass rates for each of the two common QIs and obtain in total five pass rates for the unique QIs for the given condition in the two studies. Suppose that the (mean) scores of these QIs were 30%, 35%, 40%, 55%, and 60%, then we have a proportion of two out of five QIs with a mean score above 50%. We considered two QIs as similar if they appeared to have an identical or comparable content or intent. Our matching criteria allowed for differences in targeted patient population, time frame, level of specification and small textual differences in the QI contents. The most important differences in the phrasing of QIs are highlighted in the available supplemental table S1. In the case of interventional studies, we used the QI scores of the control group for this analysis.

At level (2) the dimension of a setting was added to the analysis, to increase homogeneity between them. Specifically, we considered conditions in the same setting among the various studies. We identified per setting all conditions that had a mean score <35% or >65% in any study. This helps focus attention to the low and high scoring conditions per setting.

At level (3) we synthesized evidence for QIs regardless of study or setting. For each QI we obtained its mean score (i.e. mean pass rate) across studies. Then we calculated the percentage of QIs having mean score below or above 50% (and below 25% and above 75%).

The list of all QIs used in the included studies was compared to the complete list of the original ACOVE-1 QIs in order to identify QIs that were not assessed in any included study.
Results

The database search resulted in 347 articles. Screening the titles and abstracts yielded 45 candidate articles for inclusion, of which 17 were included after full-text review\cite{10–26}. Figure 1 (Diagram S1) shows the article selection flow diagram. Inter-rater agreement was high with Kappa of 0.76, where only five papers (5/347, 1%) necessitated the involvement of the third reviewer. Screening of the bibliographies yielded no additional studies for inclusion.

Study characteristics

Nine of the seventeen studies (53%) assessed the overall quality of care or focused on a specific domain of care. Eight studies assessed care for a specific condition. Table 1 shows the study domains (“Overall quality of care”, “Specific domain of care”, and “Specific condition”).

Eight studies used the original ACOVE QIs\cite{12,14,16,20–23,26}, all referring to the ACOVE-I set, of which one\cite{26} was performed during the second phase of ACOVE. The remaining nine studies used an adaptation of ACOVE QIs or newly developed ACOVE-like QIs\cite{10,11,13,15,17–19,24,25}.

Fifteen out of seventeen studies (88%) were done in the US and two studies were done in Europe (one in Belgium and one in the UK). Four studies\cite{12,20,22,23} used the same data sample as the study by Wenger et al.\cite{21}. Three of them\cite{20,22,23} used different QIs or a different number of QIs than those used by Wenger et al. The differences are marked in the supplemental table S1. The QIs in these four studies that overlapped with the Wenger et al. study sometimes had small differences in the pass rates, as compared to those reported in Wenger et al., perhaps related to how eligibility for QIs was determined. We treat these studies as dependent, meaning that the QIs in those studies are counted only once in the analysis. The population in the included studies ranged from age 50 and older, to age 75 and older. All but three studies\cite{13,17,19} included only patients aged 65 and older. Vulnerable elderly patients were the explicit target population in only six studies, five of which used the same patient sample, as described in the previous paragraph.

Quality of care

Table S2 shows the pass rates and number of QIs for all of the specific conditions. The number of QIs used per study ranged between three and 207, and between one to 43.
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QIs per condition or domain of care (e.g. pharmacological care). The quality of care for each condition varied greatly in the included studies. Furthermore, when the quality of care for a single condition was assessed in multiple studies, this was also highly variable. Only few conditions showed a stable range of pass rates over multiple studies. Overall, the quality scores for dementia (interquartile range: 11%–35%), depression (interquartile range: 27%–41%), osteoporosis (interquartile range: 34%–43%) and osteoarthritis

**Figure 1.** Article selection flow diagram – QoC: Quality of Care.
Quality of elderly care based on the ACOVE set

(Interquartile range: 29–41%) were notably low, regardless of setting. Medication management and use (range: 81%–90.30%), hearing loss (range: 77%–78.9%) and continuity of care (range: 76%–80%) on the other hand, scored relatively higher than other conditions.

From the seventeen studies, four studies focused on nursing home residents\textsuperscript{[10,11,18,25]}, five on managed care plans\textsuperscript{[12,20–23]}, two on patients admitted to hospital\textsuperscript{[14,24]} and four on primary care patients\textsuperscript{[15,17,19,26]}. Two studies had mixed settings\textsuperscript{[13,16]}. Because only one or two studies within a setting assessed the same condition, calculating a mean per setting for each condition was not meaningful, hence we report the score of the corresponding studies. Table 2 shows the high and low scoring conditions within each setting.

| Domain name                  | References                  | Overall quality of care | Specific domain of care | Specific condition |
|------------------------------|-----------------------------|-------------------------|-------------------------|--------------------|
| Geriatric care               | Zingmond DS et al.\textsuperscript{[15]} | X                       |                         |                    |
| Quality of hospital care     | Steel N, et al.\textsuperscript{[17]} | X                       |                         |                    |
| Pharmacologic care           | Wenger NS, et al.\textsuperscript{[21]} | X                       |                         |                    |
| Pharmacologic care           | Zingmond DS, et al.\textsuperscript{[25]} | X                       |                         |                    |
| Pharmacologic care           | Wenger NS, et al.\textsuperscript{[26]} |                         |                         |                    |
| Geriatric care               | Arora VM, et al.\textsuperscript{[24]} |                         |                         |                    |
| Pharmacologic care           | Mikuls TR, et al.\textsuperscript{[19]} |                         |                         |                    |
| Pharmacologic care           | Higashi T, et al.\textsuperscript{[23]} |                         |                         |                    |
| Appropriateness of prescribing or underuse | Spinewine A, et al.\textsuperscript{[14]} |                         |                         |                    |
| Management and detection of pain | Cadogan MP, et al.\textsuperscript{[11]} |                         |                         |                    |
| Management and detection of pain | Chodosh J, et al.\textsuperscript{[22]} |                         |                         |                    |
| Falls and instability        | Rubenstein LZ, et al.\textsuperscript{[12]} |                         |                         |                    |
| Congestive heart failure care| Asch SM, et al.\textsuperscript{[13]} |                         |                         |                    |
| Osteoarthritis               | Ganz DA, et al.\textsuperscript{[16]} |                         |                         |                    |
| Pressure ulcer care          | Bates-Jensen BM, et al.\textsuperscript{[18]} |                         |                         |                    |
| Urinary incontinence         | Schnelle JF, et al.\textsuperscript{[10]} |                         |                         |                    |
| Urinary incontinence         | Gnanadesigan N, et al.\textsuperscript{[20]} |                         |                         |                    |

Table 1. Study domains (“Overall quality of care”, “Specific domain of care”, and “Specific condition”).
Chapter 4.3

In the hospital setting, the quality of care for falls was higher than in other settings. Diabetes scores were average in all settings; nevertheless the score in the UK primary care setting was higher than in other health care settings. In the only study in the primary care setting of the UK, the pass rates for ischemic heart disease, diabetes, depression, hypertension, osteoporosis, urinary incontinence, stroke and vision care were all higher than in the US. There were three studies in primary care in the US, 

| Settings           | Low scoring conditions          | High scoring conditions          |
|--------------------|---------------------------------|----------------------------------|
| Nursing home       | Dementia (9%)                   | Medication management (90%)     |
|                    | Depression (16%)                | End-of life care (89%)          |
|                    | Stroke (20%)                    | Malnutrition (77%)              |
|                    | Ischemic heart disease (22%)    |                                  |
|                    | Heart failure (23)              |                                  |
|                    | Osteoarthritis (26 and 26%—46%)|                                  |
|                    | Osteoporosis (27%)              |                                  |
| Managed care settings | End-of-life care (9%)        | Stroke (82%)                     |
|                     | Osteoarthritis (31%)            | Medication use (81%)             |
|                     | Depression (31%)                | Continuity of care (80%)         |
|                     | Falls (34%)                     | Vision (79%)                     |
|                     | Hypertension (77%)              |                                  |
|                     | Hearing loss (77%)              |                                  |
|                     | Heart failure (71%)             |                                  |
|                     | Screening & prevention (67%)    |                                  |
| Primary care       | Osteoarthritis (29%)            | Medication management (83%)     |
|                    | Pain management (78%)           |                                  |
|                    | Hearing loss (79%)              |                                  |
|                    | Continuity of care (76%)        |                                  |
|                    | Smoking (74%)                   |                                  |
|                    | Diabetes (74%)                  |                                  |
|                    | Hypertension (72%)              |                                  |
|                    | Stroke (65%)                    |                                  |
| Hospital           | Dementia (31%)                  | Falls (83%)                      |
|                    | Hospital care (82%)             |                                  |

Table 2. High and low scoring conditions within each setting.
which used a range of three to 43 QIs to measure quality of care in one to 22 conditions, while the single UK study used 32 QIs for 12 conditions. Therefore, in terms of numbers of QIs, more QIs were used in the US studies than in the UK study.

Results per QI

Table 3 shows the QIs that were most frequently used (more than four times), regardless of setting. For the sake of brevity, Table 3 uses an abbreviated version of the QIs. The supplemental table S1 shows the full text of QIs used in all studies.

When comparing the QIs that were used with the entire original ACOVE-1 QI set, we found that 35 ACOVE-1 QIs were not used in any of the studies. All QIs for 10 conditions (diabetes, falls, hypertension, ischemic heart disease, osteoarthritis, osteoporosis, pain management, pressure ulcers, preventive care and urinary incontinence) were used in at least one study. The 35 unused QIs were distributed among the 14 remaining conditions, with a range of 7% (one out of 14 heart failure QIs) to 44% (four out of nine QIs for hospital care), and a median of 28% unused QIs within a condition. The list of the 35 QIs is provided in the supplemental table S1.

Table 3. Most frequently used QIs.

| Quality indicators | Number of unique times that QI was used |
|--------------------|----------------------------------------|
| IF analgesia required THEN NOT meperidine | 4 [11,15,21,25] |
| IF heart failure and LV ejection fraction ≤40% THEN ACE inhibitor or receptor blocker | 4 [13,14,21,25] |
| IF newly diagnosed dementia THEN measure vitamin B12 and thyroid-stimulating hormone | 4 [15,21,25,26] |
| IF depression, THEN antidepressant treatment, psychotherapy, or electroconvulsive therapy within 2 weeks | 4 [15,17,21,25] |
| IF diabetes THEN yearly HbA1C | 4 [15,17,21,25] |
| IF new heart failure THEN evaluation of LV ejection fraction | 4 [13,15,21,25] |
| IF established CHD and LDL cholesterol level >130 mg/dL THEN cholesterol-lowering medication | 4 [13,15,21,25] |
| IF female has a new diagnosis of osteoporosis, THEN hormone replacement therapy, bisphosphonates, a selective estrogen receptor modulator or calcitonin within 3 months | 4 [15,17,21,25] |

VE: Vulnerable elderly; CHD: Chronic heart disease; LDL: Low density lipoprotein; LV: Left ventricular.
From the 278 QIs that were used in the included studies (original, adapted or newly developed for the new conditions) 16% (46 QIs) scored below 25%, 50% (141 QIs) had mean pass rates below 50%, 44% (121 QIs) above 50% and 22% (62 QIs) above 75%. Sixteen QIs were reported in the included studies as having no eligible patients, therefore the pass rates could not be calculated.

Table S2 reports on the number of QIs used in the studies that had pass rates above 50%. Seventy-five percent of the QIs pertaining to medication management, hearing loss and continuity of care scored above 50%, making them the highest-scoring conditions.

Discussion

In this systematic review we described the results of 17 research papers using the ACOVE quality indicators to assess the quality of care. The assessment of care was performed in a variety of care settings, in several different elderly patient populations and for multiple conditions. Due to this heterogeneity and the fact that the studies used different subsets of the ACOVE QIs or adaptations thereof, the results of the studies cannot be directly compared and hence a quantitative meta-analysis is not justified. However, considering that many studies assessed the quality of care for multiple conditions simultaneously and 50% of the QIs had a pass rate below 50%; some general conclusions can be drawn about areas to which improvement initiatives should be focused. An overall conclusion is that there is much room for care improvement for the elderly population. Individual studies have already shown the need for greater focus on elderly care.\cite{5,27,28} This finding is supported by our review. Based on the included studies the overall quality scores for dementia, depression, osteoporosis and osteoarthritis were notably low. In addition to the conditions above, hypertension, ischemic heart disease, pressure ulcer, pain management, falls and urinary incontinence scored below 50% at the QI level.

In the interest of maintaining a good quality of life for elderly patients it is very important to treat geriatric conditions, and it may even be unethical to ignore this need. Although care for many conditions showed deficiencies, geriatric conditions like dementia and falls seem to show greater deficiencies than others. This may be due to less attention to and awareness of the need for good treatment of age-related and geriatric conditions, or poor identification of these conditions.\cite{29–32} The deficiencies may also be caused by insufficient teaching of the skills and expertise needed to perform these processes of care.\cite{33} This review cannot conclude which factors are more influential, and future studies are needed to uncover the reasons why some QIs have low pass rates. On
the other hand, medication management and use, hearing loss and continuity of care, scored markedly higher than other conditions regardless of the setting and patient population and regardless of which QIs were used to assess them. This could be due to the increased attention to medication management in general, or partly attributable to chance due to the relatively low number of studies including these conditions. Although based on only one study, quality of care for falls in the hospital setting scored markedly higher than in other settings. This difference may be explained by fewer QIs being used in the hospital study and differences in the QIs that were used in the individual studies, or by increased attention to falls in hospitals and the more intensive care given to hospitalised patients compared to other settings. There was only one UK study in the primary care setting compared to three US studies. Although different QIs were used, the care for ischemic heart disease, diabetes, depression, hypertension, osteoporosis, urinary incontinence, stroke and vision care had better quality in the UK primary care setting compared to the US. It is plausible that this is due to differences in diagnoses and treatment of these conditions between the countries, or a different prevention program. This finding does not warrant general conclusions about the differences in quality of care between the countries, and more studies are needed.

Although comparison of scores per setting was based on limited studies and QIs, it may reveal the need for extra attention to the conditions that form good candidates for quality improvement. These are the conditions that had mean scores below 50%. In managed care settings these conditions are: osteoarthritis, depression, urinary incontinence (UI), falls, dementia, end-of life care, malnutrition, pressure ulcer care, and pneumonia care. In nursing homes, dementia, depression, diabetes, falls, stroke, ischemic heart disease, heart failure, osteoarthritis, osteoporosis, atrial fibrillation, vision and hypertension had consistently low scores. Finally, in primary care, dementia, UI, falls, osteoarthritis and vision care show room for improvement.

According to the ACOVE indicators and the studies identified by our review, it appears that the quality of care for the elderly is low. However, we can only draw limited conclusions from these studies, for several reasons. First, although the QIs are generally evidence–based and have been developed in multiple Delphi rounds using expert panels, it is still possible that individual physicians will debate the content of specific QIs. Although the QIs are conjectured to represent minimal care, it is possible that low pass rates may represent legitimate differences of medical opinion. Second, undocumented patient refusal of the offered care could lead to a lower measured pass rate. Various studies, however, have taken this aspect into account and counted an indicator as passed when a patient refused the indicated care or when a contraindication existed. Third, identifying the vulnerable elderly (VE) is difficult and, probably due to this difficulty, the majority of the studies did not distinguish between the vulnerable
elderly and the general elderly population. Since ACOVE was designed for a vulnerable elderly population, this can lead to a biased score. Fourth, the reason for selecting a certain number and type of QIs for the assessment of care for a specific condition was not always clearly described in the studies. Difficulty in the assessment of some of the QIs could have lead to omitting these QIs from the assessment of that condition and consequently to selection bias. This can result in an incomplete picture of the quality of care of patients for the specific condition. Poor record-keeping can influence, positively or negatively, the pass rates of various QIs. It is plausible that correct care was performed but not documented, which can lead to lower pass rates. On the other hand, poor-record keeping for the “IF” part of a rule renders the rule as inapplicable and hence failure to provide the correct care will go undetected. Irrespective of the ability to measure QI pass rates, lack of documentation can be an indicator of poor quality because it hampers continuity of care and contributes to miscommunication. Fifth, variation in scores of quality of care could be caused by either variation in the number of QIs used per study or by the fact that QIs focused on different aspects of care for a specific condition. Moreover, variation in the study sample sizes can cause differences in the pass rates per condition. A smaller study population gives more opportunity for chance findings. We suggest that future studies should explicitly mention and discuss these factors.

To our knowledge, this is the first review on assessing quality of care of elderly patients using the ACOVE criteria. Although our literature search has been systematic and extensive in order to give a complete overview of the studies using ACOVE for assessing the elderly population care, it is still plausible that some articles were missed.

Conclusion and recommendation

Our results showed that despite the large efforts that have been expended in improving the care for elders in the last years, quality of care for elderly patients as measured by the ACOVE criteria is still poor. This is particularly worrisome as the ACOVE criteria are meant to represent a minimal standard of care for the vulnerable elderly population, although not all of the included studies included a measure of vulnerability in their inclusion criteria. The majority of the assessed conditions and domains of care seem to merit further quality improvement effort and/or a better understanding of why some QIs have low pass rates.

The ACOVE QI set provides a promising and uniquely comprehensive method for assessing the quality of care of elderly patients. However, to improve the extent to which studies can be compared, two important factors should be taken into consider-
ation. First, researchers should strive to assess all QIs for a domain of interest, instead of a small selection thereof. This is especially important because there may be an association between ease of measuring a QI and its score. Second, should one require the adaptation of original QIs, then one should measure the same underlying concept implied by the original QIs and explicitly report on the nature of the adaptation.

Supporting Information

Table S1 QI: quality indicator; *: No patients were eligible for the premise of the QI. Co: condition. Note: we rounded the percentages. †: QIs that were scored in a study, using the Wenger data set. ‡: QIs that had different pass rates than in Wenger et al. study. ††: Those QIs that were scored in the studies using the same data set as Wenger et al, but were not scored in Wenger. -: The QIs that were not used in any study.

Table S2 Measured mean pass rate of QIs per condition and proportion of unique (matched) QIs with mean score above 50% per condition. ‡: The pass rate is reported for both delirium and dementia. †: These QIs were about physical functioning. QI: quality indicator, VE: vulnerable elder(s), NH: Nursing home, PC: Primary care, PIM: Prescribing indicated Mediations, AIM: Avoiding Inappropriate Medication, ECD: Education, Continuity, and Documentation, MM: Medication Monitoring, GEM: Geriatric Evaluation and Management, CHF: Chronic Heart Failure, IHI BTS: Institute of Healthcare Improvement’s Breakthrough Series, PC: Primary Care. *: The same patient population and dataset was used as in the Wenger et al. study [21], for these common QIs we only considered the pass rates reported in [21] for our analysis.

Appendix S1 Table of extracted data. ACOVE: Assessing Care Of Vulnerable Elders; VE: Vulnerable Elder; NH: Nursing Home; QoC: Quality Of Care; QI: Quality Indicators; IHI BTS: Institute of Healthcare Improvement’s Breakthrough Series; CHF: Chronic Heart Failure; GEM: Geriatric Evaluation and Management; MAI: Medication Appropriateness Index; DM: Diabetes Mellitus; PU: Pressure Ulcer; MDS: Minimum Data Set; CI: Cognitive Impairment; UI: Urinary Incontinence; PIM: Prescribing Indicated Medication; AIM: Avoiding Inappropriate Medication; ECD: Education, Continuity, and Documentation; MM: Medication Monitoring; QoL: Quality of Life; RA: Rheumatoid Arthritis; AF: Atrial Fibrillation; OA: Osteoarthritis; 1:# =Number of quality indicators used.
Author Contributions

Conceived the preliminary study design: AA MA. Carried out the literature search: MA PW. Performed acquisition of the data: MA SE PW SM. Performed examination and analysis of the data: MA SE. Supervised and integrated the whole work: AA. Drafted the manuscript: MA. Participated in the design of the paper, the regular discussions, and read and approved the final manuscript: MA PW SE SM SdR AA.

Funding: This work was supported by ZonMw (The Netherlands Organization for Health Research and Development) by grants for the PROFIT (#300020010) and ICOVE (#311020302) projects. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

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## Appendix S1: table of extracted data

| Author(s)         | Study population (n) | Study design/ Period/ Setting | Objectives                                                                 |
|------------------|----------------------|-------------------------------|-----------------------------------------------------------------------------|
| Schnelle et al. [10] (2003) | 426 incontinent residents | Descriptive 18 NHs 50-200 beds each (US) | Demonstrate reliability and feasibility of a protocol to assess urinary incontinence in NHs |
| Cadogan et al. [11] (2005) | 542 NH residents | Descriptive 38 NHs (50-200 beds each) (US) | Demonstrate reliability and feasibility of a protocol to assess pain management in NHs and assess pain management quality |
| Rubenstein et al.[12] (2004) | 372 VEs | Retrospective observational cohort study(13-month) 2 senior health care plans each with more than 20,000 enrollees (US) | Investigate quality of care for falls and instability |
| Asch et al.[13] (2005) | 489 patients | Retrospective quasi experimental study 4 organizations participating in IHI BTS for CHF and 4 compatible comparison organizations (US) | Compare differences in indicator performance between baseline and post intervention periods for participating and nonparticipating organizations to evaluate the effects of the IHI BTS on QoC for chronic heart failure (CHF) |
| Results                                                                 | Conclusions                                                                 | # QIs used | Conditions                                      | Source of information                                      |
|------------------------------------------------------------------------|-----------------------------------------------------------------------------|------------|------------------------------------------------|-----------------------------------------------------------|
| High inter-rater agreement on scoring the QIs which facilitates replication (kappa 0.75 to 1.0); All NHs failed to document assessment for scheduling toileting | 1 to 2 days training in protocol is believed to be sufficient. Retrieval of archived data is costly. Good inter-rater reliability has been achieved | 9          | Urinary Incontinence care                       | Medical records and interviews                              |
| Excellent inter-rater reliability (kappa 0.65-1.00 and percentage agreement was 0.8-1.0). Pass rates: 10-99% | QIs can be reliably scored. Targeting residents with self-reported pain maximizes efficiency of the scoring system | 12         | Pain management and osteoarthritis              | Medical records and interviews                              |
| Of the 372 VEs, 57 had documentation of 69 episodes of 2 or more falls or fall with injury. Double this frequency was reported at interview, 47% of medical records of fallers consisted of: history of fall circumstances, co-morbidity, medications and morbidity. 85% documented 2 or more of the 4 elements. Documented physical examination was less complete. Recommendations were given in only 26% of cases | Community physicians seem to under-detect falls and gait disorders. Detected falls often receive inadequate evaluation. | 8          | Falls and instability                           | Medical records (including administrative data) and patient interview by telephone. Administrative data |
| Participating organizations showed greater improvement for 11 of 21 indicators. All indicators combined: participating sites improved more than controls (17% vs 1% p< .0001) Reliability: kappa 0.64 -0.78 for QI assessment | Organizations that participated in a disease-targeted collaborative provider interaction significantly improved counseling and education rates for CHF patients | 23         | Congestive heart failure                       | Medical records                                             |
| Author(s)                  | Study population (n)                  | Study design/ Period/ Setting                                      | Objectives                                                                                                                                                                                                 |
|---------------------------|----------------------------------------|-------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Spinewine et al.[14] (2007) | 203 patients aged >70                | RCT with patients as unit of randomization 27 Acute GEM unit (Belgium) | To evaluate the effect of pharmaceutical care provided in addition to acute GEM care on the appropriateness of prescribing, using a protocol                                                                 |
| Zingmond et al.[15] (2007)  | 100528 patients                      | Observational cohort study(2 year) Community-dwelling dual enrollees in Medicare and Medicaid, living in 19 California Counties (US) | To assess the applicability of process of care measures developed as part of ACOVE that were adapted previously for use with administrative data. To measure the QoC in community —dwelling VE.                                                                 |
| Ganz et al. [16] (2006)     | 339 elderly (>75 yrs) arthritis patients | Observational cohort study (13-months) Subgroup of 2 medical groups. One primary care group and one specialty group (US). | To describe the quality of osteoarthritis care provided to community-dwelling elderly patients and to characterize arthritis-related function in these patients                                                                 |
| Steel et al. [17] (2008)   | 8688 participants in the English longitudinal study of ageing, of whom 4417 reported diagnoses of one or more of 13 conditions | Observational cohort study Private households (UK) | To assess the receipt of effective healthcare interventions in England by adults aged 50 or more with serious health conditions                                                                 |
### Quality of elderly care based on the ACOVE set

| Results | Conclusions | # QIs used | Conditions | Source of information |
|---------|-------------|------------|------------|-----------------------|
| Intervention patients had improvement in MAI and ACOVE underuse criteria from admission to discharge (OR: 9.1, 95% CI 4.2-21.6) | Pharmaceutical care in context of acute GEM improved appropriate use of medicine during hospital stay and after discharge | 7 | 7 underuse criteria, focusing on osteoporosis/fracture, atrial fibrillation, ischemic heart disease, diabetes mellitus, heart failure, myocardial infarction | Medical records and interviews |
| 43/230 QIs were captured, overall QI pass rate was 65% (100528 patients with 930753 QIs, 9.3 QI/person) | The use of claims data-derived QoC process measures is feasible for the vulnerable older population but requires development of data elements focus on geriatric care | 43 | QIs that could be coded using administrative data by condition type or by intervention type from 22 conditions | Administrative data using linked Medicare and Medicaid |
| Overall QI pass rate: 57.0% (CI95:53.9-60.2). QI pass rates were higher for treatment QIs (63.5%, CI95: 59.8-67.2) than for medication safety QIs (43.8%, CI95: 38.2-49.4) | Quality of arthritis care for older adults is suboptimal, particularly with respect to medication safety. Quality improvement efforts should target appropriate use of, and counselling regarding medications, as well as underuse of efficacious therapy. | 8 | Osteoarthritis care | Computer assisted telephone interview, Questionnaires |
| Receipt of indicated care varied substantially by condition (29 to 83%). Substantially more indicated care was given for general medical conditions (74%, CI95: 73-76%) than for geriatric conditions (57%, CI95:55-58%) | Shortfalls in QoC of adult >50 yrs with common health conditions in the UK were most noticeable in areas associated with disability and frailty | 32 | Stroke Depression DM, Falls Hearing problems Hypertension Ischemic heart disease Osteoarthritis Osteoporosis Pain management Smoking cessation Urinary incontinence Vision | Patients (face to face interviews), expert panel |
| Author(s)                  | Study population (n)          | Study design/ Period/ Setting       | Objectives                                                                 |
|---------------------------|-------------------------------|-----------------------------------|----------------------------------------------------------------------------|
| Bates-Jensen et al.[18] (2003) | 191 residents (elderly)       | Observational study Eight NHs (US)| Reliability and feasibility of a standardized protocol to score QIs for pressure ulcer care; Assessment of Quality of PU care |
| Mikuls et al. [19] (2005)   | 63105 gout patients           | Retrospective database analysis (between 1990-1999) All gout patients in a general practice research database (US) | To examine adherence to QIs concerning the quality of allopurinol use in the treatment of gout |
| Gnanadesigan et al.[20] (2004) | 372 community-dwelling VEs    | Observational study, cohort 13-month 2 managed care plans (US) | To assess QoC provided to community-based VE with UI |
| Wenger et al. [21] (2003)   | 372 community-dwelling vulnerable elderly | Observational cohort study, 13-month 2 managed care organizations (US) | To assess QoC provided to VE by evaluating the process of care using ACOVE QIs |
| Results | Conclusions | # QIs used | Conditions | Source of information |
|---------|-------------|------------|------------|----------------------|
| Pass rate of the QIs ranged from 0-98%. Reliability medical record abstraction: kappa 0.689-1.00, agreement 80-100%; direct observation: kappa 0.979 and 0.928; thigh monitor: kappa 0.609-0.842 | Standardized QA system was feasible and had good reliability for 9 QIs for PU care | 9 | Pressure Ulcer Care | Medical records, direct observations, wireless thigh monitor observation data |
| 185 patients eligible for QI-1; 52 for QI-2 and 471 for QI-3. QI pass rates: 25 to 57%. Male sex, older age, history of chronic renal failure and a greater number of concomitant drugs were significantly associated with increased odds of inappropriate treatment for asymptomatic hyperuricaemia. | Allopurinol is frequently prescribed inappropriately; future interventions should be aimed at high-risk groups incl. older men and those receiving multiple drugs | 3 | Allopurinol use in treatment of gout and asymptomatic hyperuricaemia | National medical record database |
| In 32 patients with new or worsening UI, characteristics of voiding were documented for 75% of the patients; for 20% of the female patients pelvic examination was performed; for 42% of the male patients a rectal examination. Only 38% urinalysis, 16% a post void residual. Drug treatment was prescribed for 50% of the patients, Patient-behavioral treatments only for 13% | QoC for UI is inadequate, especially in primary care. Patient-behavioral treatments are rarely prescribed | 7 | Urinary Incontinence care | Medical record (explicit abstraction guidelines were used), telephone interview |
| Patients eligible for 1071 QIs, of which 55% were passed. No overall difference between the care organizations. Wide variation in QoC for condition, range 9-82% pass rate. Adherence to QIs concerning geriatric conditions lower than for general medical conditions (31% vs 52%, P<0.001). More treatment QIs were completed (81%) compared to the domains follow-up (63%), diagnosis (46%) and prevention (43%) | Care for VE is inadequate for a wide variety of conditions. The care for geriatric conditions is worse than for general medical conditions | 207 | 22 ACOVE conditions | Medical Record (185 QIs), patient interview (22 QIs) (approach: Written abstraction guidelines and real-time consultation with a senior nurse reviewer) |
| Author(s) | Study population (n) | Study design/ Period/ Setting | Objectives |
|-----------|----------------------|-------------------------------|------------|
| Chodosh et al. [22] (2004) | 372 community dwelling VEs (July 98-July 99) | Observational study 2 managed care plans (US) | Evaluation of QoC for chronic pain |
| Higashi et al. [23] (2004) | 372 community-dwelling VEs enrolled in managed care organizations (July 98-July 99) | Observational cohort study. 2 managed care organizations (US) | Evaluation of QoC (Pharmacological Care) |
| Arora et al. [24] (2007) | 328 VEs admitted at a general medicine ward | Prospective evaluation of QoC Academic medical center (US) | Adaptation of ACOVE QIs for QoC assessment of hospitalised elderly and use of QIs for QoC measurement |
| Zingmond et al. [25] (2009) | 21,657 NH registers, dually enrolled in Medicaid and Medicare | Retrospective cohort study Nursing homes in 19 California counties (US) | Assessing which clinical conditions are inadequately measured and adaption of ACOVE for use with routinely collected data |
| Results                                                                 | Conclusions                                                                 | # QIs used | Conditions | Source of information                           |
|------------------------------------------------------------------------|------------------------------------------------------------------------------|------------|------------|-----------------------------------------------|
| <40% of VE were screened for pain in 2 years; 33% of VE had episode of pain during study period; 86% were offered treatment; 66% had follow-up; 10% of VE receiving NSAIDs received attention for GI toxicity; 61% of VE on opioids were offered laxatives | Chronic pain management in VE is inadequate. Improvement needed in screening, clinical evaluation, follow-up, attention to toxicities of therapy | 11         | Chronic Pain | Abstraction of administrative data & medical records on in- and outpatient, patient interviews. |
| Overall pass rate: 50% for PIM ; 97% AIM; 81% for ECD; 64% MM          | Undertreatment, appropriate monitoring, documenting information, education of patients and maintaining continuity are more common problems than use of inappropriate medication | 43         | NA         | Chart abstraction and patient interview         |
| Pass rate varied from 0-100%. QIs general medical care higher pass rate than geriatric QIs (81.5% vs. 61.6% p<0.01) | Adherence to geriatric-specific QIs lower than for general hospital care QIs. QI focusing on screening may overestimate performance | 16         | General medical delirium and Dementia, Physical function Pressure ulcer | Chart abstraction (computerized tool were used) and patient interview |
| Only 50 of 283 QIs were captured. The overall QI pass rate was 76% QIs with highest pass rates measured avoidance of adverse medications and appropriate medication use | The use of claims data linked to MDS to measure the QoC is feasible for NH populations but assessment will be more valuable if additional data focused on geriatric care is used | 50         | 16 conditions: Dementia, depression, diabetes, end-of-life care, falls, heart failure, hospital care, hypertension, ischemic heart disease, malnutrition, medication use, osteoarthritis, osteoporosis, stroke/AF, urinary incontinence, vision impairment | Administrative data |
| Author(s)         | Study population (n)                                                                 | Study design/ Period/ Setting | Objectives                                                                                           |
|------------------|--------------------------------------------------------------------------------------|-------------------------------|-------------------------------------------------------------------------------------------------------|
| Wenger et al.    | Community dwelling elderly >75 yrs (357 at intervention sites and 287 at control sites) | Controlled trial 2 community medical groups (US) | To determine effect of a practice-based ACOVE-2 intervention on care for falls, UI and cognitive impairment |

ACOVE: Assessing Care Of Vulnerable Elders; VE: Vulnerable Elder; NH: Nursing Home; QoC: Quality Of Care; QI: Quality Indicators; IHI BTS: Institute of Healthcare Improvement’s Breakthrough Series; CHF: Chronic Heart Failure; GEM: Geriatric Evaluation and Management; MAI: Medication Appropriateness Index; DM: Diabetes Mellitus; PU: Pressure Ulcer; MDS: Minimum Data Set; CI: Cognitive Impairment; UI: Urinary Incontinence; PIM: Prescribing Indicated Medication; AIM: Avoiding Inappropriate Medication; ECD: Education, Continuity, and Documentation; MM: Medication Monitoring; QoL: Quality of Life; RA: Rheumatoid Arthritis; AF: Atrial Fibrillation; OA: Osteoarthritis;

$\# = \text{Number of quality indicators used.}$
| Results                                                                 | Conclusions                                                                 | # QIs used | Conditions                  | Source of information                  |
|------------------------------------------------------------------------|------------------------------------------------------------------------------|------------|-----------------------------|----------------------------------------|
| Intervention group patients received better care for falls (44% vs. 23%, p<0.001) and UI (37% vs. 22%, p<0.001), but not for cognitive impairment (44% vs. 41, p=0.67) than control patients | The practice based intervention improved care for falls and UI, although quality remained low. More intensive interventions, such as embedding interventions components into an electronic medical record, are needed | 18         | Falls (5 QIs) UI (6 QIs)    | Medical records, interviews, administrative data |
### Supplemental table S1

QI: quality indicator; *: No patients were eligible for the premise of the QI. Co: condition. Note: we rounded the percentages.

| Condition                   | Quality indicators                                                                                                                                       | Number of studies using the QI | Mean [Median (Min, Max)] |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|--------------------------|
| Falls and mobility          | All vulnerable elders should have documentation that they were asked at least annually about the occurrence of recent falls†                             | 1                             | 25                       |
|                             | All vulnerable elders should have documentation that they were asked about or examined for the presence of balance and gait disturbances at least once† | 1                             | 49 [48.5 (48;49)]        |
|                             | IF a (vulnerable elder/person aged 65 or older -Steel-) reported two or more falls in the past year or a single fall with injury requiring treatment, Then (there should be documentation that a basic fall history was performed / the physician should take a basic fall history -Steel-) | 3                             | 44 [49 (34;49)]          |
|                             | IF a vulnerable elder reported two or more falls in the past year, or a single fall with injury requiring treatment, Then there should be documentation that a basic fall physical examination was performed | 2                             | 8 [8 (3;12)]             |
|                             | IF a vulnerable elder reported two or more falls in the past year or a single fall with injury requiring treatment, Then there should be documentation of specific diagnostic and therapeutic recommendations† | 1                             | 30                       |
|                             | IF a person aged 65 or older reported 2 or more falls in the past year, or a single fall with injury requiring treatment, THEN the patient should be offered a multidisciplinary falls assessment | 1                             | 38                       |
|                             | IF a vulnerable elder reports or is found to have new or worsening difficulty with ambulation, balance, or mobility, THEN a basic gait, mobility, and balance evaluation should be performed within 6 months that results in specific diagnostic and therapeutic recommendations specific diagnostic and therapeutic recommendations† | 2                             | 22 [22 (20;33)]          |
|                             | IF a vulnerable elder demonstrates decreased balance or proprioception or increased postural sway, THEN an evaluation for an assistive device performed (Wenger 2009) and an appropriate exercise program should be offered† | 2                             | 37 [37 (12;62)]          |
| Condition     | Quality indicators                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|---------------|-------------------------------------------------------------------------------------|-------------------------------|------------------------|
|               | IF a vulnerable elder is found to have problems with gait, strength, or endurance, THEN an exercise program should be offered | 3                             | 58[70(30;71)]          |
|               | Home safety evaluation                                                               | 1                             | 4                      |
|               | treat balance problem                                                                | 1                             | 21                     |
|               | Treat strength or gait problem                                                       | 1                             | 58                     |
|               | NH resident with new balance difficulty should receive PT or an assistive device     | 1                             | 34                     |
| Dementia      | IF a vulnerable elder is admitted to a hospital or is new to a physician practice, THEN multidimensional assessment of cognitive ability and assessment of functional status should be documented | 2                             | 53[53(52;53)]          |
|               | IF a vulnerable elder is admitted to a hospital or is new to a physician practice, THEN there should be an assessment of functional status | 1                             | 18                     |
|               | IF a (vulnerable elder / NH resident -Zingmond09-) has newly diagnosed dementia, THEN serum levels of vitamin B12 and thyroid-stimulating hormone should be measured | 4                             | 14[14(2;25)]           |
|               | IF a vulnerable elder has (mild to moderate Alzheimer disease / newly diagnosed dementia -Zingmond07-), THEN the treating physician should (discuss treatment / treat -Zingmond07-) with a cholinesterase inhibitor with the patient and the primary caregiver (if available) | 3                             | 44[44(13;75)]          |
|               | IF a vulnerable elder with dementia has a caregiver (and, if capable, the patient assents), THEN the physician should discuss or refer the patient and caregiver for discussion about patient safety, provide education on how to deal with conflicts at home, and inform them about community resources for dementia | 2                             | 24[24(21;26)]          |
|               | IF a vulnerable elder has dementia, THEN he or she should be screened for depression during the initial evaluation. | 3                             | 47[50(31,2;60)]        |
|               | IF a vulnerable elder has newly diagnosed dementia, THEN the diagnosing physician should advise the patient not to drive a motor vehicle or request that the Department of Motor Vehicles (or an equivalent agency) retest the patient's ability to drive, or refer to a drivers safety course that includes assessment of driving ability | 2                             | 25[25(0;50)]           |
| Condition                                                                 | Quality indicators                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|----------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------|------------------------|
| IF a vulnerable elder with dementia has cerebrovascular disease, THEN he or she should be offered appropriate stroke prophylaxis |                                                                                      | 1                             | 100                    |
| IF a (vulnerable elder / NH resident -Zingmond09-) with dementia has depression, THEN he or she should be treated for the depression (with pharmacologic therapy or mental health referral -Zingmond07-) |                                                                                      | 3                             | 20                     |
| If a vulnerable elder with dementia is to be physically restrained in the hospital, then the target or safety issue justifying use of restraints must be identified to the consenting person and documented in the chart |                                                                                      | 1                             | 100                    |
| IF a vulnerable elder is physically restrained and the target behavioural disturbance requiring restraint is identified, then the healthcare team should include methods other than physical restraints in the care plan |                                                                                      | 1                             | 69                     |
| Classify type of dementia in medical record                                 |                                                                                      | 1                             | 40                     |
| Objective mental status test in new dementia                                |                                                                                      | 1                             | 60                     |
| Evaluation need for help with functional activities                         |                                                                                      | 1                             | 52                     |
| Evaluate decision-making capacity                                           |                                                                                      | 1                             | 27                     |
| IF a vulnerable elder presents with symptoms of dementia, THEN the physician should review the patient’s medication list for initiation of medications that might correspond chronologically to the onset of dementia symptoms |                                                                                      | 0                             | -                      |
| IF a vulnerable elder presents with symptoms of dementia that correspond in time with the initiation of new medications, THEN the physician should discontinue or justify the necessity of continuing these medications |                                                                                      | 0                             | -                      |
| IF a vulnerable elder has signs of dementia and focal neurologic findings that suggest an intracranial process, THEN he or she should be offered neuroimaging (brain computed tomography or magnetic resonance imaging), THEN he or she should be offered neuroimaging (brain computed tomography or magnetic resonance imaging) |                                                                                      | 0                             | -                      |
| Condition          | Quality indicators                                                                 | Number of studies using the QI | Mean [Median (Min, Max)] |
|--------------------|-------------------------------------------------------------------------------------|-------------------------------|-------------------------|
| Continuity of Care | IF a vulnerable elder is placed in physical restraints, THEN each of the following measures should be enacted: 1) Consistent release from the restraints at least every 2 hours; 2) Face-to-face reassessment by a physician or 3) Observation at least every 15 minutes, and more frequently if indicated by the patient’s condition, while the nurse at least every 4 hours and before renewal of the restraint order; patient is in restraints; 4) Interventions every 2 hours (or as indicated by patient’s condition or needs) related to nutrition, hydration, personal hygiene, toileting, and range of motion exercises | 0                             | -                        |
|                    | IF an outpatient, vulnerable elder is started on a new prescription medication, and he or she has a follow-up visit with the prescribing physician, THEN the medical record at the follow-up visit should document 1 of the following: 1) the medication is being taken, 2) the physician asked about the medication, or 3) the medication was not started because it was not needed or because it was changed | 1                             | 100                      |
|                    | IF a vulnerable elder is under the outpatient care of more than 2 physicians, and 1 physician prescribed a new prescription medication or a change in medications, THEN subsequent medical record entries by the non-prescription physician should acknowledge the medication change | 1                             | 42                       |
|                    | IF a vulnerable elder is discharged from a hospital to home, and he or she received a new prescription medication or a change in medication before discharge, THEN the outpatient medical record should document or acknowledge the medication change within 6 weeks of discharge | 1                             | 55                       |
|                    | IF a vulnerable elder is discharged from a hospital to home or to a nursing home, and the transfer form or discharge summary indicates that a test result is pending, THEN the outpatient or nursing home medical record should include the test result within a 6 weeks of hospital discharge | 1                             | 71                       |
| Condition | Quality indicators | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|-------------------|-------------------------------|-----------------------|
| IF a vulnerable elder is discharged from a hospital to home or to a nursing home, and the hospital medical record specifies a follow-up appointment for a physician visit or a treatment (e.g., physical therapy or radiation oncology), THEN the medical record should document that the visit or treatment took place or that it was postponed or not needed | 1 | 90 |
| IF a vulnerable elder is discharged from a hospital to home or to a nursing home, THEN there should be a discharge summary in the outpatient physician or nursing home medical record within 6 weeks | 2 | 59[59(41,76)] |
| IF a vulnerable elder is deaf or does not speak English, THEN an interpreter or translated materials should be employed to facilitate communication between the vulnerable elder and the health care provider | 1 | [*] |
| IF an outpatient vulnerable elder is referred to a consultant physician, THEN the reason for consultation should be documented in the consultant’s note | 0 | - |
| IF an outpatient vulnerable elder is referred to a consultant and subsequently visits the referring physician after the visit with the consultant, THEN the referring physician’s follow-up note should document the consultant’s recommendations, or the medical record should include the consultant’s note, within 6 weeks or at the time of the follow-up visit, whichever is later | 0 | - |
| IF the outpatient medical record documents that a diagnostic test was ordered for a vulnerable elder, THEN the medical record at the follow-up visit should document one of the following: 1) the result of the test, 2) the test was not needed or reasoned why it will not be performed, or 3) the test is still pending | 0 | - |
| IF a vulnerable elder is transferred between emergency departments or between acute care facilities, THEN the medical record at the receiving facility should include medical records from the transferring facility or should acknowledge transfer of such medical records | 0 | - |
| IF a vulnerable elder is discharged from a hospital to home or to a nursing home, THEN there should be a discharge summary in the outpatient physician or nursing home medical record within 6 weeks | 0 | - |
| Condition | Quality indicators | Number of studies | Mean [Median (Min, Max)] |
|-----------|--------------------|------------------|-------------------------|
| Depression | IF a vulnerable elder presents with new onset of one of the following symptoms: sad mood, feeling down, insomnia or difficulties with sleep, apathy or loss of interest in pleasurable activities, complaints of memory loss, unexplained weight loss greater than 5% in the past month or 10% over 1 year, or unexplained fatigue or low energy, THEN the patient should be asked about or treated for depression, or referred to a mental health professional within 2 weeks of presentation. | 1 | 26 |
| | IF a vulnerable elder presents with onset or discovery of one of the following conditions: stroke, myocardial infarction, dementia, malignancy (excluding skin cancer), chronic pain, alcohol or substance abuse or dependence, anxiety disorder, or personality disorder, THEN the patient should be asked about or treated for depression, or referred to a mental health professional within 2 months of diagnosis of the condition. | 1 | 0 |
| | IF a (vulnerable elder / person aged 50 or older -Steel-) receives a diagnosis of a new depression episode, THEN 4 (the medical record should document / the diagnosing physician should ask -Steel-) on the day of diagnosis (the presence or absence of suicidal ideation / had any thoughts about suicide -Steel-) (and psychosis (consisting of, at a minimum, auditory hallucinations or delusions). -deleted Steel-) | 2 | 23 [23 (0;45)] |
| | IF a vulnerable elder has thoughts of suicide, THEN the medical record should document, on the same date, that the patient either has no immediate plan for suicide or that the patient was referred for evaluation for psychiatric hospitalisation. | 1 | [*] |
| | IF a (vulnerable elder / NH resident-Zingmond09-/person aged 50 or older -Steel-) is diagnosed with (clinical -Steel-) depression, THEN (Treat with pharmacologic therapy or mental health referral within 2 wk-Zingmond07-/ should be treated within 2 wks of diagnosis-Zingmond09/- antidepressant treatment, psychotherapy, or electroconvulsive therapy should be offered within 2 weeks after diagnosis unless there is documentation within that period that the patient has improved, or unless the patient has substance abuse or dependence, in which case treatment may wait until 8 weeks after the patient is in a drug- or alcohol-free state) | 4 | 46 [46 (12;79)] |
| Condition                                                                 | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------------------|
| IF a (vulnerable elder / NH resident -Zingmond09-) is started on an antidepressant medication, THEN the following medications should not be used as first- (or second- -deleted Zingmond09-) line therapy: tertiary amine tricyclics (amitriptyline, imipramine, doxepin, clomipramine, trimipramine); MAOIs (unless atypical depression is present); benzodiazepines; or stimulants (except methylphenidate) | 3 92[90(89;97)]                                                                                                                                         |                              |                        |
| IF a (vulnerable elder / NH resident -Zingmond09-) with a history of (cardiac disease / coronary artery disease -Zingmond09, Zingmond07-) is started on a tricyclic antidepressant, THEN (a baseline electrocardiogram should be obtained before initiation of or within 3 months before treatment / should have a baseline ECG performed -Zingmond09-) (exclusion: Pacemaker -Zingmond07-) | 3 24[30(0;43)]                                                                                                                                         |                              |                        |
| IF a (vulnerable elder / patient with depression -Zingmond07-) is taking a serotonin reuptake inhibitor, THEN (an MAOI should not be used for at least 2 weeks after termination of paroxetine, sertraline, fluvoxamine, and citalopram or for at least 5 weeks after termination of fluoxetine / MAOI started a specified time after stopping SSRI -Zingmond07-) | 3 90[90(80,100)]                                                                                                                                         |                              |                        |
| IF a (vulnerable elder / patient with depression -Zingmond07-) is taking an MAOI, THEN (he or she should not receive medications that interact with MAOIs for at least 2 weeks after termination of the MAOI / SSRI started a specified time after stopping MAOI -Zingmond07-) | 3 66[66(32;100)]                                                                                                                                         |                              |                        |
| NH resident taking an SSRI should have an appropriate washout period before starting an MAOI, and vice versa.                                                                                      |                                                                                                                                                    |                              | [*]                    |
| IF a vulnerable elder is being treated for depression, THEN at each treatment visit suicide risk should be documented, if he or she had suicidal ideation during a previous visit |                                                                                                                                                    | 1 [*]                        |                        |
| IF a (vulnerable elder / person aged 50 or older -Steel-) has no meaningful symptom response after 6 weeks of treatment, THEN 1 of the following treatment options should be initiated by the 8th week of treatment: Medication dose should be optimized or the patient should be referred to a psychiatrist (if initial treatment was medication), or mediation should be initiated (if initial treatment was psychotherapy alone -Steel-) or referral to a psychiatrist should be offered (if initial treatment was psychotherapy alone -deleted Steel-) | 2 41[50(22;78)]                                                                                                                                         |                              |                        |
| Condition                                                                 | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean|Median(Min, Max) |
|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|-----|-----------------|
| IF a vulnerable elder responds only partially after 12 weeks of treatment, THEN 1 of the following treatment options should be instituted by the 16th week of treatment: Switch to a different medication class or add a second medication to the first (if initial treatment included medication), try psychotherapy (if the initial treatment was psychotherapy), try medication (if initial treatment was psychotherapy without medication), consider electroconvulsive therapy, or refer to a psychiatrist | IF a vulnerable elder responds only partially after 12 weeks of treatment, THEN 1 of the following treatment options should be instituted by the 16th week of treatment: Switch to a different medication class or add a second medication to the first (if initial treatment included medication), try psychotherapy (if the initial treatment was psychotherapy), try medication (if initial treatment was psychotherapy without medication), consider electroconvulsive therapy, or refer to a psychiatrist | 1           | 25            |
| IF a (vulnerable elder / NH resident -Zingmond09-) (has responded to antidepressant medication / with new depression that improves with treatment -Zingmond09-), THEN he or she should be continued (on the drug at the same dose / that antidepressant -Zingmond09-) for at least 6 months (and should make contact with a clinician at least once (office visit or phone) during that time period. -deleted Zingmond09-) | IF a (vulnerable elder / NH resident -Zingmond09-) (has responded to antidepressant medication / with new depression that improves with treatment -Zingmond09-), THEN he or she should be continued (on the drug at the same dose / that antidepressant -Zingmond09-) for at least 6 months (and should make contact with a clinician at least once (office visit or phone) during that time period. -deleted Zingmond09-) | 2           | 69            |
| NH resident with newly diagnosed depression should have TSH checked        | NH resident with newly diagnosed depression should have TSH checked                                                                                                                                                | 1           | 11            |
| IF a vulnerable elder receives a diagnosis of a new depression episode, THEN the medical record should document on the day of diagnosis the presence or absence of suicidal ideation and psychosis (consisting of, at a minimum, auditory hallucinations or delusions) | IF a vulnerable elder receives a diagnosis of a new depression episode, THEN the medical record should document on the day of diagnosis the presence or absence of suicidal ideation and psychosis (consisting of, at a minimum, auditory hallucinations or delusions) | 0           | -             |
| IF a vulnerable elder has depression with psychotic features (for example, auditory hallucinations, delusions) or has melancholic or vegetative depression with pervasive anhedonia, unreactive mood, psychomotor disturbances, severe terminal insomnia, and weight and appetite loss, THEN he or she should not be treated with psychotherapy alone, unless he or she is unable or unwilling to take medication | IF a vulnerable elder has depression with psychotic features (for example, auditory hallucinations, delusions) or has melancholic or vegetative depression with pervasive anhedonia, unreactive mood, psychomotor disturbances, severe terminal insomnia, and weight and appetite loss, THEN he or she should not be treated with psychotherapy alone, unless he or she is unable or unwilling to take medication | 0           | -             |
| IF a vulnerable elder has depression with psychotic features, THEN he or she should be referred to a psychiatrist and should receive treatment with a combination of an antidepressant and an antipsychotic, or with electroconvulsive therapy | IF a vulnerable elder has depression with psychotic features, THEN he or she should be referred to a psychiatrist and should receive treatment with a combination of an antidepressant and an antipsychotic, or with electroconvulsive therapy | 0           | -             |
| IF a vulnerable elder is being treated for depression with antidepressants, THEN the antidepressants should be prescribed at appropriate starting doses, and they should have an appropriate titration schedule to a therapeutic dose, therapeutic blood level, or remission of symptoms by 12 weeks | IF a vulnerable elder is being treated for depression with antidepressants, THEN the antidepressants should be prescribed at appropriate starting doses, and they should have an appropriate titration schedule to a therapeutic dose, therapeutic blood level, or remission of symptoms by 12 weeks | 0           | -             |
| Condition | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------|
| Diabetes  | IF a (vulnerable elder / NH resident -Zingmond09-/ person aged 50 or older -Steel-) has diabetes, THEN his or her glycosylated hemoglobin level (or fructosamine -Steel-) should be measured at least every 12 months.  
  IF a vulnerable elder has an elevated glycosylated hemoglobin level, THEN he or she should be offered a therapeutic intervention aimed at improving glycemic control within 3 months if the glycosylated hemoglobin level is 9.0% to 10.9%, and within 1 month if the glycosylated hemoglobin level is 11% or greater.  
  IF a diabetic (vulnerable elder / person aged 50 or older -Steel-) (does not have established renal disease / without renal insufficiency -Zingmond07-) and is not receiving an ACE inhibitor or ACE receptor blocker, THEN he or she should receive an annual test for proteinuria.  
  IF a diabetic (vulnerable elder / NH resident -Zingmond09-) has proteinuria, THEN (he or she should be offered / prescribe -Zingmond07-) therapy with an ACE inhibitor or ACE receptor blocker (exclusions: ACE/ARB exclusions -Zingmond07-).  
  IF a vulnerable elder has diabetes, THEN his or her blood pressure should be checked at each outpatient visit.  
  IF a diabetic vulnerable elder has a glycosylated hemoglobin level of 10% or greater, THEN he or she should be referred for diabetic education at least annually.  
  IF a diabetic vulnerable elder has elevated blood pressure, THEN he or she should be offered a therapeutic intervention to lower blood pressure within 3 months if blood pressure is 150 to 160/90 to 100 mm Hg or within 1 month if blood pressure is greater than 160/100 mm Hg.  
  ALL diabetic vulnerable elders should be offered daily aspirin therapy.  
  IF a diabetic (vulnerable elder / person aged 50 or older -Steel-) has a fasting total cholesterol level of (240 g/dL / 5 mmol/L -Steel-) or greater, THEN he or she should be offered an intervention to lower cholesterol.  
  IF a diabetic (vulnerable elder / NH resident -Zingmond09-) is not blind, THEN he or she should receive an (annual dilated eye examination performed by an ophthalmologist, optometrist, or diabetes specialist / eye examination every 2 yr -Zingmond07-/ annual dilated eye exam -Zingmond09-) | 4 | 59[61(32; 83)] |
|           |                                                                 | 1 | 61 |
|           |                                                                 | 3 | 46[36(19;83)] |
|           |                                                                 | 3 | 72[98(20,98)] |
|           |                                                                 | 1 | 59 |
|           |                                                                 | 1 | [*] |
|           |                                                                 | 1 | 79 |
|           |                                                                 | 2 | 50[ 50(41;60)] |
|           |                                                                 | 2 | 90[90(88;92)] |
|           |                                                                 | 3 | 46[48(39;51)] |
| Condition | Quality indicators                                                                                                                                                                                                                                                                                                                                 | Number of studies using the QI | Mean/Median(Min, Max) |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------|
| IF a diabetic person aged 50 or older has one additional cardiac risk factor (i.e., smoker, hypertension, hypercholesterolemia, or renal insufficiency/microalbuminuria), THEN he/she should be offered an ACE inhibitor or receptor blocker | 1                             | 48                     |
| ALL diabetic persons aged 50 or older should have an annual examination of his/her feet                                                                                                           | 1                             | 84                     |
| End of life care | ALL (vulnerable elders / NH resident -Zingmond09-) should have (an advance directive -Zingmond09/- in their outpatient charts 1) an advance directive indicating the patient's surrogate decision maker, 2) documentation of a discussion about who would be a surrogate decision maker or a discussion about a search for a surrogate, or 3) indication that there is no identified surrogate  | 2                             | 44[44(4;84)]          |
| IF a vulnerable elder with dementia, coma, or altered mental status is admitted to the hospital, THEN within 48 hours of admission the medical record should 1) contain an advance directive indicating the patient's surrogate decision maker, 2) document a discussion about who would be a surrogate decision maker or a discussion about a search for a surrogate, or 3) indicate that there is no identified surrogate | 1                             | 25                     |
| IF a vulnerable elder has a diagnosis of severe dementia, is admitted to the hospital, and survives 48 hours, THEN within 48 hours of admission, the medical record should document consideration of the patient's preferences for care or that these could not be elicited or are unknown | 1                             | 100                    |
| IF a vulnerable elder is admitted directly to the intensive care unit (from the outpatient setting or emergency department) and survives 48 hours, THEN within 48 hours of admission, the medical record should document consideration of the patient's preferences for care or that these could not be elicited or are unknown | 1                             | 17                     |
| IF a vulnerable elder indicates during an interview that he or she would rather die than live permanently comatose, ventilated, or tube fed, THEN 1) the chart should document a discussion of life-sustaining treatment preferences, 2) the chart should contain an advance directive, or 3) the patient should indicate that he or she discussed this topic with the physician or does not wish to discuss this | 1                             | 12                     |
| Condition | Quality indicators | Number of studies using the QI | Mean [Median (Min, Max)] |
|-----------|--------------------|-------------------------------|-------------------------|
| IF a vulnerable elder has an advance directive in the outpatient, inpatient, or nursing home medical record or the patient reports the existence of an advance directive in an interview, and the patient receives care in a second venue, THEN 1) the advance directive should be present in the medical record at the second venue or 2) documentation should acknowledge its existence, its contents, and the reason that it is not in the medical record | 1 | 25 |
| IF a vulnerable elder requires mechanical ventilation during a hospitalisation (except short-term and postoperative mechanical ventilation), THEN the medical record should document within 48 hours of the initiation of mechanical ventilation the goals of care and the patient’s preference for mechanical ventilation or why this information is unavailable | 1 | 100 |
| IF a vulnerable elder with decision-making capacity has orders written in the hospital or the nursing home to withhold or withdraw a particular treatment (e.g., a do-not-resuscitate order or an order not to initiate dialysis), THEN the medical record should document 1) patient participation in the decision or 2) why the patient chose not to participate in the decision | 1 | 70 |
| NH resident should have aggressiveness of care treatment preferences followed | 1 | 96 |
| IF a noncomatose vulnerable elder is not expected to survive and a mechanical ventilator is withdrawn or intubation is withheld, THEN the patient should receive (or have orders available for) an opiate or benzodiazepine or barbiturate infusion to reduce dyspnea, and the chart should document whether the patient has dyspnea | 0 | - |
| IF a vulnerable elder who had dyspnea in the last 7 days of life died an expected death, THEN the chart should document how the dyspnea was treated and follow-up should be documented about the dyspnea | 0 | - |
| IF a vulnerable elder who was conscious during the last 3 days of life died an expected death, THEN the medical record should contain documentation about pain or lack of pain during the last 3 days of life | 0 | - |
| IF a vulnerable elder who was conscious during the last 3 days of life died an expected death, THEN the medical record should contain documentation about spirituality or how the patient was dealing with death or religious feelings | 0 | - |
| Condition            | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean [Median (Min, Max)] |
|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|--------------------------|
| IF a vulnerable elder without known family or next of kin died in the hospital, THEN the chart should document a search for next of kin | 0                              | -                          |
| IF a gout patient is receiving an initial prescription for allopurinol AND has significant renal impairment (defined as a serum creat ≥ 2 mg/dl or measured/estimated Cr Cl ≤ 50 ml/min) THEN the initial daily allopurinol dose should be less than 300 mg per day BECAUSE of the risk of allopurinol-related toxicity is increased in the presence of significant renal impairment in gout patients given a daily allopurinol dose equal to or exceeding 300 mg | 1                              | 74                       |
| Dose adjustment with concomitant use of allopurinol and azathioprine (see article)                                                                                                                               | 1                              | 75                       |
| Treatment of asymptomatic hyperuricaemia (see article)                                                                                                                                                            | 1                              | 43                       |
| Hearing loss         | ALL vulnerable elders should have a hearing screening examination as part of the initial evaluation                                                                                                               | 1                              | 0                        |
| IF a (vulnerable elder / person aged 65 or older -Steel-) (fails a hearing screening / has a problem with hearing -Steel-), THEN he or she should be offered a formal audiologic evaluation within 3 months | 2                              | 85 [85 (76;94)]          |
| IF a vulnerable elder has a hearing problem or fails an audiologic screening, THEN he or she should have an ear examination within 3 months                                                                      | 1                              | 83                       |
| IF a (vulnerable elder / person aged 65 or older -Steel-) is a hearing aid candidate, THEN he or she should be offered hearing rehabilitation                                                                       | 2                              | 67 [67 (50;83)]          |
| IF a vulnerable elder has hearing problem or fails an audiologic screening, then he or she should have an ear examination within 3 months                                                                      | 0                              | -                        |
| IF a vulnerable elder has conductive hearing loss, THEN he or she should be offered a referral to an otolaryngologist                                                                                        | 0                              | -                        |
| Heart failure        | IF a (vulnerable elder / NH resident -Zingmond09-) has heart failure and left ventricular ejection fraction of 40% or less (or unknown) THEN he or she should be offered an ACE inhibitor or receptor blocker' Patient with heart failure, Prescribe ACEI or ARB; exclusions: ACEI, ARB exclusions | 4                              | 57 [65 (33;87)]          |
|                      | 1                              | 48                       |
**Chapter 4.3**

| Condition | Quality indicators (QI) | Number of studies using the QI | Mean [Median (Min, Max)] |
|-----------|-------------------------|-------------------------------|--------------------------|
| IF a vulnerable elder receives a new diagnosis of heart failure, THEN he or she should have a history taken at the time of diagnosis and hospitalisation that documents the presence or absence of previous myocardial infarction, documented coronary artery disease, revascularization, current symptoms of chest pain or angina, history of hypertension, history of diabetes, history of hypercholesterolemia, history of valvular heart disease, history of thyroid disease, smoking, current medications, and a description of functional capacity (e.g., New York Heart Association functional status) | 1 | 83 |
| IF a vulnerable elder receives a new diagnosis of heart failure, THEN he or she should have the following elements of the physical examination documented at the time of presentation: weight, blood pressure, heart rate, lung examination, cardiac examination, and abdominal or lower-extremity examination | 1 | 100 |
| IF a (vulnerable elder / NH resident) receives a new diagnosis of heart failure, THEN (he or she should undergo the following studies within 1 month of the diagnosis (unless they have already been performed within the previous 3 months) -deleted Zingmond07-): chest radiography; electrocardiography; complete blood count; and (appropriate laboratory studies -Zingmond09-) measurement of serum sodium and potassium levels, serum creatinine concentration (electrolytes -Zingmond07-), and thyroid-stimulating hormone level ((in patients with atrial fibrillation or heart failure with no obvious cause) -deleted Zingmond07) | 3 | 44 [36 (27; 67)] |
| IF a vulnerable elder receives a new diagnosis of heart failure, THEN education about disease management should be provided and documented | 2 | 37 [37 (23; 50)] |
| IF a (vulnerable elder / NH resident) receives a new diagnosis of heart failure, THEN he or she should be offered an evaluation of left ventricular ejection fraction (within 1 month -deleted Zingmond09-) | 4 | 40 [41 (2; 77)] |
| IF a vulnerable elder is hospitalised with heart failure, THEN he or she should have serum electrolyte levels, creatinine concentration, and blood urea nitrogen levels measured within 1 day of hospitalisation | 1 | 100 |
| IF a vulnerable elder has heart failure, left ventricular ejection fraction of 40% or less, and New York Heart Association class I to III disease, THEN he or she should be offered a blocker, unless a contraindication (e.g., uncompensated heart failure) has been documented | 1 | 48 |
| Condition | Quality indicators | Number of studies using the QI | Mean [Median (Min, Max)] |
|-----------|-------------------|-------------------------------|-------------------------|
| IF a vulnerable elder has heart failure, (has left ventricular ejection fraction of 40% or less -deleted Zingmond07-), does not have atrial fibrillation, THEN (from among the 3 generations of calcium-channel blocker medications -deleted Zingmond07-), he or she should not be treated with a first- or second-generation calcium-channel blocker' | 2 | 99 [99 (97;100)] |
| IF a vulnerable elder has heart failure (and left ventricular ejection fraction of 40% or less -deleted Zingmond07-), THEN he or she should not be treated with a type I antiarrhythmic agent unless an implantable cardioverter defibrillator is in place | 2 | 100 [100 (99;100)] |
| IF a vulnerable elder has heart failure and atrial fibrillation, THEN he or she should be offered anticoagulation to achieve an INR or 2.0 to 3.0 | 2 | 68 [68 (65;71)] |
| IF a vulnerable elder has heart failure and atrial fibrillation, AND he or she has documented contraindications to anticoagulation, THEN he or she should be offered aspirin | 2 | 47 [47 (33;61)] |
| (Patient / NH resident -Zingmond09-) with heart failure, Prescribe a β blocker; exclusions: β blocker exclusions‡ | 3 | 19 [19 (13;25)] |
| NH resident post-hospitalisation for HF should have follow-up visit and weight measured within 14 d after discharge | 1 | 30 |
| NH resident with HF treated with digoxin should have a digoxin level checked if a medication that can alter levels is added | 1 | 26 |
| Cr measured if on digoxin | 1 | 72 |
| BP measured | 1 | 89 |
| Electrolyte monitoring during ACE inhib Rx | 1 | 27 |
| Electrolyte monitoring during diuretic Rx | 1 | 45 |
| Visit within 4 weeks after discharge | 1 | 67 |
| Weight loss counseling | 1 | 7 |
| Water weight management plan | 1 | 4 |
| Goal Setting | 1 | 4 |
| Condition | Quality indicators | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|--------------------|------------------------------|------------------------|
| Diet counseling | | 1 | 11 |
| LDL < 100 if CAD | | 1 | 40 |
| BP<130/80 mm Hg post MI or LVEF < 40 | | 1 | 65 |
| BP<140/90 mm Hg no MI and LVDF >40 | | 1 | 58 |
| IF a vulnerable elder with heart failure is treated with digoxin, THEN the digoxin level should be checked within 1 week if signs of toxicity develop | | 0 | - |
| Hospital Care | IF a vulnerable elder is admitted to the hospital for any acute or chronic illness or any surgical procedure, THEN the evaluation should include, within 24 hours, 1) diagnoses and 2) prehospital and current medications | 1 | 97 |
| | IF a vulnerable elder is admitted to the hospital for any acute or chronic illness or any surgical procedure, THEN documentation of cognitive status should be performed within 24 hours | 2 | 13[13(5;20)] |
| | IF a vulnerable elder enters the hospital, THEN discharge planning should begin within 48 hours | 2 | 68[68(68,4)] |
| | IF a vulnerable elder has valvular or congenital heart disease, intracardiac valvular prosthesis, hypertrophic cardiomyopathy, mitral valve prolapse with regurgitation, or previous episode of endocarditis, and a high-risk procedure is planned, THEN endocarditis prophylaxis should be given | 1 | 100 |
| | IF a hospitalised vulnerable elder is at very high risk for venous thrombosis, THEN the patient should have venous thromboembolism prophylaxis | 2 | 91[91(81;100)] |
| | IF a hospitalised vulnerable elder has risk factors for stress peptic ulcers, THEN the patient should receive prophylaxis with an H2-blocker, sucralfate, or a proton-pump inhibitor | 1 | 45 |
| | IF a hospitalised vulnerable elder has a definite or suspected diagnosis of delirium, THEN an evaluation for potentially precipitating factors must be undertaken and identified causes treated | 2 | 60 |
| | IF a hospitalised vulnerable elder has a definite or suspected diagnosis of delirium, THEN identified potential causes should be treated | 1 | 44 |
| Condition                                                                 | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean [Median (Min, Max)] |
|--------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|--------------------------|
| NH resident hospitalised for nonemergent revascularization or aneurism repair should have had cardiac stress test within 12 mos of operation |                                                                                                                  | 1                            | 12                       |
| If a vulnerable elder is admitted to a hospital or is new to a physician practice, then assessment of functional status should be documented |                                                                                                                  | 1                            | 95                       |
| If a vulnerable elder with heart failure is treated with digoxin, THEN the digoxin level should be checked within 1 week if signs of toxicity develop |                                                                                                                  | 0                            | -                        |
| If a vulnerable elder enters the hospital for nonemergent peripheral revascularization or aortic abdominal aneurysm repair, THEN a cardiac stress test should be performed if one was not performed in the previous year |                                                                                                                  | 0                            | -                        |
| If a hospitalised vulnerable elder has a new fever (body temperature, 38.5 °C [101.3 °F]), THEN there should be documentation that a physician examination was performed within 4 hours (or fever evaluation performed in the last 48 hours or an alternative explanation for the fever documented in the chart) |                                                                                                                  | 0                            | -                        |
| If a hospitalised vulnerable elder has a definite or suspected diagnosis of delirium, THEN an evaluation for potentially precipitating factors must be undertaken and identified causes treated |                                                                                                                  | 0                            | -                        |
| Hypertension                                                              | IF a (vulnerable elder / NH resident -Zingmond09-) has newly diagnosed hypertension, THEN electrocardiography (and appropriate laboratory studies -Zingmond09-) (should be performed within 4 weeks of the diagnosis -deleted Zingmond09-) | 3                            | 32 [33 (28;36)]           |
| IF a vulnerable elder has a new diagnosis of hypertension, THEN there should be documentation regarding the presence or absence of other cardiovascular risk factors |                                                                                                                  | 1                            | 33                       |
| IF a vulnerable elder receives a diagnosis of hypertension and the blood pressure is below 170/90 mm Hg, THEN there should be evidence that 3 or more blood pressure measurements of 140/90 mm Hg or greater were obtained before the diagnosis |                                                                                                                  | 1                            | 33                       |
| Condition                                   | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|--------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------------|
| IF a vulnerable elder receives a diagnosis of hypertension, THEN nonpharmacologic therapy with lifestyle modification for treatment of hypertension should be recommended, including dietary sodium restriction and weight loss if the patient is more than 10% over ideal body weight | 1 33                                                                                                                                                |                             |                       |
| IF a (vulnerable elder / person aged 50 or older -Steel-) remains hypertensive after nonpharmacologic intervention, THEN pharmacologic antihypertensive treatment should be initiated | 1 68[68(64;73)]                                                                                                                                      |                             |                       |
| IF a vulnerable elder requires pharmacotherapy for treatment of hypertension in the outpatient setting, THEN a once- or twice-daily medication should be used unless there is documentation regarding the need for agents that require more frequent dosing | 1 93                                                                                                                                                |                             |                       |
| IF a (vulnerable elder / NH resident -Zingmond09-) has hypertension and has (renal parenchymal disease with a serum creatinine concentration greater than 1.5 mg/dL or more than 1 g of protein/24 h of collected urine / renal insufficiency or proteinuria -Zingmond07-/ renal disease -Zingmond09-), THEN therapy with an ACE inhibitor should be (offered / prescribe -Zingmond07-)(ACE/ARB exclusions -Zingmond07-) | 3 45[39(31;63)]                                                                                                                                      |                             |                       |
| IF a (vulnerable elder / NH resident -Zingmond09-) has hypertension and asthma, THEN blocker therapy for hypertension should not be used | 3 88[86(78;100)]                                                                                                                                       |                             |                       |
| NH resident newly prescribed a diuretic should have electrolytes checked in 10 d | 1 11                                                                                                                                                |                             |                       |
| IF a (vulnerable elder / NH resident -Zingmond09-) is hospitalised with acute myocardial infarction, THEN he or she should be offered assessment of left ventricular function ((before discharge or -deleted Zingmond07-) within 3 days after hospital discharge -deleted Zingmond09-) | 3 61[63(50;69)]                                                                                                                                       |                             |                       |
| IF a vulnerable elder has an acute myocardial infarction or unstable angina, (did not undergo angiography, and does not have contraindications to revascularization, THEN he or she should be offered noninvasive -deleted Zingmond07-)(THEN perform -Zingmond07- stress testing 4 to 21 days after the infarction or anginal event | 2 10[10(0;19)]                                                                                                                                       |                             |                       |
| IF a vulnerable elder has an acute myocardial infarction or unstable angina, THEN he or she should be given aspirin therapy within 1 hour of presentation | 1 0                                                                                                                                                |                             |                       |
| Condition                                                                 | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|--------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------|
| IF a vulnerable elder has unstable angina or an acute myocardial infarction, THEN he or she should be offered blocker therapy within 12 hours of presentation |                                                                                                                                                                                                                     | 1                             | 50                     |
| IF a vulnerable elder has an acute myocardial infarction that is measurable by electrocardiography and does not have contraindications to reperfusion therapy, THEN he or she should be offered treatment with reperfusion therapy |                                                                                                                                                                                                                     | 1                             | [*]                    |
| IF a vulnerable elder without contraindications to revascularization has an acute myocardial infarction(Zingmond2007) or unstable angina with 1 or more of the following pain refractory to medical therapy (1 h of aggressive medical therapy), recurrent angina or ischemia at rest or with low-level activities, ischemia accompanied by symptoms of heart failure THEN he or she should be offered urgent catheterization |                                                                                                                                                                                                                     | 1                             | 31                     |
| IF a vulnerable elder has significant left main or significant 3-vessel coronary artery disease with left ventricular ejection fraction less than 50%, THEN he or she should be offered coronary artery bypass graft surgery |                                                                                                                                                                                                                     | 1                             | 0                      |
| IF a vulnerable elder has established coronary artery disease and his or her cholesterol level (lipids-Zingmond07-) is not known, THEN (check lipids-Zingmond07-) he or she should undergo a fasting cholesterol evaluation, including total LDL and HDL cholesterol levels |                                                                                                                                                                                                                     | 3                             | 39[33(31;52)]          |
| IF a (vulnerable elder / NH resident-Zingmond09-) has (established CHD and an LDL cholesterol level greater than 130 mg/dL / hypercholesterolemia-Zingmond07/Zingmond09-), (and a trial of step II diet therapy was not offered or was ineffective -deleted Zingmond07/Zingmond09-), THEN he or she should be (offered / prescribe-Zingmond07/Zingmond09-) cholesterol-lowering medication |                                                                                                                                                                                                                     | 4                             | 48[47(28;64)]          |
| IF a vulnerable elder has established CHD and is not taking warfarin, THEN he or she should be offered antiplatelet therapy |                                                                                                                                                                                                                     | 2                             | 68[66(58;66)]          |
| IF a vulnerable elder with established CHD smokes, THEN he or she should be offered counseling for smoking cessation at least annually and have this documented in the medical record |                                                                                                                                                                                                                     | 1                             | 50                     |
| IF a vulnerable elder has had a recent myocardial infarction or recent coronary bypass graft surgery, THEN he or she should be offered cardiac rehabilitation |                                                                                                                                                                                                                     | 1                             | 0                      |
| Condition          | Quality indicators                                                                 | Number of studies using the QI | Mean [Median (Min, Max)] |
|--------------------|-------------------------------------------------------------------------------------|-------------------------------|--------------------------|
| Malnutrition       | IF a (vulnerable elder / NH resident -Zingmond09-) has had a myocardial infarction, THEN he or she should be (offered a blocker / prescribe ß blocker -Zingmond07/Zingmond09-); (exclusions: ß-blocker exclusions -Zingmond07-) | 3                             | 47 [38 (21; 53)]        |
|                    | ALL vulnerable elders should be weighed at each physician office visit, and these weights should be documented in the medical record | 1                             | 42                       |
|                    | IF a vulnerable elder has involuntary weight loss of more than 10% of body weight over 1 year or less, THEN weight loss (or a related disorder) should be documented in the medical record as an indication that the physician recognized malnutrition as a potential problem | 1                             | 77                       |
|                    | IF a vulnerable elder has documented involuntary weight loss or hypoalbuminemia (<3.5 g/dL), THEN she or he should receive an evaluation for potentially reversible causes of poor nutritional intake | 1                             | 52                       |
|                    | IF a vulnerable elder has documented involuntary weight loss or hypoalbuminemia (<3.5 g/dL), THEN he or she should receive an evaluation for potentially relevant comorbid conditions, including medications that might be associated with decreased appetite (e.g., digoxin, fluoxetine, anticholinergics), depressive symptoms, and cognitive impairment | 1                             | 76                       |
|                    | IF a vulnerable elder is hospitalised, THEN his or her nutritional status should be documented during the hospitalisation by evaluation of oral intake or serum biochemical testing (e.g., albumin, prealbumin, or cholesterol) | 2                             | 47                       |
|                    | IF a (vulnerable elder / NH resident -Zingmond09-) who was hospitalised for a hip fracture has evidence of nutritional deficiency ((thin body habitus or low serum albumin or prealbumin levels) -deleted Zingmond09-), THEN (oral or enteral nutritional protein—energy supplementation should be initiated postoperatively / should receive protein-energy supplementation -Zingmond09-) | 2                             | 54                       |
|                    | IF a stroke patient has persistent dysphagia at 14 days, THEN a gastrostomy or jejunostomy tube should be considered for enteral feeding | 1                             | [“]                      |
|                    | NH resident with a newly placed feeding tube should first have received a nutrition consult, feeding aid, or supplements | 1                             | 83                       |
| Condition                | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------|
| Medication management    | **IF a hospitalised vulnerable elder is unable to take foods orally for more than 72 hours, THEN alternative alimentation (for example, enteral or parenteral) should be offered**                                                                                   | 0                             | -                      |
|                          | **IF a vulnerable elder is prescribed a new drug, THEN the prescribed drug should have a clearly defined indication documented in the record**                                                                                                                    | 1                             | 98                     |
|                          | **IF a vulnerable elder is prescribed a new drug, THEN the patient (or, if incapable, a caregiver) should receive education about the purpose of the drug, how to take it, and expected side effects or important adverse reactions**                                             | 2                             | 18[18(17;18)]         |
|                          | **EVERY new drug that is prescribed to a vulnerable elder on an ongoing basis for a chronic medical condition should have a documentation of response to therapy within 6 months**                                         | 1                             | 65                     |
|                          | **ALL vulnerable elders should have a drug regimen review at least annually**                                                                                                                                          | 1                             | 68                     |
|                          | **IF a (vulnerable elder / NH resident -Zingmond09-) is prescribed warfarin, THEN an INR should be determined within 4 days after initiation of therapy and at least every 6 weeks**                                                    | 3                             | 69[78(45;84)]         |
|                          | **IF a vulnerable elder is prescribed warfarin, THEN an INR should be determined at least every 6 weeks**                                                                                                       | 1                             | 53                     |
|                          | **IF a vulnerable elder is prescribed a thiazide or loop diuretic, THEN he or she should have electrolytes checked at least yearly**                                                                                       | 2                             | 84[84(80;87)]         |
|                          | **IF a (vulnerable elder / NH resident -Zingmond09-) patient with diabetes -Zingmond07) is prescribed an oral hypoglycemic drug -deleted Zingmond07-, THEN chlorpropamide should not be used**                                      | 3                             | 99[99(99,100)]        |
|                          | **ALL (vulnerable elders / NH residents -Zingmond09-) should not be prescribed a medication with strong anticholinergic effects if alternatives are available**                                                                | 3                             | 88[84(82,98)]         |
|                          | **IF a (vulnerable elder / NH resident -Zingmond09-) does not need control of seizures, THEN barbiturates should not be used**                                                                                         | 3                             | 98[99(96,6,99)]       |
|                          | **IF a (vulnerable elder / NH resident -Zingmond09-/cadogan) (requires analgesia / All patients -Zingmond07-) , THEN meperidine should not be used**                                                                         | 4                             | 99[99(99,100)]        |
| Condition                     | Quality indicators                                                                 | Number of studies using the QI | Mean [Median (Min, Max)] |
|--------------------------------|-------------------------------------------------------------------------------------|-------------------------------|--------------------------|
|                                | IF a vulnerable elder is newly started on a diuretic, THEN serum potassium and creatinine levels should be checked within 1 month of the initiation of therapy and then annually thereafter | 2                             | 61 [61 (34; 87)]         |
|                                | NH resident receiving a diuretic should have potassium measured annually              | 1                             | 87                      |
|                                | IF a vulnerable elder is (newly started on / prescribed -Zingmond07-) an ACE inhibitor (or ARB -Zingmond07-), THEN serum potassium and creatinine levels should be checked within (1 month / 4 wk -Zingmond07-) of the initiation of therapy | 3                             | 49 [37 (88; 22)]         |
|                                | NH resident newly prescribed an ACEI, ARB, or diuretic should have potassium and creatinine checked within 30 d and annually thereafter | 1                             | 32                      |
|                                | (Patient / NH resident older than 75 -Zingmond09-) treated with warfarin, history of PUD or GI bleeding, AND treated with NSAIDS, Prescribe misoprostol or a proton pump inhibitor medication‡ | 3                             | 25 [25 (24; 27)]         |
|                                | For ALL vulnerable elders the outpatient medical record of every physician and the hospital medical record should contain an up-to-date medication list | 0                             | -                       |
| Osteoarthritis                 | IF a (vulnerable elder / person age 75 or older -Ganz-) receives a diagnosis of symptomatic osteoarthritis, THEN functional status and degree of pain should be assessed annually‡ | 2                             | 50 [50 (40; 61)]         |
|                                | IF a vulnerable elder has monoarticular joint pain associated with redness, warmth, or swelling and the patient also has an oral temperature greater than 38.0 °C and does not have a previously established diagnosis of pseudogout or gout, THEN a diagnostic aspiration of the painfully swollen red joint should be performed that day | 1                             | [^]                      |
|                                | IF an ambulatory vulnerable elder (ambulatory NH resident Cadogan) receives a new diagnosis of symptomatic osteoarthritis of the knee and has no contraindication to exercise, and is physically and mentally able to exercise, THEN a directed or supervised strengthening or aerobic exercise program should be prescribed within 3/1 months of diagnosis | 2                             | 31 [31 (16; 46)]         |
| Condition | Quality indicators | Number of studies using the QI | Mean [Median (Min, Max)] |
|-----------|-------------------|-------------------------------|-------------------------|
| IF an ambulatory (vulnerable elder / person age 75 or older -Ganz-) has had a diagnosis of symptomatic osteoarthritis of the knee for more than (12 / 3 -Ganz-) months, has no contraindication to exercise, and is physically and mentally able to exercise, THEN there should be evidence that a directed or supervised strengthening or aerobic exercise program was prescribed at least once since the time of diagnosis | 2 | 22 [22 (0;44)] |
| IF an ambulatory (vulnerable elder / person age 75 or older -Ganz-) has had a diagnosis of symptomatic osteoarthritis for more than 6 months, THEN there should be evidence that education regarding the natural history, treatment, and self-management of the disease was offered at least once | 2 | 52 [52 (36;69)] |
| IF an ambulatory vulnerable elder has had a diagnosis of symptomatic osteoarthritis of the knee for more than 12 months, THEN there should be evidence that the patient was offered education at least once since the time of diagnosis | 1 | 33 |
| IF oral pharmacologic therapy is initiated to treat osteoarthritis, THEN acetaminophen should be the first drug used, unless there is a documented contraindication to use | 3 | 53 [43 (26;59)] |
| IF oral pharmacologic therapy for osteoarthritis is changed from acetaminophen to a different oral agent, THEN there should be evidence that the patient has had a trial of maximum-dose acetaminophen (suitable for age and comorbid conditions) | 2 | 35 [33 (33;37)] |
| IF a (vulnerable elder / person age 75 or older -Ganz-) is treated with cyclooxygenase nonselective NSAIDS, THEN there should be evidence that the patient was advised of the risks associated with these drugs | 2 | 21 [21 (4;39)] |
| IF a person age 75 or older is treated with a COX-2 NSAID, THEN the patient should be advised of the risks associated with the drug | 1 | 50 |
| IF a vulnerable elder (NH resident Cadogan) is older than age 75 years or has a history of peptic ulcer disease, gastrointestinal bleeding, or current coumadin use, AND the patient is being treated with a cyclooxygenase nonselective NSAID, THEN he or she should be offered concomitant treatment with misoprostol or a proton-pump inhibitor | 2 | 11 |
| IF a person age 75 or older is treated with a COX nonselective NSAID, THEN he or she should be offered concomitant treatment with either misoprostol or a proton-pump inhibitor | 1 | 27.4 |
| Condition | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------|
|           | IF a (vulnerable elder / person age 75 or older -Ganz/- a person aged 50 or older -Steel-) with severe symptomatic osteoarthritis of the knee or hip has not responded to nonpharmacologic and pharmacologic therapy, THEN the patient should be offered referral to an orthopedic surgeon to be evaluated for total joint replacement within 6 months unless a contraindication to surgery is documented | 2                             | 66[73(90;36)]          |
|           | NH resident is bedfast should receive mobilization                                                                                                                                                            | 1                             | 30                     |
| Osteoporosis | ALL female vulnerable elders should be counseled at least once regarding intake of dietary calcium and vitamin D and weight-bearing exercises                                                                                       | 1                             | 47                     |
|           | ALL female vulnerable elders who smoke should be counseled annually about smoking cessation                                                                                                                          | 1                             | 48                     |
|           | ALL female vulnerable elders should be counseled about estrogen replacement therapy at least once                                                                                                               | 1                             | 23                     |
|           | IF a vulnerable elder has a new diagnosis of osteoporosis, THEN during the initial evaluation period an underlying cause of osteoporosis should be sought by checking medication use and current alcohol use | 1                             | 42                     |
|           | IF an ambulatory vulnerable elder has an osteoporotic fracture diagnosed, THEN physical therapy or an exercise program should be offered within 3 months                                                                 | 1                             | 0                      |
|           | IF a (vulnerable elder / person aged 50 or older -Steel-) has (untreated -Steel-) osteoporosis, THEN calcium and vitamin D (and biphosphonate-Spinewine-) supplements should be recommended at least once | 2                             | 27[27(26;28)]          |
|           | IF a vulnerable elder is taking corticosteroids for more than 1 month, THEN the patient should be offered calcium and vitamin D                                                                                         | 2                             | 65[62(54;71)]          |
|           | IF a female (vulnerable elder / aged 50 or older -Steel/- NH resident -Zingmond09-) has a new diagnosis of osteoporosis, THEN the patient should be offered (pharmacologic treatment -Zingmond09/-treatment with hormone replacement therapy, biphosphonates, a selective estrogen receptor modulator (or PTH -Zingmond07/- or calcium and vitamin D -Steel-) or calcitonin within 3 months of diagnosis) | 4                             | 44[46(20;60)]          |
|           | IF a male vulnerable elder has osteoporosis and is hypogonadal, THEN he should be offered testosterone treatment                                                                                             | 1                             | [*]                   |
| Condition            | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------------------|
| Pain management      | IF an ambulatory NH resident is newly diagnosed with symptomatic osteoarthritis (OA) of the knee, has no contraindication to exercise, THEN a directed or supervised care plan should be developed within 1 month. | 1                            | 46                     |
|                      | ALL (vulnerable elders / NH residents -Cadogan-) should be screened for chronic pain during the initial evaluation period (with documentation in the primary care provider's note during the initial evaluation period and at least quarterly -Cadogan-)  | 3                            | 55[70(15;80,2)]        |
|                      | ALL vulnerable elders should be screened for chronic pain every 2 years.† | 1                            | 41                     |
|                      | IF a vulnerable elder has a newly reported chronic painful condition, THEN a targeted history should be performed within 1 month.† | 1                            | 40                     |
|                      | IF a (vulnerable elder / NH resident -Cadogan-) has been prescribed a cyclooxygenase nonselective NSAID for treatment of chronic pain, THEN the medical record should indicate whether he or she has a history of peptic ulcer disease and, if a history is present, justification of NSAID use should be documented.† | 2                            | 11[11(10,12)]          |
|                      | IF a (vulnerable elder / NH resident -Cadogan-) with chronic pain is treated with opioids, THEN he or she should be offered a bowel regimen, or the medical record should document the potential for constipation or explain why bowel treatment is not needed.† | 2                            | 32[32(0;64)]           |
|                      | IF a vulnerable elder has a newly reported chronic painful condition, THEN treatment should be offered.                                                                                                         | 2                            | 82[82(78,86)]          |
|                      | IF a (vulnerable elder/NH residents -Cadogan-) is treated for a chronic painful condition THEN he or she should be assessed for a response within 6/3 months.                                                              | 2                            | 55[55(44;66)]          |
|                      | IF a NH resident has pain on MDS screen or is diagnosed with chronic pain, THEN the resident should be evaluated for depression by a PCP within 1 month.                                                                 | 1                            | 49                     |
|                      | IF a NH resident has a positive MDS screen for pain, THEN a quantitative pain assessment using a standard pain scale should be used (with its use not precluded but modified for cognitive impairment).                                         | 1                            | 90                     |
| Condition | Quality indicators | Number of studies using the QI | Mean [Median (Min, Max)] |
|-----------|--------------------|------------------------------|-------------------------|
| Pneumonia | IF a (vulnerable elder / NH resident -Cadogan-) has a newly reported painful condition, THEN a targeted H & P should be done by the PCP and documented within 1 month | 1 | 10 |
| | IF a patient is treated with a COX nonselective NSAID, THEN there should be evidence that the patient was advised of the risk for gastrointestinal bleeding associated with these drugs | 1 | 54 |
| | IF a vulnerable elder with no history of allergy to the pneumococcal vaccine is not known to have already received a pneumococcal vaccine or if the patient received it more than 5 years ago (if before age 65 years), THEN a pneumococcal vaccine should be offered | 1 | 29 |
| | IF a vulnerable elder has no history of anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine, THEN the patient should be offered an annual influenza vaccination | 1 | 66 |
| | IF a smoker develops pneumonia, THEN the smoker should be advised to quit smoking | 1 | 33 |
| | IF a vulnerable elder is admitted to the hospital with pneumonia, THEN antibiotics should be administered within 8 hours of hospital arrival | 1 | 88 |
| | IF a vulnerable elder is admitted to the hospital with community-acquired pneumonia with hypoxia, THEN the patient should receive oxygen therapy | 1 | 100 |
| | IF a vulnerable elder has an empyema, THEN drainage is required | 1 | [*] |
| | IF a vulnerable elder with community-acquired pneumonia is to be discharged home, THEN the patient should not be unstable on the day before or the day of discharge | 1 | 100 |
| | IF a vulnerable elder is hospitalised and he or she is eligible for vaccination (that is, is not up-to-date with and influenza (during flu season) | 0 | - |
| | IF pneumococcal or influenza vaccination rates among patients of a health delivery organization are low (60% of persons at risk for pneumococcal and influenza disease and, 90% of institutionalized elderly), THEN methods to increase the rate of vaccination should be used | 0 | - |
| Condition | Quality indicators | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|--------------------|-------------------------------|-----------------------|
| IF a health care organization cares for vulnerable elders, THEN it should have a formal plan to offer and encourage influenza vaccination among its employees | 0 | - |
| IF a vulnerable elder with community-acquired pneumonia is to be switched from parenteral to oral antimicrobial therapy, THEN the patient must meet all of the following criteria: a clinically improving condition, hemodynamic stability, and tolerance of oral medication or food and fluids | 0 | - |
| Pressure ulcer | IF a (vulnerable elder / NH resident – Bates-Jansen-) is admitted to an intensive care unit or a medical–surgical unit of a hospital and is unable to reposition himself or herself or has limited ability to do so, THEN risk assessment for pressure ulcers should be performed on admission (and weekly for the first 4 weeks -Bates-Jansen-) | 3 | 74[62(59;100)] |
| | IF a vulnerable elder is identified as at risk for pressure ulcer development or a pressure ulcer risk assessment score indicates that the person is at risk, THEN preventive intervention must be instituted within 12 hours, addressing repositioning needs and pressure reduction (or management of tissue loads) | 1 | 0 |
| | IF a vulnerable elder is identified as at risk for pressure ulcer development and has malnutrition (involuntary weight loss of >10% of body weight over 1 year or low albumin or prealbumin levels), THEN nutritional intervention or dietary consultation should be instituted | 1 | 83 |
| | IF a (vulnerable elder / NH resident - Bates-Jansen-) presents with a pressure ulcer, THEN the pressure ulcer should be assessed for 1) location, 2) depth and stage, 3) size, and 4) presence of necrotic tissue | 3 | 27[32(0;33)] |
| Condition                                                                 | Quality indicators                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------|------------------------|
| IF a vulnerable elder presents with a clean full-thickness pressure ulcer and has no improvement at 4 weeks post-treatment, THEN 1) the appropriateness of the treatment plan and 2) the presence of cellulitis or osteomyelitis should be assessed | 1                                                                                | 50                             |
| Has a full-thickness PU with no improvement in 4 weeks or a partial thickness PU with no improvement in 2 weeks, THEN reassess the treatment plan and Stage III/IV PU for cellulitis or osteomyelitis | 1                                                                                | 17                             |
| IF a vulnerable elder presents with a partial-thickness pressure ulcer and has no improvement at 2 weeks post-treatment, THEN the appropriateness of the treatment plan should be assessed | 1                                                                                | 33                             |
| IF a vulnerable elder presents with a full-thickness sacral or trochanteric pressure ulcer covered with necrotic debris or eschar, THEN debridement interventions using sharp, mechanical, enzymatic, or autolytic procedures should be instituted within 3 days of diagnosis | 1                                                                                | 17                             |
| IF a vulnerable elder with a full-thickness pressure ulcer presents with systemic signs and symptoms of infection such as elevated temperature, leukocytosis, or confusion and agitation, and these signs and symptoms are not due to another identified cause, THEN the ulcer should be debrided of necrotic tissue within 12 hours | 2                                                                                | 0                              |
| IF a vulnerable elder with a full-thickness pressure ulcer presents with systemic signs and symptoms of infection, such as elevated temperature, leukocytosis, or confusion and agitation, and these signs and symptoms are not due to another identified cause, THEN a tissue biopsy or needle aspiration sample should be obtained and sent for culture and sensitivity testing within 12 hours | 2                                                                                | [*]                            |
| Has a (stage two or greater -Arora-)PU, THEN a topical antiseptic should not be used on the wound | 2                                                                                | 90[90(82;98)]                   |
| Has a clean full-thickness or a partial-thickness PU, Then a moist wound-healing environment should be provided with topical dressings | 2                                                                                | 59[59(40;78)]                   |
| IF a vulnerable elder has a stage 2 or greater pressure ulcer, THEN a topical antiseptic should not be used on the wound | 0                                                                                | -                              |
| Condition                        | Quality indicators                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|---------------------------------|------------------------------------------------------------------------------------|-------------------------------|-----------------------|
| Screening and prevention        | ALL vulnerable elders newly admitted to a physician practice should receive the elements of a comprehensive geriatric assessment within 6 months | 1                             | 14                    |
|                                 | ALL vulnerable elders newly admitted to a physician practice should receive within 6 months recommendations from the comprehensive geriatric assessment | 1                             | 44                    |
|                                 | IF the elements of a comprehensive geriatric assessment are performed, THEN follow up should assure the implementation of recommendations | 1                             | 100                   |
|                                 | ALL vulnerable elders should be screened to detect problem drinking and hazardous drinking by taking a history of alcohol use or by using standardized screening questionnaires (e.g., CAGE, AUDIT) at least once | 1                             | 49                    |
|                                 | ALL vulnerable elders should receive screening for tobacco use and nicotine dependence | 1                             | 83                    |
|                                 | IF a vulnerable elder uses tobacco regularly, THEN he or she should be offered counseling or pharmacologic therapy to stop tobacco use at least once | 3                             | 65[56(38;83)]         |
|                                 | ALL vulnerable elders should receive an assessment of their activity level and be provided with counseling to promote regular physical activity at least once | 2                             | 43[43(12;74)]         |
|                                 | ALL vulnerable elders should be offered screening for colorectal cancer at least once with fecal occult blood testing or should have had sigmoidoscopy in the past 5 years or colonoscopy in the past 10 years | 1                             | 76                    |
|                                 | IF a female vulnerable elder is younger than age 70 years, THEN she should be offered mammographic screening for breast cancer every 2 years | 1                             | 100                   |
| Stroke and atrial fibrillation  | IF a male vulnerable elder has carotid artery symptoms, receives a diagnosis of TIA or nondisabling stroke, and has had carotid imaging documenting at least 70% carotid stenosis on the side ipsilateral to the hemisphere producing the symptoms, and the medical record does not document that no facility is available with 30-day morbidity and mortality rates of less than 6%, THEN he should receive referral for evaluation for carotid endarterectomy within 4 weeks of the diagnostic study or event, whichever is later | 1                             | [+]                   |
| Condition | Quality indicators | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|--------------------|-------------------------------|------------------------|
| IF a male vulnerable elder has carotid artery symptoms and is diagnosed with TIA or nondisabling stroke, and the medical record does not document that the patient is not a candidate for carotid surgery, THEN a carotid artery imaging study should be performed within 4 weeks | 1 | 100 |
| IF a (vulnerable elder / NH resident -Zingmond09-) has atrial fibrillation (for more than 48 hours and -deleted Zingmond07/Zingmond09-) has any high-risk condition ((impaired left ventricular function; female _75 years of age; hypertension or systolic blood pressure _ 160 mm Hg; previous ischemic stroke, TIA, or systemic embolism) -deleted Zingmond07/Zingmond09-)), THEN (he or she should be offered oral anticoagulation, or antiplatelet therapy / prescribe anticoagulant -Zingmond07-) (if the medical record documents a reason not to give anticoagulant therapy -deleted Zingmond09-) | 3 | 46[23(21;94)] |
| IF a (vulnerable elder / NH resident -Zingmond09-)) has a presumed stroke (with hemispheric symptoms -Zingmond09-), THEN CT or MRI of the head should be performed (before initiation or continuation of thrombolytic treatment, anticoagulant therapy, or antiplatelet therapy -deleted Zingmond09-) | 2 | 79[79(58;100)] |
| IF a vulnerable elder is taking warfarin for atrial fibrillation, THEN the INR should be checked within 4 days of the first dose and at least every 6 weeks | 1 | 67 |
| IF a vulnerable elder is taking warfarin for atrial fibrillation, THEN the INR should be checked at least every 6 weeks | 1 | 64 |
| IF a vulnerable elder has a diagnosis of acute atherothrombotic ischemic stroke or a TIA, THEN antiplatelet treatment should be offered within 48 hours following the stroke or TIA, unless the patient is already receiving anticoagulant treatment | 1 | 100 |
| IF a vulnerable elder has a TIA or stroke, THEN the medical record should document that smoking status was assessed and that smokers were counseled to stop smoking | 1 | 100 |
| Condition | Quality indicators | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|--------------------|-------------------------------|------------------------|
| Quality of elderly care based on the ACOVE set | IF a vulnerable elder is started on thrombolytic therapy for a stroke, THEN all of the following should be true: head CT or MRI should precede initiation of thrombolytic therapy; sulcal effacement, mass effect, edema, or possible hemorrhage should not be present on neuroimaging; time from symptom onset to initiation of thrombolytic therapy should be documented in the medical record and should not exceed 3 hours; absence of absolute contraindications to thrombolysis should be documented in the medical record; tissue plasminogen activator should be used; AND National Institute of Neurological Disorders and Stroke exclusion criteria should not be present | 1 | [*] |
| | IF a vulnerable elder is admitted to the hospital with a diagnosis of acute ischemic or hemorrhagic stroke, THEN he or she should be admitted to a specialized acute or combined acute and rehabilitative stroke unit, or hospital. transferred to a specialized stroke unit if such a unit is available in the hospital | 1 | 50 |
| | NH resident <70 yrs old has a thrombotic CVA or TIA and hypercholesterolemia should be offered treatment to lower cholesterol | 1 | 31 |
| | IF for a vulnerable elder the combined risk of surgery (patient characteristics and hospital or surgeon experience) is 10% or greater, THEN carotid endarterectomy should not be performed | 0 | - |
| Urinary incontinence | ALL vulnerable elders should have documentation of the presence or absence or urinary incontinence during the initial evaluation | 1 | 50 |
| | ALL vulnerable elders should annually have documentation of the presence or absence of urinary incontinence | 1 | 31 |
| | IF a (vulnerable elder / person aged 65 or older -Steel-) has new urinary incontinence that persist for more than 1 month(Gandadesigan) or urinary incontinence at the time of a new evaluation, THEN a targeted history should be obtained that documents each of the following: 1) characteristics of voiding, 2) ability to get to the toilet, 3) previous treatment for urinary incontinence, 4) importance of the problem to the patient, and 5) mental status | 3 | 17[19(11;20)] |
| | IF a (vulnerable elder / person aged 65 or older -Steel-) has new urinary incontinence(Gandadesigan) that persists for more than 1 month (or urinary incontinence at the time of a new evaluation -deleted Steel-), THEN a targeted physical examination should be performed that documents 1) a rectal examination and 2) a genital system examination (including a pelvic examination for women) | 3 | 34 [31(22;50)] |
| Condition | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean[Median(Min, Max)] |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------|
|           | IF a (vulnerable elder / person aged 65 or older -Steel-) has new urinary incontinence (Gandadesigan) that persists for more than 1 month or urinary incontinence at the time of a new evaluation, THEN a dipstick urinalysis (and post-void residual / and/or midstream urine sample -Steel-) should be obtained                      | 3                             | 43[43(13;74)]          |
|           | IF a (vulnerable elder / person aged 65 or older -Steel-) has new urinary incontinence or (or worsening -Gandadesigan-) urinary incontinence at the time of a new evaluation, THEN treatment options should be discussed                             | 3                             | 49[59(26;61)]          |
|           | IF a (cognitively intact -deleted Zingmond09-) (vulnerable elder / NH resident -Zingmond09-) who is capable of independent toileting (has documented stress, urge, or mixed incontinence without evidence of hematuria or high post-void residual / with UI -Zingmond09-), THEN behavioral treatment should be offered | 3                             | 22[13(5;49)]           |
|           | IF a vulnerable elder undergoes surgery or periurethral injections for urinary incontinence, THEN subtracted cystometry should be performed before the procedure        | 1                             | 0                      |
|           | IF a female vulnerable elder has documented stress urinary incontinence caused by isolated intrinsic sphincter deficiency or isolated intrinsic sphincter deficiency with coexistent hypermobility and she undergoes surgical correction, THEN a sling or artificial sphincter procedure should be used | 1                             | 100                    |
|           | IF a vulnerable elder has clinically significant, newly discovered overflow urinary incontinence, and indwelling urethral catheterization is used, THEN there should be documentation that the patient is not a candidate for alternative interventions as a result of severe physical or mental impairments or does not want alternative interventions | 1                             | [*]                   |
| Vision care | Follow up on incontinence                                                                                                                                                                                                | 1                             | 17                     |
| Vision care | Classify type of incontinence in medical record                                                                                                                                                                           | 1                             | 26                     |
| Vision care | NH resident with UI should be on a toileting assistance program                                                                                                                                                        | 1                             | 98                     |
| Vision care | ALL (vulnerable elders / NH resident -Zingmond09-) should be offered an eye evaluation (every 2 years / annually -Zingmond09-) (that includes the essential components of a comprehensive eye examination -deleted Zingmond07-) | 3                             | 69[69(49;86)]          |
| Vision care | IF a vulnerable elder has sudden-onset visual changes, eye pain, corneal opacity, or severe purulent discharge, THEN the patient should be examined within 72 hours by an ophthalmologist | 1                             | 80                     |
| Condition                                                                 | Quality indicators                                                                                                                                                                                                 | Number of studies using the QI | Mean [Median (Min, Max)] |
|---------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|--------------------------|
| IF a vulnerable elder develops progression of a chronic visual deficit that now interferes with his or her ability to carry out needed or desired activities, THEN he or she should have an ophthalmic examination by a person skilled at ophthalmic examination within 2 months | 1                                                                                                                                                    | 100                          |
| IF a vulnerable elder is diagnosed with a cataract, THEN assessment of visual function with respect to his or her ability to carry out needed or desired activities should be performed every 12 months | 1                                                                                                                                                    | 31                           |
| IF a vulnerable elder (NH resident) has a new diagnosis of primary open-angle glaucoma, THEN the initial evaluation of each eye should include the essential components of a comprehensive eye examination AND documentation of the optic nerve appearance, visual field testing, and determination of an initial target pressure | 1                                                                                                                                                    | [*]                         |
| NH resident with new primary open angle glaucoma should have a comprehensive eye exam | 1                                                                                                                                                    | 41 [41(32;50)]               |
| NH resident with primary open angle glaucoma should have appropriate yearly eye exam | 1                                                                                                                                                    | 27                           |
| IF a vulnerable elder with diabetes has a retinal examination, THEN the presence and degree of diabetic retinopathy should be documented | 1                                                                                                                                                    | 88                           |
| IF a (vulnerable elder / NH resident -Zingmond09-) receives a diagnosis of proliferative diabetic retinopathy, THEN a dilated eye examination should be performed at least every 4 months | 3                                                                                                                                                    | 22                           |
| IF a vulnerable elder with diabetes receives a diagnosis of macular edema, THEN a dilated eye examination should be performed at least every 6 months | 2                                                                                                                                                    | 69 [69(39;100)]              |
| IF a (vulnerable elder / person aged 50 or older -Steel-) receives a diagnosis of a cataract that limits the patient's ability to carry out needed or desired activities, THEN cataract extraction should be offered | 2                                                                                                                                                    | 72 [76(57;86)]               |
| IF a (vulnerable elder / NH resident -Zingmond09-) undergoes cataract surgery, THEN (a follow-up ocular examination should occur within 48 hours and -deleted Zingmond07/Zingmond09-) reexamination should occur within 3 months | 3                                                                                                                                                    | 43 [16(14;100)]              |
### Condition Quality indicators

| Condition                        | Quality indicators                                                                                                                                                                                                                                                                                                                                 | Number of studies using the QI | Mean [Median (Min, Max)] |
|----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|--------------------------|
| Cardio-vascular disease          | **IF a person aged 50 or older has had a previous stroke, THEN the patient should be offered antihypertensive medication**                                                                                                                                                                                                                      | 1                             | 65                       |
| Patient-oriented questions       | **Some people with diabetes receive training to help manage their diabetes themselves. Have you ever participated in a course or class about diabetes, or received special training on how you can live with your diabetes from day-to-day?**  
  **How much do you think you know about managing your diabetes? ('just about everything you need to know' or 'most of what you need to know')**  
  **Has a doctor or nurse explained high cholesterol in a way you could understand?**  
  **Have doctors or nurses taken your preferences into account when making treatment decisions about your high cholesterol?**                                                                                                                                   | 1                             | 25 78 49                |
| Condition | Quality indicators                                                                 | Number of studies using the QI | Mean/Median (Min, Max) |
|-----------|-------------------------------------------------------------------------------------|-------------------------------|------------------------|
|           | Has a doctor or nurse explained high blood pressure in a way you could understand at any time since you were first told you had high blood pressure? | 1                             | 68                     |
|           | In general, have doctors or nurses given you any choice about how to treat your high blood pressure? | 1                             | 42                     |
|           | Has any doctor or nurse ever talked to you about what the specific purpose of the treatment for your arthritis or joint pain is? | 1                             | 78                     |
| Condition ID | Conditions                          | # of QI used | # of QIs in each cond. Above 50% | Percentage of QIs above 50% | Proportion(%) of QIs not used (from ACOVEI set) | Mean of the Mean(per QI) per condition |
|-------------|------------------------------------|--------------|----------------------------------|-----------------------------|------------------------------------------------|--------------------------------------|
| 1           | Falls and morbidity disorder       | 13           | 2                                | 0,15                        | 0                                              | 32,7                                 |
| 2           | Dementia                           | 15           | 6                                | 0,40                        | 28                                             | 46,1                                 |
| 3           | Continuity of care                 | 8            | 6                                | 0,75                        | 38                                             | 68,9                                 |
| 4           | Depression                         | 15           | 4                                | 0,27                        | 23                                             | 42,7                                 |
| 5           | Diabetes                           | 12           | 8                                | 0,67                        | 0                                              | 63,2                                 |
| 6           | End of life care                   | 9            | 4                                | 0,89                        | 35                                             | 54,3                                 |
| 7           | Gout                               | 3            | 2                                | 0,67                        | -                                              | 64,0                                 |
| 8           | Hearing loss                       | 4            | 3                                | 0,75                        | 33                                             | 58,7                                 |
| 9           | Heart failure                      | 28           | 12                               | 0,43                        | 7                                              | 51,2                                 |
| 10          | Hospital care                      | 10           | 6                                | 0,60                        | 44                                             | 62,4                                 |
| 11          | Hypertension                       | 9            | 3                                | 0,33                        | 0                                              | 48,4                                 |
| 12          | Ischemic heart disease             | 13           | 2                                | 0,15                        | 0                                              | 32,2                                 |
| 13          | Malnutrition                       | 8            | 5                                | 0,63                        | 12                                             | 61,6                                 |
| 14          | Medication management              | 16           | 12                               | 0,75                        | 8                                              | 68,3                                 |
| 15          | Osteoarthritis                     | 14           | 3                                | 0,21                        | 0                                              | 36,3                                 |
| 16          | Osteoporosis                       | 10           | 1                                | 0,10                        | 0                                              | 37,6                                 |
| 17          | Pain management                    | 12           | 5                                | 0,42                        | 0                                              | 47,6                                 |
| 18          | Pneumonia                          | 7            | 4                                | 0,57                        | 36                                             | 69,3                                 |
| 19          | Pressure ulcer                     | 16           | 7                                | 0,44                        | 9                                              | 46,5                                 |
| 20          | Screening and prevention           | 9            | 5                                | 0,56                        | 0                                              | 63,8                                 |
| 21          | Stroke and atrial fibrillation     | 11           | 6                                | 0,55                        | 10                                             | 70,8                                 |
| 22          | Urinary incontinence               | 13           | 2                                | 0,15                        | 0                                              | 40,6                                 |
| 23          | Vision care                        | 15           | 8                                | 0,53                        | 13                                             | 62,6                                 |
| 24          | Cardiovascular disease             | 1            | 1                                | 1,00                        | -                                              | 65,4                                 |
| 25          | Patient-oriented questions         | 7            | 4                                | 0,57                        | -                                              | 59,7                                 |
### Table S2

Measured mean pass rate of QIs per condition and proportion of unique (matched) QIs with mean score above 50% per condition.

| Conditions      | Reference                          | Settings                      | Patient population          | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|-----------------|------------------------------------|-------------------------------|-----------------------------|------------|-------------------|------------------------------------------------------------------|
| Continuity of care | Wenger et al.[21] (2003)          | Two managed care organizations (US) | 372 community-dwelling VE | 8          | 80%               | 75% (6/8)                                                       |
|                  | Zingmond et al.[15] (2007)        | PC (US)                       | Community-dwelling elderly >75 yrs | 1          | 76%               |                                                                  |
| Dementia        | Wenger et al.[21] (2003)          | Two managed care organizations (US) | 372 community-dwelling VE | 9          | 35%               | 40% (6/15)                                                       |
|                  | Zingmond et al.[25] (2009)        | NH (US)                       | 21657 NH residents          | 2          | 9%                |                                                                  |
|                  | Zingmond et al.[15] (2007)        | PC (US)                       | Community-dwelling elderly >75 yrs | 3          | 11%               |                                                                  |
|                  | Arora et al.[24] (2007)           | Academic medical center (US)  | 328 VE admitted at a general medicine ward‡ | 5          | 31%               |                                                                  |
|                  | Wenger et al.[26] (2009)          | Two managed care organizations (US) | Community dwelling elderly >75 yrs | 7          | 44% (in inter. group) vs 41% |                                                                  |
| Depression       | Wenger et al.[21] (2003)          | Two managed care organizations (US) | 372 community-dwelling VE | 13         | 31%               | 26% (4/15)                                                       |
|                  | Steel et al.[17] (2008)           | Private households (UK)-PC    | 8688 participants in the English longitudinal study of ageing | 3          | 64%               |                                                                  |
|                  | Zingmond et al.[25] (2009)        | NH (US)                       | 21657 NH residents          | 6          | 16%               |                                                                  |
|                  | Zingmond et al.[15] (2007)        | PC (US)                       | Community-dwelling elderly >75 yrs | 5          | 33%               |                                                                  |
| Conditions                        | Reference                          | Settings                          | Patient population                  | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|----------------------------------|------------------------------------|-----------------------------------|-------------------------------------|------------|-------------------|---------------------------------------------------------------|
| Diabetes mellitus                | Wenger et al. [21] (2003)          | Two managed care organizations (US) | 372 community-dwelling VE           | 10         | 57%               | 58% (7/12)                                                    |
|                                 | Steel et al. [17] (2008)           | Private households (UK)-PC         | 8688 participants in the             | 5          | 74%               |                                                               |
|                                 |                                    |                                   | English longitudinal study of ageing |            |                   |                                                               |
|                                 | Zingmond et al. [25] (2009)        | NH (US)                           | 21657 NH residents                  | 3          | 49%               |                                                               |
|                                 | Zingmond et al. [15] (2007)        | PC (US)                           | Community-dwelling elderly >75 yrs  | 4          | 56%               |                                                               |
| End-of-life care                 | Wenger et al. [21] (2003)          | Two managed care organizations (US) | 372 community-dwelling VE           | 8          | 9%                | 44% (4/9)                                                     |
|                                 | Zingmond et al. [25] (2009)        | NH (US)                           | 21657 NH residents                  | 2          | 89%               |                                                               |
| Falls, instability and physical function | Rubenstein et al.* [12] (2004)     | Two managed care organizations (US) (US) | 372 VE                                 | 8          | 3 -71%            | 15% (2/13)                                                   |
|                                 | Wenger et al. [21] (2003)          | Two managed care organizations (US) | 372 community-dwelling VE           | 8          | 34%               |                                                               |
|                                 | Steel et al. [17] (2008)           | Private households (UK)-PC         | 8688 participants in the             | 2          | 44%               |                                                               |
|                                 |                                    |                                   | English longitudinal study of ageing |            |                   |                                                               |
|                                 | Zingmond et al. [25] (2009)        | NH (US)                           | 21657 NH residents                  | 1          | 31%               |                                                               |
| Conditions       | Reference          | Settings                                      | Patient population            | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|------------------|--------------------|-----------------------------------------------|------------------------------|------------|-------------------|------------------------------------------------------------------|
| Quality of elderly care based on the ACOVE set               |                    |                                               |                |             |                   |                                                                  |

| Arora et al. [24] (2007) | Academic medical center (US) | 328 VE admitted at a general medicine ward † | 2 | 83% |                  |
| Wenger et al. [26] (2009) | Two community medical groups (US) | Community dwelling elderly >75 yrs (357 at intervention sites and 287 at control sites) | 5 | 44% (in inter. group) vs. 23% | |
| Hearing loss Wenger et al. [21] (2003) | Two managed care organizations (US) | 372 community-dwelling VE | 4 | 77% | 75%(3/4) |
| Steel et al. [17] (2008) | Private households (UK)-PC | 8688 participants in the English longitudinal study of ageing | 2 | 79% | |
| Heart failure Wenger et al. [21] (2003) | Two managed care organizations (US) | 372 community-dwelling VE | 12 | 71% | 46%(13/28) |
| Asch et al. [13] (2005) | 4 organizations participating in IHI BTS for CHF and 4 compatible comparison organizations (US) | 489 patients | 23 | Median pass rates for all the QIs increased from 57 (baseline) to 61%(after BTS) | |
| Zingmond et al. [25] (2009) | NH (US) | 21657 NH residents | 6 | 23% | |
| Zingmond et al. [15] (2007) | PC (US) | Community-dwelling elderly >75 yrs | 6 | 63% | |
| Hospital care Wenger et al. [21] (2003) | Two managed care organizations (US) | 372 community-dwelling VE | 8 | 61% | 60%(6/10) |
| Zingmond et al. [25] (2009) | NH (US) | 21657 NH residents | 1 | 12% | |
| Conditions       | Reference                        | Settings                      | Patient population                                      | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|------------------|----------------------------------|-------------------------------|----------------------------------------------------------|------------|-------------------|-----------------------------------------------------------------|
| Hypertension     | Wenger et al.[21] (2003)         | Two managed care organizations (US) | 372 community-dwelling VE                                | 8          | 77%               | 33%(3/9)                                                        |
|                  | Steel et al.[17] (2008)          | Private households (UK)-PC    | 8688 participants in the English longitudinal study of ageing | 1          | 72%               |                                                                 |
|                  | Zingmond et al.[25] (2009)       | NH (US)                       | 21657 NH residents                                       | 4          | 38%               |                                                                 |
|                  | Zingmond et al.[15] (2007)       | PC (US)                       | Community-dwelling elderly >75 yrs                       | 3          | 51%               |                                                                 |
| Ischemic heart disease | Wenger et al.[21] (2003)         | Two managed care organizations (US) | 372 community-dwelling VE                                | 13         | 55%               | 15%(2/13)                                                       |
|                  | Steel et al.[17] (2008)          | Private households (UK)-PC    | 8688 participants in the English longitudinal study of ageing | 5          | 83%               |                                                                 |
|                  | Zingmond et al.[25] (2009)       | NH (US)                       | 21657 NH residents                                       | 3          | 22%               |                                                                 |
|                  | Zingmond et al.[15] (2007)       | PC (US)                       | Community-dwelling elderly >75 yrs                       | 6          | 42%               |                                                                 |
| Malnutrition     | Wenger et al.[21] (2003)         | Two managed care organizations (US) | 372 community-dwelling VE                                | 7          | 47%               | 62%(5/8)                                                        |
|                  | Zingmond et al.[25] (2009)       | NH (US)                       | 21657 NH residents                                       | 2          | 77%               |                                                                 |
| Conditions       | Reference               | Settings                                      | Patient population   | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|------------------|-------------------------|-----------------------------------------------|----------------------|------------|--------------------|------------------------------------------------------------------|
| Osteoporosis     | Wenger et al.[21] (2003)| Two managed care organizations (US)           | 372 community-dwelling VE | 9          | 36%                | 21%(3/14)                                                        |
|                  | Steel et al.[17] (2008) | Private households (UK)-pc                    | 8688 participants in the English longitudinal study of ageing | 2          | 53%                |                                                                  |
|                  | Zingmond et al.[25] (2009)| NH (US)                                       | 21657 NH residents   | 2          | 27%                |                                                                  |
|                  | Zingmond et al.[15] (2007)| PC (US)                                       | Community-dwelling elderly >75 yrs | 1          | 39%                |                                                                  |
| Osteoarthritis   | Cadogan et al.[11] (2005)| 38 NHs (50-200 beds each) (US)                | 542 NH residents     | 3          | 26-46%             | 10%(1/10)                                                        |
|                  | Wenger et al.[21] (2003)| Two managed care organizations (US)           | 372 community-dwelling VE | 11         | 31%                |                                                                  |
|                  | Ganz et al.[16] (2006) | Subgroup of 2 medical groups One primary care group and 1 special group (US) | 339 elderly arthritis patients (>75 yrs) | 8          | Overall QI pass rate: 57% pass rate range: 27 — 73% |                                                                  |
|                  | Steel et al.[17] (2008) | Private households (UK) -PC                  | 8688 participants in the English longitudinal study of ageing | 4          | 29%                |                                                                  |
| Pain management  | Zingmond et al.[25] (2009)| NH (US)                                       | 21657 NH residents   | 1          | 27%                |                                                                  |
|                  | Cadogan et al.[11] (2005)| 38 NHs (50-200 beds each) (US)                | 542 NH residents     | 9          | 10-99%,            | 58%(7/12)                                                        |
|                  | Chodosh et al.[22] (2004)| Two managed care plans (US)                   | 372 community-dwelling VE | 11         | 10 — 99%           |                                                                  |
| Conditions          | Reference                        | Settings                              | Patient population                  | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|---------------------|----------------------------------|---------------------------------------|-------------------------------------|------------|-------------------|--------------------------------------------------------------------|
| Pressure Ulcer      | Bates-Jensen et al.[18] (2003)   | Eight NHs (US)                        | 191 NH residents                    | 9          | 0-98%             | 43% (7/16)                                                         |
|                     | Wenger et al.[21] (2003)         | Two managed care organizations (US)   | 372 community-dwelling VE          | 9          | 41%               |                                                                    |
|                     | Arora et al.[24] (2007)          | Academic medical center (US)          | 328 VEs admitted at a general medicine ward † | 5          | 76%               |                                                                    |
| Pneumonia           | Wenger et al.[21] (2003)         | Two managed care organizations (US)   | 372 community-dwelling VE          | 7          | 49%               | 57% (4/7)                                                          |
| Screening and       | Wenger et al.[21] (2003)         | Two managed care organizations (US)   | 372 community-dwelling VE          | 9          | 67%               | 55% (5/9)                                                          |
| prevention          |                                   |                                       |                                     |            |                   |                                                                    |
| Smoking             | Steel et al.[17] (2008)          | Private households (UK)-PC            | 8688 participants in the English longitudinal study of ageing | 1          | 74%               |                                                                    |
| Stroke and          | Wenger et al.[21] (2003)         | Two managed care organizations (US)   | 372 community-dwelling VE          | 10         | 82%               | 54% (6/11)                                                         |
| Conditions          | Reference            | Settings                        | Patient population                                      | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|---------------------|----------------------|---------------------------------|---------------------------------------------------------|------------|-------------------|-------------------------------------------------------------------|
|                     | Steel et al.[17]     | Private households (UK)-PC      | 8688 participants in the English longitudinal study of ageing | 1          | 65%               |                                                                   |
|                     | Zingmond et al.[25]  | NH (US)                         | 21657 NH residents                                      | 3          | 20%               |                                                                   |
|                     | Zingmond et al.[15]  | PC (US)                         | Community-dwelling elderly >75 yrs                      | 1          | 23%               |                                                                   |
| Urinary Incontinence| Schnelle et al.[10]  | 18 NHs, 50-200 beds each (US)   | 426 incontinent residents                               | 9          | 0-98%.            | 23% (3/13)                                                       |
|                     | Gnanadesigan et al.[20] (2004) | 2 managed care plans (US)     | 372 community-dwelling VE                               | 7          | 13-59%            |                                                                   |
|                     | Wenger et al.[21]    | Two managed care organizations (US) | 372 community-dwelling VE                               | 10         | 29%               |                                                                   |
|                     | Steel et al.[17]     | Private households (UK)-PC      | 8688 participants in the English longitudinal study of ageing | 4          | 51%               |                                                                   |
|                     | Zingmond et al.[25]  | NH (US)                         | 21657 NH residents                                      | 2          | 97%               |                                                                   |
|                     | Wenger et al.[26] (2009) | Two community medical groups (US) | Community dwelling elderly >75 yrs (357 at intervention sites and 287 at control sites) | 6          | 37% (in intervention group) vs. 22% |                                                                   |
| Vision              | Wenger et al.[21]    | Two managed care organizations (US) | 372 community-dwelling VE                               | 13         | 79%               | 53% (8/15)                                                       |
| Conditions | Reference | Settings | Patient population | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|------------|-----------|----------|-------------------|------------|-------------------|----------------------------------------------------------------|
| Steel et al. [17] (2008) | Private households (UK)-PC | 8688 participants in the English longitudinal study of ageing | 1 | 58% | |
| Zingmond et al. [25] (2009) | NHs in 19 California counties (US) | 21657 NH residents | 5 | 37% | |
| Zingmond et al. [15] (2007) | PC (US) | Community-dwelling elderly >75 yrs | 5 | 44% | |
| Wenger et al. [21] (2003) | Two managed care organizations (US) | 372 community-dwelling VE | 13 | 81% | 75%(12/16) |
| Zingmond et al. [25] (2009) | NH (US) | 21657 NH residents | 7 | 90% | |
| Zingmond et al. [15] (2007) | PC (US) | Community-dwelling elderly >75 yrs | 8 | 83% | |
| Higashi et al.* [23] (2004) | Two managed care organizations (US) | 372 community-dwelling VE | 43 | Overall pass rate: 50%. Per domain: PIM; 97% AIM; 81% for ECD; 64% MM | - |
| Conditions | Reference | Settings | Patient population | No. of QIs | Reported pass rate | % of QIs with mean score > 50% among unique QIs (No.) per condition |
|------------|-----------|----------|--------------------|------------|-------------------|----------------------------------------------------------------|
| Spinewine et al.[14] (2007) | 27 Acute GEM unit (Belgium) | 203 hospitalised patients aged 70+ yrs | 7 | 7 QIs for 6 conditions focusing on underuse: Osteoporosis (28%), Atrial fibrillation (61%), Ischemic heart disease (58%), Diabetes mellitus (60%), Heart failure (58%, 31%), and Myocardial infarction (39%). | |
| Mikuls et al.[19] (2005) | All gout patients in an General Practice (US) | 63105 gout patients | 3 | QI pass rates range for allopurinol use in treatment of gout and asymptomatic hyperuricaemia: 25 to 57% | |

‡: The pass rate is reported for both delirium and dementia. †: These QIs were about physical functioning. QI: quality indicator, VE: vulnerable elder(s), NH: Nursing home, PC: Primary care, PIM: Prescribing indicated Mediations, AIM: Avoiding Inappropriate Medication, ECD: Education, Continuity, and Documentation, MM: Medication Monitoring, GEM: Geriatric Evaluation and Management, CHF: Chronic Heart Failure, IHI BTS: Institute of Healthcare Improvement's Breakthrough Series, PC: Primary Care.

*: The same patient population and dataset was used as in the Wenger et al. study [21], for these common QIs we only considered the pass rates reported in [21] for our analysis.
4.4 Quality of in-hospital pharmaceutical care of elderly assessed by quality indicators is not associated with survival and readmissions

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Abstract

Background: Since medication-related problems are highly prevalent among vulnerable elderly patients due to polypharmacy, age-related physiological changes, non-adherence and co-morbidity, assessment of the quality of pharmaceutical care in order to improve the pharmaceutical care provided to elderly patients is important. Because of the shortcomings of unstructured chart review followed by expert opinion judgment, the traditional method for measuring medication safety, other strategies have to be considered. Focusing on processes instead of outcomes provides an alternative strategy to measure medication safety. For this purpose the Academic Medical Center (AMC) developed an explicit screening tool consisting of 87 quality indicators.

Objective: The aim of this research project was to assess the quality of pharmaceutical care provided to vulnerable elderly patients admitted to the internal medicine ward at the AMC. A secondary objective was to examine the association between quality of pharmaceutical care and survival, readmission rate.

Methods: A retrospective cohort study in a tertiary 1002-bed teaching hospital. Elderly patients who used more than five drugs and who were admitted to the Internal Medicine ward between March and December 2007 were included. Quality of pharmaceutical care received by patients was measured by a set of 87 quality indicators. Data on readmissions within 90 days after discharge and death within 500 days after discharge were obtained.

Results: The median pass rates for the four domains ‘Using indicated medication’, ‘Avoiding inappropriate medication’, ‘Continuity and documentation’ and ‘Medication monitoring’ were 63.6%, 100%, 20.3% and 37.3% respectively. The 200 participating patients had a mean quality score of 42.9%, SD 13.4%. After adjustment for potential confounders no difference was found in survival 500 days after discharge between patients with a low and high quality score (hazard ratio=1.351, p=0.237). A difference in readmission rate and mortality 90 days after discharge was not found either (p=0.516).

Conclusions: The quality of pharmaceutical care of the elderly was insufficient. This research project demonstrated that improvements in 3 out of 4 domains of pharmaceutical care are needed. According to the indicators a better quality of pharmaceutical care is not associated with an improved 500-day survival and fewer readmissions within 90 days. The vulnerable elderly patients received, on average, less than half of the pharmaceutical care recommended. The set of process indicators is useful, but will be further developed by selecting indicators with sufficient distinctiveness (high number
of patients, low success rate) and study clusters of indicators that show a relationship with outcomes.

Introduction

People over the age of 65 years have a higher prevalence of chronic illnesses, disabilities and dependency use medication more frequently than younger people\(^1\)\(^2\). Although pharmacotherapy is an essential component of medical treatment for elderly patients, medication is also responsible for many adverse events in this age group\(^3\)\(^4\), resulting in patient harm and increased costs\(^5\). Many elderly patients take multiple drugs for the treatment of several conditions. This polypharmacy is often responsible for an increased risk of adverse drug events (ADEs) in older adults\(^6\). Furthermore, elderly develop altered pharmacokinetics and -dynamics and often have multiple co-morbidities with sometimes conflicting medical treatment\(^7\). The complex characteristics of ageing and geriatric medicine mentioned above affect medication prescribing and render the selection of appropriate medication a challenging process.

As a consequence of the difficulties involved in prescribing medication to elderly patients (potentially) inappropriate prescribing in the elderly is highly prevalent in the United States and Europe, ranging from 12% in community-dwelling elderly to 40% in nursing home residents\(^8\). Inappropriate prescribing is defined as the use of medicines that introduce a significant risk of an ADE where there is evidence for an equally or more effective but lower-risk alternative therapy available for treating the same condition. Inappropriate prescribing encompasses also the use of medicines at a higher frequency and for longer than clinically indicated, the use of multiple medicines that have known drug-drug interactions and the under-use of beneficial medicines that are clinically indicated but not prescribed\(^8\). There is a high variety in incidence rates of ADEs among different studies. The main cause is probably the poor reliability of the available methods to measure the incidence rate of ADEs\(^9\)\(^10\). Because of the shortcomings of chart review, other strategies to measure quality of care should be considered. Focusing on processes instead of outcomes provides an alternative strategy to measure medication safety. It can be beneficial to measure processes instead of outcomes, because processes are under relatively greater control of providers, need a shorter time frame and do not require statistical adjustment for severity of illness\(^11\).

Earlier, we described the development of a 87 item quality indicator (QI) set meant to assess the quality of in-hospital pharmaceutical care of Dutch elderly\(^12\). This set is based on the original ACOVE indicators\(^13\)\(^14\) and showed good feasibility and excellent
interrater reliability. However, our indicator set has, up till now, not been applied to a representative patient population to assess the quality of in-hospital pharmaceutical care.

Also, in order to be a meaningful measure of quality, a process of care has to be related to improved patient outcomes. For many quality indicators the association between processes of care and improved patient outcomes is based on clinical evidence and professional opinion. However, the association between performance of processes and health outcomes is a largely untested assumption\(^\text{[15]}\). Literature on the association between performance of process measures during usual care and subsequent patient outcomes is scarce. Only a few studies are available\(^\text{[15,16]}\). These studies however, used a different QI set and/or a different elderly population. Their findings therefore cannot be extrapolated to our QI set, which was developed specifically for in-hospital pharmaceutical care, for the Dutch healthcare setting, and which can be assessed solely by using documented medical information\(^\text{[12]}\).

The objective of this study was to assess the quality of pharmaceutical care of hospitalised elderly patients using at least five drugs by a quality indicator set and to determine the association between the measured quality and survival outcomes and readmissions.

### Methods

#### Design

The study was designed as a retrospective cohort study.

#### Population

Patients of 65 years and older with at least five drugs, and longer than 24 hours admitted on an internal medicine department were selected in the period from March to December 2007. Exclusion criteria were a planned admission for chemotherapy, transplantation, radiotherapy or a transfer from another hospital or department. The study was approved by the Medical Ethics Committee.

#### Measurements

For each patient quality indicators were scored using medical record data and discharge letters (see Appendix for complete indicator set). The medical data from the admitted patients were assessed with a standardized method. A Case Report Form (CRF) was
developed to collect data from medical charts. This CRF contained a flow-chart on how to collect data from medical records and was linked to an instructive handbook. This had to guarantee an objective and consistent measurement and therefore minimal interrater variability. Each indicator had a pass rate calculated:

\[
\text{Pass rate per quality indicator} = \frac{\text{Number of eligible patients who passed the quality indicator}}{\text{Number of eligible patients}} 
\]

**Figure 1.** Quality indicator pass rate calculation

To be able to better analyze and later improve the quality of pharmaceutical care the indicators were grouped into four domains\cite{[14]}: ‘Prescription of indicated drugs’, ‘Avoidance of inappropriate drugs’, ‘Continuity and documentation of care’ and ‘Monitoring of medication’. For these domains, the median pass rate was calculated. These domains correspond to the 4 steps of prescribing medication: choosing the right drug; providing medication along with proper documentation and education in concert with the care of other physicians; and follow-up of the patient.

Furthermore, a patient Quality Score was calculated for each patient to be able to have a measure of quality for an individual patient:

\[
\text{Quality score per patient} = \frac{\text{Number of quality indicators passed}}{\text{Number of quality indicators for which the patient was eligible}} 
\]

**Figure 2.** Patient quality score calculation

Data analysis

Descriptive statistics were applied on the measurements of the quality of in-hospital pharmaceutical care.

The association between the quality of in-hospital pharmaceutical care and the outcomes survival 500 days after admission and readmission within 90 days was assessed by dividing the quality scores of all patients into a ‘high score’ (≥ median quality score) and a ‘low score’ (≤ median quality score) group. Kaplan-Meier survival
curves for survival and time to readmission for both groups were made. In the analysis in which readmissions were examined, death within 90 days was also seen as an event. The log-rank test was used to examine differences in readmissions. For survival, an adjusted analysis using the Cox proportional-hazards survival model was applied. Co-variates were age, gender, hospital stay, emergency admission, active malignancy, and the number of (co-)morbidities. SPSS (version 17) was used for the statistical analyses.

Results

Quality of in-hospital pharmaceutical care

A total of 200 patients fulfilled the inclusion criteria and were available for quality-of-pharmaceutical-care assessment.

The vulnerable elderly patients had a mean age of 76.6 (SD 7.92) years; exactly half of them were women and the mean length of hospital stay was 8.0 days. During the study period from March 2007 to December 2008, 69 (34.5%) patients died.

More than half of the patients had hypertension and about 40% had diabetes and/or ischemic heart disease. In addition, about 30% of patients had arrhythmia and/or heart failure. Pain medication was the most frequently used drug class among participating patients (54.5%). Sleeping medication and coumarins were used by 40% and 30% of patients respectively. Patient characteristics are summarized in table 1.

A total of 92% of the 87 quality indicators was scored at least once.

Indicator pass rates per domain are shown in appendix 1. The indicators were stratified into 4 domains of pharmaceutical care. The median pass rates for the 4 different domains are shown in table 2.

The ‘prescribing indicated medication’ domain contained 39 quality indicators, with individual pass rates ranging from 0% to 100%. The median pass rate for the first domain was 63.6%. Notable among these quality indicators was that only 26.5% of patients that had a transient ischaemic attack (TIA) or stroke (and no history of atrial fibrillation) received prophylaxis with acetyl salicylic acid in combination with dipyridamole. Drugs to prevent osteoporosis were underused; only 17.9% of patients taking corticosteroids (≥ 7.5 mg prednisolone or equivalent) for more than 1 month were offered calcium, vitamin D and a biphosphonate. 63.6% patients at high risk for venous thrombo-embolism (VTE) received VTE prophylaxis with a low molecular weight heparin. Approxi-
Table 1. Patient Characteristics of the entire population and of the patient groups with a quality score above and below the median

| Variable                                 | Patients (n=200) | High quality score (>median) n=102 | Low quality score (<median) n=98 | p-value |
|------------------------------------------|------------------|------------------------------------|----------------------------------|---------|
| Age (mean ± SD)                          | 76.6 ± 7.9       | 77.7 ± 8.1                         | 75.5 ± 7.7                       | NS$     |
| Gender (% Female)                        | 50.0             | 52.9                               | 46.9                             | NS¤     |
| Length of stay (days) (mean ± SD (median; range)) | 8.0 ± 7.7        | 9.2 ± 8.1                           | 6.7 ± 7.2                        | 0.03$   |
| Readmissions within 90 days after discharge (%) | 29.5             | 24.5                               | 34.7                             | NS¤     |
| Number of medications at admission (mean ± SD (median; range)) | 8.3 ± 3.1        | 8.6 ± 3.1                           | 7.9 ± 3.0                        | NS$     |
| Number of co-morbidities (mean ± SD (median; range)) | 3.1 ± 1.9        | 3.3 ± 1.9                           | 2.8 ± 1.8                        | NS$     |
| Acute admissions (%)                     | 67.0             | 62.7                               | 71.4                             | NS¤     |
| Active malignancy (%)                    | 24.0             | 28.4                               | 19.4                             | NS¤     |
| Morbidity* (%)                           |                  |                                    |                                  |         |
| Hypertension                             | 57.0             | 62.7                               | 51.0                             | NS¤     |
| Diabetes                                 | 39.5             | 37.3                               | 41.8                             | NS¤     |
| Ischemic heart disease                   | 38.5             | 42.2                               | 34.7                             | NS¤     |
| Arythmias                                | 31.0             | 30.4                               | 31.6                             | NS¤     |
| Heart failure                            | 28.0             | 29.4                               | 26.5                             | NS¤     |
| Medication# (%)                         |                  |                                    |                                  |         |
| Pain medication                          | 54.5             | 68.6                               | 39.8                             | 0.00¤   |
| Sleep medication                         | 41.5             | 52.9                               | 29.6                             | 0.00¤   |
| Cumarins                                 | 25.0             | 19.6                               | 30.6                             | NS¤     |
| Opioids                                  | 29.5             | 36.3                               | 22.4                             | 0.03¤   |
| Corticosteroids                          | 21.5             | 21.6                               | 21.4                             | NS¤     |
| Digoxin                                  | 17.5             | 24.5                               | 10.2                             | 0.01¤   |

Number of co-morbidities of the 15 co-morbidities measured: osteoarthritis, arythmias, CVA, delirium, dementia, depression, diabetes, heart failure, hypertension, ischemic heart disease, gout, falls, osteoporosis, Parkinson's disease, pneumonia. Sorted by size.

# Medication groups measured by quality indicators. Sorted by size

$ calculated by independent samples T-test

¤ calculated by Pearson Chi-square test

NS: not significant

# Medication groups measured by quality indicators. Sorted by size

$ calculated by independent samples T-test

¤ calculated by Pearson Chi-square test

NS: not significant
Approximately half of the patients in whom ACE-inhibitor or AT-2 receptor blocker therapy were indicated because of hypertension and renal parenchymal disease (creatinine > 150 µmol or microalbuminurea) did receive these drugs. All patients using a NSAID and at risk for an adverse event were receiving adequate prophylaxis with a proton-pump inhibitor or misoprostol. In addition, most patients (95.5%) received haloperidol when diagnosed with delirium.

The ‘avoiding inappropriate medication’ domain contained 14 quality indicators. The median pass rate was 100%, indicating that few inappropriate drugs were prescribed. The lowest pass rate in this domain pertained to the use of strong anticholinergic drugs. One out of 2 patients received a drug with strong cholinergic effects despite available alternatives. All other quality indicators had pass rates of 91.6% and higher.

In the ‘continuity and documentation’ domain 26 quality indicators were included. The pass rates ranged from 0 to 100% with a median pass rate of 20.3%. When an elderly patient was admitted to the hospital, the evaluation of (differential) diagnoses, pre-hospital medication and a current therapy plan was almost always documented in the patient’s medical record within one day post-admission. Patients were (according to the documentation), however, not or incidentally screened for depression, delirium and dementia when admitted to the hospital. Furthermore, the advice to evaluate the response to a drug started during hospital admission within three months was missing in every discharge letter. A clearly defined indication for a newly prescribed drug was found in only half of the cases. About 75% of the discharge letters was incomplete, for example information on medication at admission or discharge was missing, or not sent to the outpatient physician or nursing home within two weeks. Furthermore, reasons for changes in pre-hospital medication or new drugs were included in only 36% of the discharge letters. More than half of the patients who have been prescribed an ocular therapeutic regimen before hospital admission did not continue to receive this regimen in the hospital.

The fourth domain contained 8 quality indicators related to medication monitoring. Six out of the eight quality indicators had at least one eligible patient. The pass rates ranged

| Domain                               | Median pass rate (%) | Median eligible patients |
|--------------------------------------|----------------------|-------------------------|
| 1 Using indicated medication         | 63.6 (0.0-100.0)     | 9 (1-165)               |
| 2 Avoiding inappropriate medication  | 100.0 (50.0-100.0)   | 13 (2-100)              |
| 3 Continuity and documentation       | 20.3 (0.0-100.0)     | 32.5 (1-200)            |
| 4 Medication monitoring              | 37.3 (30.0-100.0)    | 4.5 (2-33)              |
from 30.0% to 100%, with a median pass rate of 37.3%. Electrolyte and renal function monitoring after initiating therapy with diuretics and ACE-inhibitors was adequate in a third of the cases. About 80% of the patients on a maintenance dose digoxin did not receive more than the recommended maximal dosage of 0.125 mg a day. The possible causes of supra-therapeutic INR were evaluated and a dosage adjustment was made for about 40% of the patients with an INR higher than the advised range.

Comparison of the domains showed that quality indicators related to avoiding inappropriate medication generally achieved the highest pass rates. Most quality indicators in the other 3 domains had lower pass rates with large variations in individual quality indicator pass rates.

The lowest median pass rate was found for the ‘continuity and documentation’ domain.

Association of measured quality with survival and readmissions

Patients received an average of 42.9% of the care recommended in the indicators (based on patient’s quality score). The average quality score in the high score group was 53.6% in the low score group, 31.8%. Characteristics of both groups are shown in Table 1 column 2 and 3.

![Figure 3. Kaplan-Meier Survival curves for 500 days survival after admission (A) and readmission or dead after 90 days (B) (unadjusted)](image-url)
A statistically significant difference in mean length of hospital stay was identified after splitting the sample in half on the basis of median quality score. Patients with a high quality score stayed on average 2.5 days longer in the hospital than patients with a low quality score. In addition, patients with a high quality score were using pain medication, sleeping medication, opioids and digoxin more frequently than patients with a low quality score. The other patient characteristics showed no statistically significant differences between patients with a high and low quality score.

The survival of 500 days after admission were 58.8% and 72.4% for patients in respectively the high score group and low score group (Figure 3A). After adjustment for covariates, there was no significant association between high patient mortality score and more quality (hazard ratio=1.351, p=0.237). The percentage of patients that had not been readmitted after 90 days or deceased was 51.0% for the high score group and 57.1% for patients for the lower score group (Figure 3B). The difference was not significant (p=0.516).

Discussion

The quality of in-hospital pharmaceutical care of the elderly is insufficient. Furthermore, according to the indicators a better quality of pharmaceutical care is not associated with an improved 500-day survival and fewer readmissions within 90 days.

Quality of pharmaceutical care

Improvements are needed in prescribing indicated medications, documentation and continuity of care and monitoring of medication. The prescription of inappropriate medicines is not a problem. This is in line with findings of other researchers. Higashi et al.[14] evaluated the quality of pharmaceutical care for community-dwelling high-risk patients 65 years of age or older in 2 managed care organizations. They concluded that improvements in medication management should focus on prescribing indicated medication and avoiding adverse events by monitoring, documentation, education and continuity. In both studies the highest overall pass rate was found for the ‘avoiding inappropriate medication’ domain (100% vs. 97% by Higashi et al.). The median pass rate for the ‘prescribing indicated medication’ domain was slightly higher in our study (63.6%) than the overall pass rate in Higashi’s study (50%). Overall pass rates for the ‘continuity and documentation’ and ‘medication monitoring’ domains were far higher in the study by Higashi et al. (81% and 64%) than in this research project (20.3% and 37.3%). The differences in the overall pass rates could be explained by the different health care settings studied (hospital vs. primary care/managed care). The patients in the study
by Higashi were probably treated for a longer time period by one or more physicians, hence enabling better continuity of care, documentation, and better monitoring of therapy.

The underuse of indicated medication is in line with previous studies which demonstrated that elderly patients are less likely to receive potentially beneficial medication than younger patients [18-20]. Explanations for underuse of indicated medication in elderly patients might be the physicians’ fear of polypharmacy or the perception that the elderly patients being treated are going to die in the near future anyway [14].

Our approach had certain limitations. Information bias may have occurred since the scoring of the indicators depended on the extent to which information was recorded. Care could have been delivered, but not or incorrectly been documented. This could have caused a lower quality score. It is known that chart abstraction underestimates the true quality of care [17]. Incomplete documentation itself causes also low pass rates in the ‘continuity and documentation’ domain which causes a further decrease in quality score. Another limitation is the sometimes low number of patients eligible for a specific indicator. For forty indicators there were less than 10 patients eligible, so drawing conclusions should be done with caution.

Additionally, this study was conducted in one Dutch academic institution; therefore our results could be limitedly generalizable.

Survival and readmission

No significant differences were found between the high (≥ median) and low (< median) quality score groups with regard to both outcomes. Higashi et al. reported an association between a high quality of care and improved survival. However, this association was significant only after 500 days, and the indicators focused mainly on the primary care [15]. Since Higashi et al. did not detect any difference in survival within 500 days either, the 500-day time frame might have been too short to detect a difference between patients with higher and lower quality scores. However, recently Arora et al. found an association between 1 year survival and quality of care of hospitalised vulnerable elderly [16].

Failure to adjust for severity of co-morbidities, may account for the absence of an association in our study. There may be more patients with serious illnesses in the high group than in the low quality group. The significantly higher use of pain medications and opiates, the longer length of stay (2.5 days longer) and the increased use of sleep medications, and digoxin in the high group may indicate that these patients were more ill. In
addition, physicians may devote more attention to severely ill patients, which can result in a more complete documentation and thus higher quality score. The recent comparable study by Arora et al. did establish an association between higher quality of care of hospitalised elderly and postdischarge survival. However, they excluded patients that were discharged to hospice or comfort care and hence were likely to die soon[16]. These patients may have been present in our high quality care group, thereby contributing to the lack of association between quality of care and survival. Furthermore both Higashi and Arora selected only vulnerable elderly patients according to the VES-13 score. In our study all patient of 65 years or older were eligible. This may have contributed to our findings.

Improved quality of pharmaceutical care was not associated with fewer readmissions and deaths within 90 days after discharge. A study by Hastings et al. investigated the association between suboptimal pharmacotherapy and visits to the emergency room, hospitalisations and deaths within 90 days after discharge. Patients with suboptimal pharmacotherapy showed a trend towards an increased risk of adverse outcomes seen above (hazard ratio=1.32, CI95: 0.95 to 1.84)[21]. In our analysis, the reason for the readmission was not known. In our study the reason of readmission was not registered and therefore readmissions unrelated to the first admission were not excluded. Readmissions that may have no relationship with aspects of care that were measured by the QIs during the first admission could have been included in our analysis. The high quality group may have contained more readmissions unrelated to the first admission period, which could explain the lack of difference in readmissions between both groups.

The limitations of an explicit screening tool containing a selection of QIs, could also explain the lack of any association between quality score and 500-day survival and readmission and mortality rate 90 days after discharge. The 87 quality indicators assessed only a proportion of the pharmaceutical care provided to the vulnerable elderly patients. The proportion of pharmaceutical care not measured by the QI set could be responsible for deaths and readmissions if this care was provided poorly.

For many quality indicators used in our QI set the association between processes of pharmaceutical care and improved patient outcomes is based on clinical evidence. However, a proportion of quality indicators are based on expert opinion, for example some quality indicators in the ‘continuity and documentation’ domain. The fact that many of those expert-opinion based indicators do not have a described association in scientific studies with the specific outcomes that were studied in this research project, may explain part of the lack of association between quality score and mortality and readmissions.
In conclusion, this study applying quality indicators in 200 elderly patients showed evidence that improvements in pharmaceutical care are needed. Elderly patients received less than half the recommended pharmaceutical care. Interventions to improve quality of pharmaceutical care should focus on the prescription of indicated medication, continuity of care and documentation and monitoring of drug therapy. A better quality of pharmaceutical care according to the indicators was not associated with improved 500-day survival or fewer readmissions within 90 days. The set of process indicators is useful, but will be further developed by selecting indicators with sufficient distinctiveness (high number of patients, low success rate) and by studying clusters of indicators that show a relationship with outcomes.

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## Appendix

Indicator pass rates per domain

### Domain I: Using indicated medication

| Indicator                                                                                                                                  | Pass rate (%) | Patients |
|--------------------------------------------------------------------------------------------------------------------------------------------|---------------|----------|
| ALL diabetic elders with elevated blood pressure (SBP>140 mmHg) should be offered one of the following drugs (in order of choice) as an antihypertensive treatment: diuretic, calcium inhibitor, ACE inhibitor, AT2 receptor blocker or beta receptor blocker | 90.4          | 52       |
| IF an elder is diagnosed with delirium and a pharmacologic intervention is needed, THEN Haloperidol (0.25-2.5 mg once or twice daily) should be the first-line treatment option UNLESS there is a known contraindication such as Parkinson's disease or Lewy-bodies dementia | 95.5          | 22       |
| IF a hospitalised elder needs or already uses a NSAID and has one or more solitary risk factors such as age > 70 years or untreated H. pylori or previous ulcer, THEN the patient should receive prophylaxis with either a proton-pump inhibitor in combination with a NSAID or misoprostol in combination with a NSAID | 100.0         | 19       |
| IF an elder is presented with heart failure with AF without a sufficiently controlled ventricular response OR an elder is presented (or diagnosed in hospital) with heart failure without AF but with remaining complaints of heart failure despite treatment with ACE inhibitors, diuretics and beta blockers and/or spironolactone, THEN digoxin treatment should be initiated or given | 100.0         | 17       |
| ALL elders WITH a TIA and/or a cerebrovascular infarction in their history AND a plasma cholesterol > 5.0 mmol/l OR a LDL concentration > 2.5 mmol/l, THEN prophylaxis with cholesterol lowering medication should be considered | 100.0         | 6        |
| IF there are two or more cumulative risk factors present in an elder (age 65-70 years, use of acetyl salicylic acid/anticoagulants, serious Rheumatoid Arthritis, high dose NSAIDs (> DDD), use of corticosteroids, use of SSRIs, Diabetes or Heart Failure), THEN the physician should consider giving the patient prophylaxis with either a proton-pump inhibitor in combination with a NSAID or misoprostol in combination with a NSAID | 80.0          | 5        |
| IF an elder had a recent TIA or a non-invalidating stroke due to AF, THEN a prophylaxis should be offered. The first-choice treatment is oral anticoagulation aiming at the INR range of 2.5-3.5. If there is a contraindication for OA, then ASA 30-300 mg a day | 100.0         | 9        |
| IF an elder has unstable angina or an acute MI, THEN he or she should be offered beta blocker therapy within 12 hours of presentation | 100.0         | 2        |
Indicator  | Pass rate (%) | Patients
--- | --- | ---
If an elder admitted to a hospital has dementia complicated by a problematic behavior, THEN a pharmacologic treatment should be offered according to 'flowchart problem behavior' if other non-pharmacologic interventions fail | 100.0 | 5
If an elder has established IHD AND his or her LDL cholesterol level > 2.5 mmol/l, THEN he or she should be offered cholesterol-lowering medication (statins) | 75.0 | 8
If an elder has heart failure and atrial fibrillation, THEN anticoagulation should be offered to achieve an international normalized ratio of 2.5 to 3.5 | 56.7 | 30
ALL diabetic elders with proven cardiovascular disease should be offered daily aspirin therapy (80-100 mg per day) OR ELSE an increased risk for cardiovascular complications will exist | 75.8 | 33
If a diabetic elder has an LDL level > 2.5 mmol/l, or a TC level > 4.5 mmol/l, THEN an intervention to lower cholesterol (statin) should be considered. This should be mentioned in the patient’s record | 77.8 | 9
If an elder is started on or is already treated with an antidepressant medication, and an additional sleeping disorder or fear episodes are present and additional short treatment is started with benzodiazepines, THEN short t1/2 benzodiazepines should be used. Benzodiazepines with a long t1/2 (diazepam, flurazepam, flunitrazepam, clorazepate or cloridiazepoxide) should NOT be used OR ELSE there will be an increased risk of falls and fractures, respiratory depression, polyurea and incontinence (due to long half-life benzodiazepines) | 80.0 | 5
If an elder has established ischemic heart disease (IHD) and is not receiving a coumarin, THEN he or she should be offered antiplatelet therapy consisting of aspirin and/or clopidogrel | 84.5 | 58
If an elder has a newly reported chronic painful condition THEN treatment should be offered according to the pain scheme of the WHO pain ladder | 90.2 | 51
If an elder has hypertension and has renal parenchymal disease with a lowered glomerular filtration rate (creatinine > 150 µmol/l) or microalbuminuria, THEN therapy with an ACE inhibitor or AT2 receptor blocker should be offered | 56.1 | 57
If a hospitalised elder is at a very high risk for VTE (one of the following risk factors are present: heart failure, immobility, severe respiratory disease, severe acute infections, active malignancy, history of VTE, acute neurological diseases or inflammatory bowel diseases), THEN the patient should be offered venous thromboembolism prophylaxis with a LMWH UNLESS the patient is already taking coumarins or UNLESS it is contraindicated | 63.6 | 165
If an elder with chronic pain is treated with opioids, THEN he or she should be offered a laxative OR the medical record should document the potential for constipation or give an explanation why bowel treatment is not needed | 58.9 | 56
| Indicator                                                                                                                                                                                                                                                                                                                                                           | Pass rate (%) | Patients |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|----------|
| IF a diabetic elder has proteinuria, THEN he or she should be offered therapy with an ACE inhibitor or an AT2 receptor blocker                                                                                                                                                                                                                                     | 56.8         | 37       |
| ALL elders diagnosed with delirium and presumed vitamin B (B1 and/or B12) deficiency should be offered an adequate supplementation                                                                                                                                                                                                                                    | 77.8         | 9        |
| IF an elder has had a MI, THEN he or she should be offered a beta blocker                                                                                                                                                                                                                                                                                           | 58.0         | 50       |
| IF an elder is admitted to the hospital with pneumonia, THEN the correct antibiotics should be administered within eight hours of hospital arrival. Check the kind of antibiotics against current local pneumonia antibiotic guidelines  | 78.1         | 32       |
| IF an elder is taking corticosteroids (≥ 7.5 mg prednisolone or equivalent) for more than one month, THEN the patient should be offered calcium and vitamin D AND a bisphosphonate                                                                                                                                                                                      | 17.9         | 28       |
| ALL elders with repeating incidence of blood pressure > 185/95 mmHg in the chronic phase after stroke should be offered blood-pressure-lowering treatment consisting of beta blocker and thiazide diuretics as a secondary prevention                                                                                                                                     | 50.0         | 4        |
| IF an elder has heart failure AND left ventricular ejection fraction of 40% or less (or unknown), THEN he or she should be offered an ACE inhibitor or a AT2 receptor blocker in combination with a diuretic                                                                                                                                                                           | 33.3         | 6        |
| IF an elder had a TIA or non-invalidating stroke and no history of AF, THEN a prophylaxis should be offered. The first choice for treatment is 38-100 mg a day acetyl salicylic acid (ASA) in combination with dipyridamole 2 dd 200 mg (slow release). Both are to be given life-long. IF there is a contra-indication for ASA, THEN clopidogrel should be given | 26.5         | 34       |
| IF an elder has a new diagnosis of osteoporosis, THEN the use of calcium (when daily diet is insufficient) and vitamin D supplements (when exposure to sunlight is scarce) should be recommended                                                                                                                                                                                  | 0.0          | 3        |
| IF an elder has a new diagnosis of osteoporosis, THEN the patient should be offered treatment with bisphosphonates                                                                                                                                                                                                                                                  | 33.3         | 3        |
| IF an elder has heart failure and atrial fibrillation AND he or she has documented contra-indications to anticoagulation, THEN he or she should be offered aspirin                                                                                                                                                                                                 | 28.6         | 14       |
| IF a diabetic elder has proven cardiovascular disease AND a total cholesterol > 4.5 mmol/l or an LDL cholesterol > 2.5 mmol/l, THEN medical treatment (statins, aspirin, beta receptor blocker and ACE inhibitors) has to be given unless contra-indicated                                                                                                                                               | 0.0          | 7        |
| IF an elder has an acute MI or unstable angina, THEN he or she should be given aspirin therapy within one hour of presentation (300 mg loading dose, 100 mg per day continuously)                                                                                                                                                                                                                              | 0.0          | 2        |
| Indicator                                                                 | Pass rate (%) | Patients |
|---------------------------------------------------------------------------|---------------|----------|
| IF an elder is started on a new pharmacologic antidepressant treatment during his or her hospital stay, THEN the first-line treatment should be a TCA (preferred are nortriptyline or clomipramine and NOT amitriptyline) or an SSRI (regular sodium concentration check) or venlafaxine or mirtazapine | 0.0           | 1        |
| IF an elder is diagnosed with delirium and a pharmacological intervention is needed but haloperidol is contra-indicated by Parkinson's disease or Lewy-bodies dementia or causes too many side-effects, THEN as a second-line treatment, an atypical antipsychotic (order of preference: 1) Olanzapine or Quetiapine, 2) Risperidon, 3) Clozapine and 4) Rivastigmine) can be considered UNLESS there is known contra-indication such as cardiovascular disease | 40.0          | 5        |
| IF an elder has stable heart failure AND a left ventricular ejection fraction of 40% or less, THEN a beta blocker should be offered (recommended beta blockers are carvedilol, bisoprolol and metoprolol) UNLESS the patient has a documented contraindication (for example, uncompensated heart failure) | 50.0          | 4        |
| IF an elder has valvular or congenital heart disease or an intracardiac valvular prosthesis or hypertrophic cardiomyopathy or mitral valve prolapse with regurgitation or a previous episode of endocarditis AND a high-risk procedure is planned, THEN endocarditis prophylaxis should be given according to current local guidelines | 0.0           | 4        |
| IF an elder receives a diagnosis of acute ischemic stroke during his or her hospital stay or at admission, THEN antiplatelet treatment with aspirin (loading dose of at least 160 mg aspirin) within 48 hours after the stroke should be offered and continued for at least 14 days | -             | 0        |
| IF an elder receives a diagnosis of acute ischemic stroke during hospital stay or at admission AND has tension > 220-230/125-135 mmHg, THEN an intravenous treatment with blood-pressure-lowering drugs that can be titrated should be offered | -             | 0        |
| IF oral pharmacologic therapy is initiated to treat osteoarthritis in an elder, THEN acetaminophen should be the first drug used, UNLESS there is a documented contraindication | 100.0         | 4        |
Domain II Preventing inappropriate medications

| Indicator                                                                 | Pass rate (%) | Patients |
|---------------------------------------------------------------------------|---------------|----------|
| IF An elder requires analgesia, THEN mepiridine should not be used OR ELSE there is risk for severe confusion | -             | 0        |
| IF an elder has hypertension and pharmacologic antihypertensive treatment is initiated, THEN alpha-blocking agents such as doxazosin, prazosin and terazosin should not be used | 96.8          | 31       |
| IF an elder is treated for a chronic painful condition, THEN he or she should not be treated with indomethacin OR ELSE there is a risk a for gastropathy, neurologic side effects and salt and water retention | 100.0         | 100      |
| IF an elder has cardiac arrhythmias AND therapy with an anti-arrhythmic is started, THEN disopyramide should not be used OR ELSE there could be a worsening of heart failure and fluid retention and strong anticholinergic effects | 91.7          | 12       |
| IF an elder has hypertension and asthma or COPD, THEN beta blocker therapy for hypertension should not be used UNLESS no other option remains | 91.7          | 24       |
| IF an elder has dementia, THEN do NOT use a long half-life benzodiazepine such as diazepam, flurazepam, flunitrazepam, clorazepate or chlordiazepoxide | 100.0         | 17       |
| IF an elder has a history of gout or an acute episode of gout, THEN DO NOT prescribe a thiazide diuretic to treat hypertension OR ELSE gout attacks could happen | 92.9          | 14       |
| IF an elder has a history of postural hypotension or heart block or glaucoma or urinary retention, THEN a tricyclic antidepressant should NOT be used because of anticholinergic effects of TCAs | 100.0         | 5        |
| IF an elder has Parkinson's disease, THEN do NOT use a classical antipsychotic or metoclopramide UNLESS the patient is delirious, THEN clozapine is indicated | 100.0         | 3        |
| An elder should not be prescribed a medication with strong anticholinergic effects IF alternatives are available OR ELSE there is a risk for acute glaucoma, urine retention, constipation and delirium | 50.0          | 2        |
| IF an elder has a cardiac, cardiovascular or cerebrovascular disease and a chronic painful condition, THEN he or she should NOT be treated with COX-2 selective NSAIDs because of an increased cardiovascular risk long-term | 100.0         | 60       |
If an older adult is treated for a sleeping disorder or for anxiety during his or her hospital stay or at admission, THEN long half-life benzodiazepines (diazepam, flurazepam, flunitrazepam, clorazepate or chlordiazepoxide) should NOT be used OR ELSE there is an increased risk of falls and fractures, respiratory depression, polyurea and incontinence.

If an older adult has heart failure AND left ventricular ejection fraction of 40% or less AND atrial fibrillation, THEN he or she should NOT be treated with a type I antiarrhythmic agent (disopyramide, kinidine, procainamide, phenytoin, lidocaine, flecainide or propafenone) UNLESS an implantable cardioverter-defibrillator is in place. Only amiodarone (class III) is allowed for treatment patient with heart failure and AF.

If an older adult has heart failure AND left ventricular ejection fraction of 40% or less AND no atrial fibrillation, THEN calcium-channel-blocking medication should NOT be used.

### Domain III: Continuity and documentation of care

| Indicator                                                                 | Pass rate (%) | Patients |
|---------------------------------------------------------------------------|---------------|----------|
| If an older adult is admitted to a hospital for any acute or chronic illness OR for any surgical procedure, THEN the evaluation should include within one day: 1) diagnoses, 2) pre-hospital medications and 3) a current therapy plan | 96.0          | 200      |
| If a new drug is prescribed to an older adult on an ongoing basis for a chronic medical condition, THEN the prescribed drug should have a clearly defined indication documented in the patient’s record | 54.4          | 79       |
| If an older adult who has been prescribed an ocular therapeutic regimen becomes hospitalised, THEN the regimen should be administered in the hospital unless discontinued by an ophthalmologic consultant | 47.1          | 17       |
| If an older adult is hospitalised with heart failure or develops heart failure during hospital stay, THEN the following parameters should be measured within one day of hospitalisation or diagnosis: serum electrolytes (sodium and potassium), creatinine, blood urea, Hb, Ht, TSH and glucose | 9.1           | 44       |
| If an older adult admitted to a hospital has dementia AND there is an acute decrease in cognitive functions and worsening of behavior, THEN a diagnosis of delirium should be considered and a geriatrist should be consulted. This consultation should be noted in the patient’s record (clinical diagnosis or CAM score) | 66.7          | 12       |
| If an older adult is discharged from a hospital to his or her home or to a nursing home, THEN there should be a discharge summary sent to the outpatient physician or nursing home within 14 days including information on medication at admission and discharge | 24.7          | 174      |
| Indicator | Pass rate (%) | Patients |
|-----------|---------------|----------|
| IF an elder is discharged from a hospital to his or her home or to a nursing home AND he or she received a new drug (excluding temporary during admission) OR a change in pre-hospital medication before discharge, THEN the general physician or nursing home physician should be acknowledged (including reasons of changes in medication and route of administration and information on dosing) by a discharge letter | 35.9 | 142 |
| IF an elder presents him- or herself with symptoms of cognitive dysfunction THEN the patient’s medication possibly associated with these symptoms should be evaluated. Risky interactions should also be considered. This evaluation should be noted in the patient’s record | 27.8 | 36 |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure THEN he or she should receive diagnostic screening for delirium (CAM score). This is to be documented in the patient’s record | 0.0 | 200 |
| IF an elder presents him- or herself with symptoms of delirium at admission or during his or her hospital stay, THEN the patient’s medication possibly associated with these symptoms should be evaluated and risky interactions that could enhance the anti-cholinergic effects should also be considered. This evaluation should be noted in the patient’s record | 21.9 | 32 |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure, THEN he or she should receive a cognitive function evaluation (MMSE score). This is documented in the patient’s record | 2.5 | 200 |
| IF a new drug is prescribed to an elder on an ongoing basis for a chronic medical condition, THEN the advice to evaluate the response to therapy within three months should be mentioned in the discharge letter | 0.0 | 79 |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure, THEN he or she should be examined for dementia AND this evaluation should be noted in the patient’s record | 2.5 | 200 |
| IF an elder is admitted to a hospital for any acute or chronic illness or any surgical procedure, THEN he or she should be examined for depression (GDS score) AND this evaluation should be noted in the patient’s record | 0.0 | 200 |
| ALL diabetic elders with proven cardiovascular disease should be examined for lipid metabolism disorders (TC, LDL, HDL and TG) and lab value evaluations should be noted in these patients’ records | 6.1 | 33 |
| IF pain treatment is altered or newly begun in an elder, THEN he or she should be assessed for a response within six months AND this advice should be mentioned in his or her discharge letter | 3.0 | 33 |
| Indicator                                                                 | Pass rate (%) | Patients |
|--------------------------------------------------------------------------|---------------|----------|
| IF an elder is admitted to a hospital after a fall incident or has a fall incident during his or her hospital stay, THEN the patient’s medication should be screened for drugs that are associated with increased incidence of falling (hypnotics, tranquilizers, long acting benzodiazepines, antidepressives, sedatives, neuroleptics and antipsychotics) AND this evaluation should be noted in the patient's record | 17.4          | 23       |
| IF the attending physician suspects that an elder is depressed or has a depressive episode, THEN a geriatrist or psychiatrist should be consulted AND the medical record should document the symptoms and grade of severity and whether medication is started or not, and why | 12.5          | 8        |
| IF an elder has newly diagnosed heart failure, THEN left ventricular ejection fraction should be evaluated during his or her hospital stay | 18.8          | 16       |
| IF an elder admitted to a hospital receives a diagnosis of dementia OR has dementia diagnosed previously, THEN the patient's medication that possibly caused or worsened dementia-like symptoms should be evaluated (drugs with anticholinergic effects) AND this evaluation should be noted in the patient's record | 55.6          | 18       |
| IF an elder has a new diagnosis of osteoporosis, THEN during the initial evaluation period, an underlying cause of osteoporosis should be sought by checking medication use and current alcohol use AND this should be noted in the patient's record | 33.3          | 3        |
| IF an elder is started in-hospital on chronic coumarin treatment, THEN there should be an evaluation of the risk factors of bleeding during therapy before the patient is discharged AND the evaluation should be reported in the patient’s record and at discharge to the GP | 0.0           | 2        |
| IF an elder is admitted to a hospital and after evaluation it is stated that there is no meaningful symptom response after four to six weeks of pharmacologic antidepressant treatment begun in the outpatient setting, THEN one of the following should be initiated: the diagnosis should be reconsidered OR precipitating factors evaluated OR concordance should be evaluated OR the medication dosage should be optimized OR TDM should be performed (if applicable) OR the patient should be referred to a psychiatrist or psychotherapy should be offered | -             | 0        |
| IF an elder with a history of cardiac disease is started on a tricyclic antidepressant, THEN baseline electrocardiography should be performed before initiation of or within three months before treatment | -             | 0        |
| IF an elder has a presumed stroke during his or her hospital stay or at admission, THEN a CT or an MRI of the head should be obtained before the initiation or continuation of thrombolytic treatment (r-TPA), anticoagulant therapy (OA), or antiplatelet therapy (ASA, dipyridamole, clopidogrel) | 100.0         | 1        |
| IF oral pharmacologic therapy for osteoarthritis in an elder is changed from acetaminophen to a different oral agent, THEN there should be evidence that the patient has had a trial of maximum dose acetaminophen (suitable for age and co-morbid conditions) | 100.0         | 1        |
**Domain IV** Medication monitoring

| Indicator                                                                 | Pass rate (%) | Patients |
|---------------------------------------------------------------------------|---------------|----------|
| IF an elder is newly started on a diuretic for chronic use, THEN during hospital admission, serum potassium and creatinine levels should be checked within one month after discharge and yearly thereafter the parameters (potassium and creatinine) should be checked again. This advice should be mentioned in the discharge letter | 30.0          | 10       |
| IF an elder begins receiving an angiotensin-converting enzyme (ACE) inhibitor, THEN serum potassium and creatinine levels should be checked within one month of initiation of therapy and thereafter yearly AND this advice should be mentioned in the discharge letter | 33.3          | 6        |
| IF an elder uses a maintenance dose digoxin, THEN the maximal dosage per day is 0.125 mg UNLESS a lower dosage has previously been insufficiently effective for the patient AND TDM has shown therapeutic blood levels at this high dosage | 78.8          | 33       |
| IF an elder has an INR higher than the advised range (depending on the indication), THEN the possible causes of this elevation including interacting medications should be evaluated AND the coumarin dosage adjusted until the INR returns within the therapeutic range | 41.2          | 17       |
| IF an elder is newly prescribed a coumarin, THEN an INR should be determined by at least five to seven days after initiation, in-hospital or by the thrombosis service. The patient should be enrolled in the program of the thrombosis service AND this should be mentioned in the patient’s records | 33.3          | 3        |
| IF an elder is started on a new SSRI antidepressant treatment during his or her hospital stay, THEN the evaluation of sodium levels should be performed by the prescribing physician (min. once during hospital stay) OR should be continued after discharge by a GP (yearly) OR ELSE hyponatraemia could occur | -             | 0        |
| IF an elder is started on a new pharmacologic antidepressant treatment during hospital stay, THEN a frequent evaluation of effectiveness and side effects should be performed during the first four weeks of treatment (every week) by the prescribing physician OR IF patient leaves hospital before this term, THEN this advice should be stated in the discharge letter | -             | 0        |
| IF an elder uses an oral anticoagulant (acenocoumarol or fenprocoumon) AND also cotrimoxazole OR cefomandol OR metronidazole OR miconazole OR fluconazole OR itraconazole OR ketoconazole OR voriconazole, THEN INR should be monitored at least every week during concomitant use OR ELSE INR could rise and hemorrhagic events could result | 100.0         | 2        |
5.1 The effect of an active on-ward participation of hospital pharmacists in internal medicine teams on preventable adverse drug events in elderly inpatients:

Protocol of the WINGS study (Ward-oriented pharmacy In Newly admitted Geriatric Seniors).

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Abstract

Background: The potential of clinical interventions, aiming at reduction of preventable Adverse Drug Events (preventable ADEs) during hospital stay, have been studied extensively. Clinical Pharmacy is a well-established and effective service, usually consisting of full-time on-ward participation of clinical pharmacists in medical teams. Within the current Hospital Pharmacy organisation in the Netherlands, such on-ward service is less feasible and therefore not yet established. However, given the substantial incidence of preventable ADEs in Dutch hospitals found in recent studies, appears warranted. Therefore, “Ward-Oriented Pharmacy”, an on-ward service tailored to the Dutch hospital setting, will be developed. This service will consist of multifaceted interventions implemented in the Internal Medicine wards by hospital pharmacists. The effect of this service on preventable ADEs in elderly inpatients will be measured. Elderly patients are at high risk for ADEs due to multi-morbidity, concomitant disabilities and polypharmacy. Most studies on the incidence and preventability of ADEs in elderly patients have been conducted in the outpatient setting or on admission to a hospital, and fewer in the inpatient setting. Moreover, recognition of ADEs by the treating physicians is challenging in elderly patients because their disease presentation is often atypical and complex. Detailed information about the performance of the treating physicians in ADE recognition is scarce.

Methods/Design: The design is a multi-centre, interrupted time series study. Patients of 65 years or older, consecutively admitted to Internal Medicine wards will be included. After a pre-measurement, a Ward-Oriented Pharmacy service will be introduced and the effect of this service will be assessed during a post-measurement. The primary outcome measures are the ADE prevalence on admission and ADE incidence during hospital stay. These outcomes will be assessed using structured retrospective chart review by an independent expert panel. This assessment will include determination of causality, severity and preventability of ADEs. In addition, the extent to which ADEs are recognised and managed by the treating physicians will be considered.

Discussion: The primary goal of the WINGS study is to assess whether a significant reduction in preventable ADEs in elderly inpatients can be achieved by a Ward-Oriented Pharmacy service offered. A comprehensive ADE detection method will be used based on expert opinion and retrospective, trigger-tool enhanced, chart review.
Background

Harmful events caused by medication are a widely recognised problem, both in hospital and outpatient settings\[^{[1-5]}\]. These events are known as Adverse Drug Events (ADEs), usually defined as ‘any injury due to the use of medication’. ADEs may occur during the normal use of medication as a result of an unavoidable pharmacological effect (side effects or Adverse Drug Reactions (ADRs)), or as a result of a medication error (preventable ADEs)\[^{[6]}\]. Preventable ADEs are associated with substantial morbidity, increased mortality, a longer length of stay in the hospital and costs\[^{[7-9]}\].

To increase medication safety, many interventions to reduce preventable ADEs have been studied and were found to be successful\[^{[6, 10, 11]}\]. Full-time on-ward participation of clinical pharmacists in medical teams is an effective intervention in the hospital setting\[^{[12-15]}\]. Nowadays, these services, often referred to as “Clinical Pharmacy”, are routinely offered in most Anglo-Saxon countries\[^{[16-18]}\]. In The Netherlands however, the Hospital Pharmacy organisation is mainly product-oriented. Also, most of the hospital pharmacists’ time is taken up by activities such as quality assurance of medication compounding, verification of parenteral medication prepared by pharmacy technicians, therapeutic drug monitoring and medication logistics. In addition, the number of Dutch hospital pharmacists is low. On average, there are fewer hospital pharmacists per 100 hospital beds (0.75) in comparison to United Kingdom (1.42) and United States of America (14.1)\[^{[19]}\]. As a consequence, routine clinical activities by Dutch hospital pharmacists are usually limited to off-ward services such as an on-call duty for consultations and checking of automated alerts pertaining to drug-drug interactions, drug-drug duplications and overdosages. The disadvantage of such a back-office organisation is that it gives hospital pharmacists limited insight into the relevant medication risks incurred by patients in the wards. The substantial incidence of preventable ADEs in Dutch hospitals found in recent studies\[^{[20-23]}\] warrants an extension of the current off-ward clinical activities by an on-ward pharmacy service. To maximise its effectiveness, such a service should primarily be aimed at the highest medication risks both at patient and organisation levels. For efficiency reasons, an adaptation of Clinical Pharmacy to the Dutch hospital setting is needed because Dutch hospital pharmacists are scarce.

In this study, we choose to limit the on-ward pharmacy service to elderly hospitalised patients using five or more medications on the day of admission. Especially in elderly patients, pharmacotherapy management is challenging as polypharmacy, multi-morbidity and concomitant disabilities are often present. Altered physiological functions and cognitive decline even further increase the risk for ADEs in this vulnerable patient group\[^{[24-26]}\]. A number of studies have described ADE incidence and preventability in
elderly patients in the outpatient setting and on admission to hospitals\cite{27-33}. However, limited data exist regarding these outcomes in the inpatient setting\cite{34-36}. Furthermore, none of these studies have addressed the extent to which ADEs detected by the researchers were also recognised and managed by the treating physicians in the wards. Correct diagnoses in elderly patients are difficult to make because such patients often present with atypical symptoms\cite{37}. One study found that only 51\% of ADEs were recognised by the treating physicians\cite{38}. However, the generalisability of these results to the inpatient setting is limited, because only Emergency Department physicians were involved. It thus appears that our knowledge on ADE recognition and management in the elderly inpatients is limited and further study is needed.

Numerous studies have investigated the effect of on-ward pharmacy services in the elderly hospital population by measuring surrogate end-points, such as inappropriate prescribing\cite{39-42}. Only a few studies have measured clinical outcomes such as the number of ADEs\cite{43, 44}. However, the measurements conducted in these studies were limited to one specific type of preventable ADEs (e.g. only coagulation-related)\cite{44} or limited in the number of participants and conducted in one academic hospital\cite{43}. Thus, the results of these studies cannot readily be generalised to other hospital settings. The WINGS study is a multicentre study, designed to assess the reduction of ADE incidence in a high-risk population deploying limited pharmacist resources, focusing on ADE recognition and management by treating physicians, using clinical outcome as an effect measure. The on-ward pharmacy service designed in this study will be called “Ward-Oriented Pharmacy” as opposed to Clinical Pharmacy because hospital pharmacists will be attributed only part-time to this service.

The primary goals of this study are 1) to determine the number of ADEs on admission and during hospital stay in elderly patients, and to assess their causality, preventability, severity, recognition and management of ADEs by treating physicians, 2) to design and implement an effective and feasible on-ward pharmacy service for elderly patients in the Dutch hospital setting and 3) to measure the effect of this service on the incidence of preventable ADEs.

Methods/Design

Study design

The design is a multi-centre interrupted time series study. The interrupted time series (ITS) model follows the Cochrane Effective Practice and Organisation of Care Review Group criteria for short time series\cite{45}. This type of series consists of pre-
and post-intervention phases and needs to have at least three observation points in
the pre-intervention phase and three in the post-intervention phase. Every data point
needs to have at least 30 observations.

The six data points needed will be strategically spread over pre- and post-measurement
periods. The study will be conducted during a period of three years. An advantage of
an ITS design is that it allows for the statistical investigation of potential biases such
as secular trends in the estimate of the effect of the intervention[46]. ITS is also more
feasible than a Randomized Controlled Trial in measuring the effect of interventions
that require organisational change to a health care delivery system, which is the case
in the WINGS study[45].

Study setting

The participating hospitals are one academic hospital, the Academic Medical Centre in
Amsterdam, and two non-academic hospitals, the Westfriesgasthuis Hospital in Hoorn
and the Spaarne Hospital in Hoofddorp, the Netherlands. All internal medicine wards
of these hospitals participate in the study.

Study population

All consecutive patients of 65 years or older with an expected length of stay of 24
hours or longer, using 5 or more medications on the day of hospital admission and
admitted to an internal medicine ward during measurement phases will be included.
Patients admitted for scheduled chemotherapy, radiation therapy or transplantation,
as well as patients transferred from another hospital or from a ward other than an
internal medicine ward within the same hospital will be excluded. No patient will be
included more than once.

Intervention

During the whole study, all regular off-ward services, as described in the Introduction
section, will be offered to Internal Medicine wards by the participating Hospital
Pharmacy departments. During the intervention period, a designed Ward-Oriented
Pharmacy service will be added to regular off-ward pharmacy services offered to all
Internal Medicine wards of the participating hospitals. A Ward-Oriented Pharmacy
service will consist of multifaceted interventions such as pharmacotherapy education,
writing and implementation of drug protocols, face-to-face pharmacotherapy guidance
of prescribers, participation in ward-rounds and medication reviews. Multifaceted
interventions are reported to be more effective than single interventions, especially
when these are complementary and not overly complex. To promote implementation of a Ward-Oriented Pharmacy service, the three participating hospitals can choose different types of interventions to include in this service.

To be able to choose efficient interventions and to design a feasible Ward-Oriented Pharmacy service, the following steps will be taken:

1. An analysis of preventable ADEs based on the pre-measurement results will be conducted to identify most frequent medication risks in elderly inpatients. These risks will be categorised in patient-related medication risks and organisational medication risks. Patient-related medication risks refer to patients’ characteristics, for example use of specific medication or the presence of specific co-morbidities, which might be associated with a higher risk for preventable ADEs. Organisational risks refer to ward characteristics, for example the extent to which pharmacotherapy guidelines or protocols are available and the level of existing knowledge and education. Lacking or insufficient pharmacotherapy guidelines, protocols or knowledge could entail a higher risk for preventable ADEs.

2. The results from step one will be presented to a multidisciplinary group consisting of Internal Medicine and Hospital Pharmacy staff members and residents of all three participating hospitals. These groups will prioritise risks and choose interventions tailored to local needs and possibilities to design a specific Ward-Oriented Pharmacy service. Tools and strategies like Bow-Tie risk analysis and the Swiss Cheese model will be used to structure this process.

3. To further assure a successful implementation process, a finally designed Ward-Oriented Pharmacy service will be presented to all personnel in the participating departments. A one-month introduction period will be used to fine-tune the interventions. To keep the participating departments informed about the progress of the study, periodic evaluations will be planned and a newsletter will be distributed. After 7 months we expect the implementation of a Ward-Oriented Pharmacy service to be finalised.

Study Outcomes

The primary outcomes of this study are 1) the number, severity and preventability of ADEs present at admission calculated per 100 hospitalisations, 2) the number, severity and preventability of ADEs during hospital stay calculated per 100 hospitalisations, 3) the percentage of ADEs recognised and appropriately managed by the treating physicians.
The secondary outcomes of this study are 1) the number of medication errors per number of medication orders and 2) the number of readmissions within three months after the index hospitalisation.

Depending on the type of the interventions that will be implemented, additional secondary outcomes will be measured to monitor the implementation of these specific interventions. For example, pharmacotherapy consultations given by hospital pharmacists on the wards can be monitored by recording the number of advices given to the physicians and nurses.

Data collection and outcome assessment

The flow charts of the data collection process and the outcome assessment process are shown in Figures 1 and 2 and have been adapted from previous studies. First, trained research nurses and pharmacy students will collect all information available about the index hospitalisation of included patients, after discharge of each patient. All charts, laboratory results, rapport of diagnostic procedures and medication prescriptions will be assembled. A Case Report Form (CRF) will be completed for every included patient. In the CRF, a selection of ADE triggers is listed and can be checked off when applicable. The selection of included ADE triggers was based on available trigger tools and expert opinion. Second, copies of the gathered information and the CRF of all included patients will be presented to two independent experts: a senior specialist in Internal Medicine and a senior clinical pharmacist specialised in geriatrics. The two experts will first review the presented information independently from each other. This first review is an implicit process based on expert judgment, which is still the “gold standard” in adverse events determination. In this study we use implicit judgment of a pharmacist and physician team because their knowledge has shown to be complementary. Third, the two experts will discuss their findings in an expert panel meeting. During this second review, the causality between the adverse events found during the first review and commission or omission of medication will be assessed. Only ADEs for which the experts meet consensus on causality will be recorded and subsequently assessed on preventability, severity and, when applicable, on type of medication error. If consensus cannot be reached, the opinion of a third expert will be sought.

For the ADE causality assessment used in the second review, we developed a structured method based on the World Health Organization – Uppsala Medical Centre (WHO-UMC) system. The causality will be scored on a 3-point scale: nearly certain (> 90% certainty that there is a causal relationship between adverse event and a drug), probable/likely (> 65-90% certainty that there is a causal relationship between...
adverse event and a drug), possible (33-65% certainty that there is a causal relationship between adverse event and a drug). ADEs with 32% or less certainty in causality will not be recorded and therefore not further assessed. The severity of ADEs will be scored according to the Common Terminology Criteria for Adverse Events version 3.0 (CTCAEv3) developed by the U.S. National Cancer Institute\[^57\]. CTCAEv3 is a descriptive terminology used to report adverse events in many clinical trials. For each ADE, a 5-points scale of seriousness is included: mild, moderate, severe, life-treating, fatal.

An innovative item in our ADE assessment is the determination of recognition and management of ADEs by the treating physicians during hospitalisation. For every ADE present on admission or occurred during the index hospitalisation, the experts will assess if it was recognised by the treating physicians in the Internal Medicine wards. When applicable, the experts will assess whether the chosen management was timely and sufficient to stop or preclude further harm.

ADEs that will be included in this study are shown in Figure 3. The index hospitalisation is the hospitalisation sampled. ADEs will be included if they were present on admission or occurred during the index hospitalisation. For each included patient, one of the experts (CS) will also score a predefined set of medication errors that occurred during the index hospitalisation, but did not cause patient harm. Medication errors will be classified according to the Dutch Central Medication Incidents Registration.

**Definitions**

The definitions used in this study were adapted from the Glossary of Terms Related to Patient and Medication Safety by Expert Group On Safe Medication Practices\[^6\].

*Adverse Drug Event (ADE)* is any injury occurring during the patient’s drug therapy and resulting either from appropriate care, or from unsuitable or suboptimal care. ADEs include non-preventable *Adverse Drug Reactions (ADRs)* during normal use of medication, and any harm secondary to a medication error (preventable ADEs), both errors of omission and commission will be included. An ADE can result in different clinical outcomes, for example: abnormal laboratory values, worsening of the existing disease, lack of any expected disease improvement, or outbreak of new symptoms or diseases.

*Harm:* temporary or permanent impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting there from requiring intervention. In this study also abnormal laboratory values will be counted as harm.

*Medication error:* any preventable event that may cause or lead to inappropriate medi-
cation use or patient harm while the medication is in the control of the health care professional or patient. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

Sample size calculation and data analysis

The power-calculation for this study was based on the expected incidence of 15 ADEs per 100 hospitalisations and a clinically relevant 50% reduction by a Ward-Oriented Pharmacy service in the post-measurement period. This assumption was made based on the findings of two controlled studies that assessed active clinical pharmacists participation in medical teams on the wards, showing a reduction of 66% and 78% respectively\textsuperscript{[12,13]}. To be able to identify a significant reduction from 15 ADEs to 7.5 ADEs per 100 hospitalisations, 496 patient admissions are needed, equally divided between pre- and post-measurement period ($\alpha=0.05$ and $\beta=0.8$). This sample size enables to identify a reduction of 19 ADEs or more from the expected 38 ADEs in 248 admissions during the pre-measurement period.

Descriptive statistics will be used to summarise patient characteristics for the three participating hospitals and to check for any imbalance in variables between pre- and post-measurement groups. By comparing the pre- and post-measurement periods, the effect of a Ward-Oriented Pharmacy service will be analysed using a suitable generalised linear model for a short interrupted time series. Adjustment will be made for any case mix imbalances between pre- and post-measurement periods and background trend in the ADE rate over time.

Exploratory analyses are also planned to examine the effect of factors like age, sex, length of hospital stay, Charlson Co-morbidity Index Score\textsuperscript{[58]}, renal function on the primary and secondary outcomes. For this purpose unadjusted univariate and adjusted multivariate Poisson regression analyses are planned.

Quality assurance

To ensure quality of data collection, research nurses and pharmacy students will be trained by an experienced member of the research team (JK) to collect the data and how to complete the CRFs. Before the start of the study, research nurses and pharmacy students involved in data-collection will test whether the designed CRF is explicit, comprehensive, and user-friendly. When necessary, the CRF will be adjusted to improve it and a manual will be written to guide the data-collectors during the whole
process. This manual will also be tested to assure that it is explicit, comprehensive, and user-friendly.

Before the start of the study, the structured outcome assessment by the expert panel will be tested by the experts on a sample of 10 patients to ensure that it is explicit, comprehensive and user-friendly. If necessary, the assessment will be adjusted to

Figure 1. Process of data collection and outcome assessment
1 CPOE, Computer Physician Order Entry
2 ADEs, Adverse Drug Events (preventable and non-preventable)
Figure 2. Process of outcome classification and scoring
1 ADR, Adverse Drug Reaction, non-preventable
2 ADE, Adverse Drug Event (preventable and non-preventable)

improve these characteristics. Furthermore, the intra-rater and inter-rater reliability of the assessment process by the expert team will be assessed. For this purpose the kappa statistic (κ) will be calculated. A kappa value of 0.00 will be considered as poor agreement, 0.01–0.20 as slight agreement, 0.21–0.40 as fair agreement, 0.41–0.60 as moderate agreement, 0.61–0.80 as substantial agreement, and 0.81–1.00 as almost perfect agreement[59].
Figure 3. ADEs included in the study

- **Protocol WINGS study**

- **HOME**
  - General Practitioner/Outpatient Clinic

- **INDEX HOSPITALISATION**

- **HOSPITAL**
  - Specialist/Resident

- Medication is prescribed
- Patient is taking medication
- Event
  - OR
  - Event is not recognised, no actions taken
  - OR
  - Event is not timely recognised, but actions taken are sufficient
  - OR
  - Event is timely recognised, but actions taken are not sufficient
  - OR
  - Event is recognised, actions are timely and sufficient

- Indicated medication is NOT prescribed
  - Omission
  - Event
  - OR
  - Event is not recognised, no actions taken
  - OR
  - Event is not timely recognised, but actions taken are sufficient
  - OR
  - Event is timely recognised, but actions taken are not sufficient
  - OR
  - Event is recognised, actions are timely and sufficient

- **INDEX HOSPITALISATION**

- Medication is prescribed
- Patient is taking medication
- Event
  - OR
  - Event is not recognised, no actions taken
  - OR
  - Event is not timely recognised, but actions taken are sufficient
  - OR
  - Event is timely recognised, but actions taken are not sufficient
  - OR
  - Event is recognised, actions are timely and sufficient

- Indicated medication is NOT prescribed
  - Omission
  - Event
  - OR
  - Event is not recognised, no actions taken
  - OR
  - Event is not timely recognised, but actions taken are sufficient
  - OR
  - Event is timely recognised, but actions taken are not sufficient
  - OR
  - Event is recognised, actions are timely and sufficient
Study organisation and management

The research protocol was submitted to the Medical Ethics Committee of the Academic Medical Centre (AMC) before the start of the study. The Medical Ethics Committee of AMC judged the protocol as not needing an approval because the Dutch Medical Research Involving Human Subjects Act (WMO) does not apply to the WINGS study. In this research, we use a retrospective chart review to evaluate the effect of an intervention aimed at quality improvement. Therefore, the integrity of the patients is not influenced. All patient data will be analysed anonymously by coding every patient by a 6-digit number. In every hospital a group of representatives of the Internal Medicine Department and Hospital Pharmacy Department has been formed. The main investigator (JK) and project manager (LL) will meet at least monthly with these representatives to oversee the progress of the study.

The WINGS study is part of the CAREFUL (pharmacist Coordinated ADE Reducing Efforts For Use in all Levels of healthcare) research program, based on a cooperation of Leiden University Medical Centre, Academic Medical Centre Amsterdam, University Medical Centre Groningen and University Medical Centre Utrecht/Utrecht University. Within this program, interventions are studied that are aimed at promoting medication safety in hospital and outpatient settings.

Discussion

Clinical Pharmacy as practised in Anglo-Saxon countries has shown to be successful in reducing preventable ADEs in various hospital patient populations\[12-15\]. In this study, the effect of a Ward-Oriented Pharmacy service on preventable ADEs in elderly inpatients will be investigated. The Ward-Oriented Pharmacy service is an on-ward pharmacy service based on the successful Clinical Pharmacy practice but tailored to the Dutch hospital setting. The Ward-Oriented Pharmacy service will include multifaceted interventions implemented in Internal Medicine wards by hospital pharmacists. Adapting Clinical Pharmacy practice to the Dutch hospital setting is necessary, because Clinical Pharmacy entails a full-time participation of clinical pharmacists in medical teams on the wards, a time investment that is not feasible within the current organisation of Hospital Pharmacy in the Netherlands. This applies also to many other European countries\[19\]. Moreover, active on-ward participation of pharmacists in medical teams is a practice Dutch physicians are not familiar with. This could raise barriers that also need to be considered.
The results of the WINGS study will add insight into the effectiveness of Ward-Oriented Pharmacy on the reduction of ADEs in elderly inpatients. Also the extent to which this service is feasible in the Dutch setting will be explored. By measuring ADEs across the process of admission and subsequent hospitalisation, the extent to which ADEs are recognised and appropriately managed by treating physicians will be investigated. Especially in elderly patients, ADE awareness is essential to be able to practice the safest possible pharmacotherapy\cite{37}.

The method of data collection and chart review used in the WINGS study differs from the standard trigger-tool based chart review method used in other ADE studies\cite{35}. According to the standard method, only charts with one or more triggers are subjected to further review by a physician. Therefore, only a selection of ADEs can be scored and this selection depends on the predefined selection of triggers used in the first step of data collection and examination procedure. In contrast, the trigger-tool based CRF in this study serves only as an aid to help the experts. Trigger-tools have shown to be able to increase the detection of ADEs and can be computerised or used manually\cite{60}. We will use manual screening for ADE triggers in patient files instead of electronic trigger-tools, because by the manual method, the narrative information, such as progress notes or discharge letters, can be screened. Symptoms like constipation, dizziness, falls and hypotension are examples of ADE triggers in narrative information sources. By subjecting all included patients to further review and applying the above described method, a more sensitive ADE assessment by the experts is expected. In our setting, where the magnitude of medication risks in elderly inpatients is unclear, such a comprehensive approach is needed to gain detailed insight into this problem. The time-consuming character of our method is not a barrier, because it is used for research purposes.

In the WINGS study, the primary outcome (ADE) is assessed by using a combination of implicit expert judgment with structured causality assessment based on the WHO-UMC system\cite{56}. Because the WHO-UMC system was developed for ADRs causality assessment, we added or discarded items to design a causality assessment strategy for ADEs and therefore assessment of ADRs and preventable ADEs. Furthermore, both errors of omission and commission are considered as causes of preventable ADEs in our assessment\cite{50}.

The expert judgment is the most popular and most widely used method, even given limitations like lack of reproducibility, poor inter- and intra-rater agreement and a lack of standardised clinical evaluation. Algorithms for ADR causality assessment have been developed to overcome the limitations of expert judgment\cite{61}. However, as mentioned before, ADE assessment in elderly patients could be complicated by factors like multi-morbidity, polypharmacy and atypical presentation of diseases. Therefore,
opinion of clinically experienced reviewers, who are able to weigh drug causation considering all these factors, is essential. In order to do so, less flexible and less specific algorithms are not suitable in this study. It has also been shown that reproducibility of results from the use of such algorithms can drastically decrease, yielding low inter-rater variability, because clinical judgment is always necessary to be able to answer all the questions included[61].

To improve the validity of the method used in this study, we have taken three measures:

1) by using a CRF we help the experts to standardise their clinical evaluation,

2) by combining implicit review followed by structured causality assessment we lower the subjectivity of the expert's decisions

3) by deployment of the same expert team in ADE assessment in the pre- and post-measurement phases the problem of low inter-rater agreement seen in studies using expert judgment can be partly overcome[55].

Competing interests

The author(s) declare that they have no competing interests.

Authors’ contributions

JK, PW, SM, SdR and LL conceptualised the study and developed the study design and methods. JK, PW and SM drafted the protocol. JK is responsible for data collection and overseeing the running of the study. LA, CS and PK helped in developing of methods for data-collection and outcome assessment used in this study. LA and CS will access the outcomes of the study. MD helped with an analysis-plan and drafting of the protocol.

All authors read and approved the final manuscript.

Acknowledgments

The WINGS study was supported by a grant from the Netherlands Organisation for Health Research and Development (ZonMW), The Hague, The Netherlands.
The authors would like to thank the residents, staff and other personnel of Internal Medicine and Hospital Pharmacy Departments, pharmacy students and research nurses who have so far participated in the study.

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5.2 Recognition of adverse drug events in older hospitalised medical patients

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*Eur J Clin Pharmacol. 2013 Jan; 69(1): 75-85*
Abstract

Objective: To assess medical teams’ ability to recognize adverse drug events (ADEs) in older inpatients.

Methods: The study cohort comprised 250 patients aged 65 years or older consecutively admitted to Internal Medicine wards of three hospitals in the Netherlands between April and November 2007. An independent expert team identified ADEs present upon admission or occurring during hospitalisation by a structured retrospective patient chart review. For all ADEs identified, the expert team assessed causality, severity, preventability, and recognition by medical teams.

Results: The medical teams did not recognize 19.9% of all ADEs present upon admission [60.4 ADEs [95% confidence interval (CI) 51.5–70.8] per 100 hospitalisations] and 20.3% of all ADEs occurring during the hospital stay [47.2 ADEs (95% CI 39.4–56.5) per 100 hospitalisations]. Unrecognized ADEs were significantly more often ADEs with possible causality (p=0.014, df=1), ADEs caused by medication errors (p<0.001, df=1), and ADEs not manifesting as new symptoms (p<0.001, df=1). The medical teams did not recognize 23.2% of mild to moderately severe ADEs and 16.5% of severe, life-threatening, or fatal ADEs. The recognition of ADEs varied with event type.

Conclusions: The recognition of ADEs by medical teams was substantial for those ADEs with evident causality and with clinically apparent and severe consequences. ADEs mimicking underlying pathologies with a lower severity went unrecognized much more often, as did those resulting only in abnormal laboratory values. Tools to improve the recognition of ADEs by medical teams should, therefore, focus on those ADEs that are more challenging to detect.
Introduction

Adverse Drug Events (ADEs) are the most frequent type of adverse events in medical inpatients[^1] and are associated with a prolonged hospital stay, a twofold increase in the risk of death, and higher costs[^2]. Approximately 50% of ADEs are preventable[^3]. A widely accepted definition of an ADE is any harm occurring during drug therapy which may result from either appropriate care (non-preventable ADE) or from suboptimal care (preventable ADE) (i.e., a medication error[^4]).

It is widely acknowledged that older patients are especially at risk for ADEs[^5, 6], primarily due to multiple co-morbidities, polypharmacy, and higher vulnerability due to decreased organ function, increased susceptibility to drugs, and frequently present cognitive impairment[^7, 8]. Furthermore, correct and timely diagnosis is often hampered by atypical disease presentation, such as falls or delirium[^5, 9]. Therefore, not only avoiding ADEs in older inpatients, but also, when they do occur, timely recognition of ADEs may pose a significant challenge for medical teams[^9, 10]. Failure to recognize ADEs during the hospital stay may lead to inappropriate actions causing even more harm[^10]. The study by Nebeker et al.[^11] reports that in a general inpatient population, 24% of ADEs subsequently identified by the researchers were not recognized by the medical teams.

Although the body of literature on the occurrence of (preventable) ADEs in older hospitalised patients is extensive[^5, 12–22], data on medical teams’ ability to timely recognize ADEs in this vulnerable patient population are limited to the Emergency Department setting[^23].

Therefore, we conducted a multicenter cohort study with the aim to gain a detailed insight into recognition of ADEs by medical teams in older inpatients. In order to do so, both ADEs present upon admission and those occurring during the hospital stay were included in our analysis.

Material and methods

Study setting

The study was performed in the Internal Medicine wards of three teaching hospitals in the Netherlands: the Academic Medical Center (AMC) in Amsterdam, a 1,002-bed academic hospital, the Westfriesgasthuis (WFG) in Hoorn, a 506-bed regional teaching
hospital, and the Spaarne Hospital (SH) in Hoofddorp, a 520-bed tertiary teaching hospital. The Internal Medicine wards were staffed by teams consisting of attending physicians, junior and senior residents, and interns on rotation, caring together for an average of ten adult patients daily. All three Hospital Pharmacy Departments offered only off-ward, daily clinical services, including preparation of parenteral medications by pharmacy technicians, on-call availability of a hospital pharmacist for pharmacotherapeutic or toxicological consultations, and therapeutic drug monitoring (TDM). In addition, Computerized Physician Order Entry (CPOE) systems with limited clinical decision support were in place in all three participating hospitals. These clinical decision support systems (CDSSs) generated three types of alerts based only on the prescribing data: drug–drug interactions, drug–drug duplications, and overdoses. No other sources, such as laboratory values or diagnostic tests results, were linked to these operating CDSSs.

Study design

Data presented in this study are baseline results of an interrupted time-series study on the effects of the Ward-oriented pharmacy In Newly admitted Geriatric Seniors (WINGS) study[24]. Over a period of 8 months (April–November 2007), 250 patients aged 65 years or older were included in the study during three sampling periods: 90, 80, and 80 consecutively admitted patients were enrolled during the first (April–May 2007), second (July–August 2007) and third (October–November 2007) sampling period, respectively.

The WINGS study was conducted within the framework of the CAREFUL (pharmacist Coordinated ADE Reducing Efforts For Use in all Levels of healthcare) research program based on a cooperative effort between Leiden University Medical Center, AMC Amsterdam, University Medical Center Groningen, and University Medical Center Utrecht/Utrecht University.

Patients

All patients aged 65 years or older who were taking five or more medications on the day of admission and who were admitted to an Internal Medicine ward of the participating hospitals during one of the three sampling periods were eligible for enrolment in the study. Patients were excluded if they were scheduled for chemotherapy, radiation therapy, or stem cell/kidney transplantation, were discharged within 24 h, and/or had been transferred from other hospitals or other non-medical wards within the study hospitals. Only the first hospitalisation during the baseline period per each included patient was reviewed (index hospitalisation). The index hospitalisation included the day
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of admission and all days of the subsequent hospitalisation until the patient was discharged home, transferred to a non-medical ward within the same hospital, or transferred to another healthcare facility (e.g., hospital, nursing home).

Measurement and classification of ADEs

No golden standard currently exists for the measurement, definition, and assessment of ADEs. The definitions used in this study, as well as the method and assessment of ADEs follow recommendations by experts and are also widely accepted. An ADE was classified as any harmful event occurring during drug therapy that resulted either from appropriate care (non-preventable ADEs) or from medication errors (preventable ADE). Both errors of omission or commission were included in this study. Harmful events were defined as either abnormal laboratory values or clinical symptoms. ADEs were included if they resulted in an outbreak of new symptoms/pathology, in worsening of existing or new symptoms/pathology, or in a delay or lack of any expected improvement of existing or new symptoms/pathology.

A detailed description of the method applied in this study can be found elsewhere. In summary, after an included patient was discharged or transferred, trained research nurses and pharmacy students first gathered all information available on the index hospitalisation (medical and nurse patients' files, medication charts, discharge letters and other medical correspondence, laboratory and diagnostic results) and completed a case report form (CRF) in which 'so-called' triggers were incorporated. These triggers were adapted from the Institute of Healthcare Improvement (IHI) ADE trigger-tool. Examples of IHI ADE triggers are the ordering of vitamin K which may be related to overanticoagulation with coumarines, or a digoxin level of >2.0 µg/L which may be related to digoxin toxicity. These triggers were ticked off by the researchers when applicable, with an aim to prompt expert team attention to specific events which may potentially be ADEs. Second, the information collected on the index hospitalisation together with the CRFs were presented to two independent experts, namely, a senior specialist in Internal Medicine (LA) and a senior clinical pharmacist specializing in geriatric medicine (CS), both of whom were experienced in systematic ADE identification. These two experts reviewed all data independently and subsequently discussed their findings during scheduled meetings. A structured ADE assessment was used to determine the causality between a drug and an adverse event, preventability and severity of an ADE, recognition of ADEs by medical teams, and, when applicable, type of underlying medication error. Only ADEs with a causality score of nearly certain, probable, and possible, as assessed according to the World Health Organization–Uppsala Medical Centre (WHO-UMC) criteria were included. ADEs caused by a medication error were classified as preventable. The severity of an ADE was scored.
Recognition of adverse drug events in older hospitalized patients according to Common Terminology Criteria for Adverse Events ver. 3.0 (CTCAE\textsuperscript{v3}) developed by the U.S. National Cancer Institute\textsuperscript{[32]}. For example, for hyperkalemia, severity of the ADE is classified as mild if the potassium concentration is higher than the upper limit of normal (5.5 mmol/L), as moderate if higher than 5.5–6.0 mmol/L, as severe if higher than 6.0–7.0 mmol/L, and as life-threatening if >7.0 mmol/L. Medication errors were classified according to the Dutch Central Medication Incidents Registration\textsuperscript{[33]} and defined as errors in drug prescribing, transcribing, processing, compounding, stocking, dispensing, administering, or monitoring\textsuperscript{[33]}. To assess if a medication error occurred, we utilized prevailing national\textsuperscript{[34]} and local pharmacotherapeutic guidelines, as well as all alerts generated by the CDSSs operating in the participating hospitals.

The expert team assessed an ADE as unrecognized if, based on the patient charts reviewed, no indication was found that a medical team involved recognized patient harm as being medication related and/or no certain documented actions were targeted at that specific ADE. During the scheduled meetings, the experts reached consensus on all aspects of the ADE assessment for an ADE to be included.

**Main outcome measures**

The main outcome measures were: (1) rate of ADEs present upon admission and (2) rate of ADEs occurring during the hospital stay. Both outcomes were expressed as rates per 100 hospitalisations.

**Statistical methods**

Descriptive statistics were applied for the analysis of patient characteristics, including means, standard deviations (SD), medians, and percentiles. To test for differences between patients included in the three hospitals, normally distributed continuous variables were compared using a one-way analysis of variance test and categorical variables were analyzed by using the chi-square test. Non-normally distributed continuous variables were compared using the Kruskall–Wallis test.

To compare the distributions of ADE severity, causality, type of harm manifestation, and type of events between unrecognized and recognized ADEs, we used the chi-square test or Fisher's exact test.

Multivariable backward logistic regression analyses were conducted to determine which patient factors were independently associated with no recognition of ADEs present upon admission and which factors led to no recognition of ADEs occurring during hospitalisation. Variables in the model for no recognition of ADEs present
upon admission included age, sex, number of preadmission medications, the type of admission (elective or acute), the presence of cognitive impairment on admission (yes/no), and the Charlson Comorbidity Index score\(^{35}\). Variables in the model for no recognition of ADEs occurring during the hospital stay included age, sex, number of hospital medications, length of stay on an Internal Medicine ward, the presence of cognitive impairment on admission (yes/no), and the Charlson Comorbidity Index score\(^{35}\). A p value of <0.05 was considered to be statistically significant. Computer software SPSS ver. 18.0 (SPSS, Chicago, IL) was used for the calculations.

Ethical considerations

The WINGS study protocol\(^{24}\) was presented to The Medical Ethics Committee of the University of Amsterdam. The Medical Ethics Committee discussed the protocol and exempted it from review and official approval. According to the Dutch Medical Research Involving Human Subjects Act, such a review and approval were not required because the study did not involve direct interaction with human subjects. This research used retrospective patient chart review to assess the extent of suboptimal care related to ADEs. Therefore, the integrity of patients was not influenced, and all patient data were analyzed anonymously by coding each patient included in the study by a 6-digit number.

Results

Study population

Demographic characteristics of the 250 patients included in the study are shown in Table 1. The three groups of patients in the participating hospitals only differed in the median length of hospital stay on an Internal Medicine ward (median, with 25th and 75th percentile: AMC, 5.6 days (3.6, 7.9 days); WFG, 5.9 days (2.8, 8.1 days); SH, 7.4 days (4.8, 11.8 days); \(p=0.025\)). Therefore, patients’ characteristics are in Table 1 presented after pooling.

Main outcomes

A total of 269 ADEs in 164 patients were identified. We found 60.4 ADEs (95 % CI 51.5–70.8) present upon admission per 100 hospitalisations (151 ADEs), of which 19.9 % (30/151) remained unrecognized during the subsequent hospitalisation. During the hospital stay, we found 47.2 ADEs (95 % CI 39.4–56.5) per 100 hospitalisations (118 ADEs) to have occurred, of which 20.3 % (24/118) remained unrecognized (Table 2).
Table 1. Patient characteristics

| Characteristic                                      | Total (n=250)    |
|-----------------------------------------------------|------------------|
| Age, years (mean ± SD)                             | 76.9±7.5         |
| Female, n (%)                                       | 133 (53.2)       |
| Living independent, n (%)                          | 211 (84.4)       |
| Acute admission, n (%)                             | 213 (85.2)       |
| Length of stay, days, median (25th, 75th percentile)| 5.9 (3.6, 9.6)   |
| Specialty of wards, n (%)                          |                  |
| General internal medicine                          | 98 (39.2)        |
| Gastroenterology                                   | 51 (20.4)        |
| Nephrology                                         | 46 (18.4)        |
| Oncology and hematology                            | 37 (14.8)        |
| Rheumatology                                       | 18 (7.2)         |
| Number of preadmission medications (mean ± SD)     | 7.3±3.2          |
| Number of hospital medications (mean ± SD)         | 11.0±4.1         |
| Number of concomitant diseases (mean ± SD)         | 3.16±1.7         |
| Most frequent types of diseases, n (%)              |                  |
| Cardiovascular                                     | 179 (71.6)       |
| Malignancy                                         | 94 (37.6)        |
| Diabetes mellitus                                  | 84 (33.6)        |
| Muscle skeletal                                    | 52 (20.8)        |
| Renal                                               | 41 (16.4)        |
| Pulmonary                                          | 39 (15.6)        |
| Gastrointestinal                                   | 30 (12.0)        |
| Neurologic                                         | 22 (8.8)         |
| Psychologic                                        | 15 (6.0)         |
| Charlson Comorbidity Index score, n (%)            |                  |
| 0 points                                            | 24 (9.6)         |
| 1–2 points                                         | 108 (43.2)       |
| 3–4 points                                         | 63 (25.2)        |
| ≥5 points                                          | 55 (22.0)        |
| MDRD eGFR b (ml/min/1.73 m²), n (%)                 | (n=240)          |
| ≥90                                                 | 21 (8.8)         |
| 60–89                                               | 73 (30.4)        |
| 29–59                                               | 88 (36.7)        |
| 15–28                                               | 34 (14.2)        |
| <15                                                 | 24 (10.0)        |

SD, Standard deviation; MDRD study, Modification of Diet in Renal Disease study; eGFR, estimated glomerular filtration rate; aLength of stay on the Internal Medicine wards; b For 10 patients no laboratory tests were run during the hospital stay to assess renal function.
When only severe, life-threatening, or fatal ADEs were considered, the overall proportion of unrecognized ADEs decreased from 20.1 to 7.8%. When only ADEs assessed as having nearly certain or probable event–drug causality were considered, the overall proportion of unrecognized ADEs decreased from 20.1 to 15.2%.

The expert team assessed 135 ADEs as preventable (50.2%), i.e., caused by medication errors, of which the medical teams did not recognize 30.4%. Medication errors most often identified were: omissions in prescribing (25.2%), prescribing of too high or too low doses (25.2%), prescribing of medication while contra-indicated (20.0%), wrong pharmacotherapy choice for a known indication (excluding economic considerations) (11.1%), drug–drug interactions (combinations should have been avoided or dosages adjusted) (7.4%), drug administration errors (5.9%), and lack of TDM (5.2%).

The intra-rater agreement of the involved expert team (initial vs. second review by LA and CS 1 year later) was substantial for presence of an ADE (κ=0.74), preventability of

Table 2. Characteristics of adverse drug events identified and their in-hospital recognition by medical teams.

| Characteristics                              | Unrecognized ADEs (n=54) | Recognized ADEs (n=215) | p value and degrees of freedom |
|----------------------------------------------|--------------------------|-------------------------|--------------------------------|
| Time of identification                       |                          |                         |                                |
| ADE present upon admission                   | 30 (55.6)                | 121 (56.3)              | 0.924; df=1                    |
| ADE occurred during the hospital stay        | 24 (44.4)                | 94 (43.7)               |                                |
| Severity                                     |                          |                         |                                |
| Mild to moderate                              | 33 (61.1)                | 109 (49.3)              | 0.171; df=1                    |
| Severe or worse (life-threatening or fatal)   | 21 (38.9)                | 106 (50.7)              |                                |
| Causality                                    |                          |                         |                                |
| Nearly certain or probable/likely            | 41 (75.9)                | 191 (88.8)              | 0.014; df=1                    |
| Possible                                     | 13 (24.1)                | 24 (11.2)               |                                |
| Preventability                                |                          |                         |                                |
| Non-preventable                              | 13 (24.1)                | 121 (56.3)              | <0.001; df=1                   |
| Preventable                                  | 41 (75.9)                | 94 (43.7)               |                                |
| Type of events                                |                          |                         |                                |
| Clinical symptom                              | 27 (50.0)                | 135 (62.8)              | 0.086; df=1                    |
| Laboratory abnormality                        | 27 (50.0)                | 80 (37.2)               |                                |
| Type of harm manifestation                    |                          |                         |                                |
| New harm                                     | 9 (16.7)                 | 174 (80.9)              | <0.001; df=1                   |
| Sustained/worsened harm or delayed recovery   | 45 (83.3)                | 41 (19.1)               |                                |

ADE, Adverse drug event; df, degrees of freedom; Data are presented as the number of patients, with the percentage given in parenthesis.
ADEs (κ=0.68), and severity (κ=0.93).

Characteristics of recognized and unrecognized ADEs

A substantial number of ADEs identified by the expert team caused serious patient harm (47.2%; 127/269 ADEs were scored as severe, life-threatening, or fatal). Of these ADEs 16.5% were not recognized by the medical teams (Table 2). We identified four fatal ADEs (all recognized by the medical teams) and 38 ADEs which caused life-threatening patient harm [5 (15.2%) unrecognized by the medical teams]. Differences in distributions between the unrecognized and recognized ADEs were found for causality (p=0.014, df=1), preventability (p<0.001, df=1), and type of harm due to an ADE (p<0.001, df=1). In comparison with recognized ADEs, unrecognized ADEs were more often ADEs with a possible drug–event causality score, preventable ADEs, and less often ADEs which resulted in new symptoms or pathology. The most frequent events related to ADEs (87.0% of all ADEs identified), their severity and causality, and recognition are shown in Table 3, as well as medications most frequently involved in those ADEs listed per event type.

All ADEs resulting in hemorrhage raised International Normalization Ratio (INR), skin reaction, and, except for one event per category, all ADEs resulting in constipation or ileus, and hyper- and hypoglycemia were recognized by the medical teams involved (Table 3). Causality of those events with medication was assessed as nearly certain or probable for 64.3% of the ADEs resulting in raised INR to 100.0% of the skin reaction ADEs and ADEs resulting in constipation/ileus. More than half of ADEs resulting in hemorrhage (56.5%) and hyper-hypoglycemia (66.7%), and all ADEs resulting in raised INR (100.0%) were severe or worse according to the CTCAEv3 criteria[32].

The proportions of unrecognized ADEs were higher for events in the following categories: central nervous system (CNS), (23.8% unrecognized), hypotension/bradycardia (27.8% unrecognized), anemia (40.0% unrecognized), nausea and vomiting (44.4% unrecognized), raised creatinine/renal insufficiency (47.1% unrecognized), and raised liver transaminases (LTs)/liver insufficiency (53.3% unrecognized) (Table 3). Of the latter two categories, 75.5% manifested as an abnormal laboratory test result only. The majority of these ADEs was assessed as having nearly certain or probable drug causality (66.7% for CNS events to 94.4% for hypotension/bradycardia). The proportions of severe or worse ADEs according to CTCAEv3 criteria[32] were, except for CNS events, lower (26.7% for anemia to 44.4% for hypotension/bradycardia) than those for ADEs which were (almost) all recognized. Of the CNS events, 66.7% was scored as severe or worse.
Multivariable analyses

The Charlson Comorbidity Index score\textsuperscript{[32]} was the only characteristic independently associated with no recognition of ADEs present upon admission [odds ratio (OR) 0.76, 95\% CI, 0.59–0.97; \( p=0.026 \)]. Patients with cognitive impairment on admission seemed to have a higher risk for unrecognized ADEs being present upon admission in comparison to patients without cognitive impairment (OR 2.4, 95\% CI 1.00–5.85; \( p=0.05 \)). No independently associated patient characteristics were found for having an unrecognized ADE occurring during the hospital stay.

Discussion

Our study focused on medical teams' ability to recognize ADEs in hospitalised older patients aged 65 years or older and included an assessment of both ADEs present upon admission and ADEs occurring during the hospital stay. We found that of all 269 ADEs identified by our expert team, 20\% remained unrecognized by medical teams during the hospital stay. Of the unrecognized ADEs, more than a half (56\%) were ADEs present upon admission, and the majority (76\%) were ADEs caused by medication errors. Our results show that patients' characteristics as well as ADE characteristics impact the ability of medical teams to recognize ADEs in older inpatients.

The rates of both ADEs present upon admission (60.4 per 100 hospitalisations) and ADEs occurring during the hospital stay (47.2 per 100 hospitalisations) identified in this study are markedly higher than those reported in previous ADE studies in older patients\textsuperscript{[5, 12–22]}. These differences can partly be explained by differences in the type of identification method used, the clinical setting, and in the definitions of the outcomes applied\textsuperscript{[25, 36, 37]}. In this study, we used a definition of an ADE which included not only new ADEs, but also worsened and sustained harm or delayed recovery from harm due to both preventable and non-preventable ADEs\textsuperscript{[4, 24]}. Furthermore, by utilizing an adapted IHI ADE trigger-tool\textsuperscript{[29]} as an aid, our chart review was more structured and may, therefore, be more accurate\textsuperscript{[27, 30, 38]}. We also deployed a physician–pharmacist team to review patient charts because the professional knowledge of this combination is complementary\textsuperscript{[39]}. These combined aspects of our methodology may have resulted in a higher number of ADEs being identified. In addition, we included patients with five or more medications on the day of admission. It is well acknowledged that a higher number of medications significantly increases the risk of an ADE\textsuperscript{[40]}. The distribution of ADEs in our study per severity category, however, is comparable to that in other published ADE studies reporting on severity classification\textsuperscript{[23, 41]}, indicating that the high
ADE yield gained in this study was, therefore, also not merely a result of a higher identification of less clinically relevant ADEs. Although a direct comparison of our results on ADE recognition in older medical inpatients with those of previous studies is not possible, some aspects of our findings can be compared. In a study by Hohl et al.\textsuperscript{[23]} conducted in an Emergency Department (ED) setting, the medical teams did not recognize 50% of ADEs present upon admission in older patients, whereas in our study this proportion was 20%.

This lower proportion can be explained by several factors. First, the ED study of Hohl et al.\textsuperscript{[23]} was conducted in a Canadian hospital\textsuperscript{[23]} and our study was conducted in three hospitals in the Netherlands. As such, the level of medical training in geriatrics and/or ADEs awareness may differ between the physicians involved in these two studies. Differences between healthcare settings are known to have an impact on ADE rates\textsuperscript{[36]}. Second, in comparison to the relatively short ED visit, the time available to critically review admission medication during the hospital stay is longer. Third, because more than 80% of our patients were acutely admitted, they were often first seen in the ED. Hospital admission summaries written by ED physician’s sometimes included possible medication-related causes promoting further examination by the treating physicians on medical wards. Interestingly, the percentage of unrecognized ADEs in our study is in line with that reported in a study in a general inpatient population where 24% of ADEs were not recognized by the medical team\textsuperscript{[11]}. Given the complexity of older patients’ cases, one could expect the proportion of unrecognized ADEs in our study to be much higher. Unfortunately, detailed data on the type of unrecognized ADEs were not presented by Nebeker et al.\textsuperscript{[11]}, which hampers further exploration of this point.

Patient characteristics and ADEs recognition

The results of our multivariate analyses showed that the odds for having an unrecognized ADE on admission decreased by 24% with each one point increase in the Charlson Comorbidity Index score\textsuperscript{[33]} (95% CI 0.59–0.97; \( p=0.026 \)), while these odds appeared to be 2.4-fold higher in patients with cognitive impairment (95% CI 1.00–5.85; \( p=0.05 \)). The former results indicate that the physicians were well aware of the frail state of multi-morbid patients; the latter results suggest, however, that they were insufficiently aware of medication-related harm in patients with cognitive impairment on admission. A possible explanation for the better recognition of ADEs in multi-morbid patients is probably the investment of more time and/or involvement of other medical specialties. Previous studies have shown that a multidisciplinary approach is successful in improving prescribing in older patients\textsuperscript{[42–44]}. Cognitive impairment is a well-known and highly prevalent atypical symptom in hospitalised elderly patients\textsuperscript{[45]}. Atypical disease presentation often hampers correct and timely diagnosis and treatment\textsuperscript{[19]}. Therefore, such presentation may be an extra barrier in distinguishing between disease and med-
### Table 3. Most frequently identified ADEs and their recognition by the medical teams during the hospital stay

| Type of events (examples of most often involved medication) | No. of all events identified by the expert team (% unrecognized) | No. of severe or worse events (% unrecognized) | No. of nearly certain and probable events (% unrecognized) |
|-----------------------------------------------------------|---------------------------------------------------------------|-------------------------------------------------|--------------------------------------------------------|
| Electrolyte disturbances (diuretics/RAAS inhibitors)      | 43 (18.6)                                                     | 11 (27.3)                                      | 34 (17.6)                                              |
| Hemorrhage (coumarines/anti-platelet medication, omissions of gastro-protective medication) | 23 (0.0)                                                      | 13 (0.0)                                       | 19 (0.0)                                               |
| Central nervous system events<sup>a</sup> (opiates/benzodiazepines/beta-blockers) | 21 (23.8)                                                     | 14 (21.4)                                      | 14 (7.1)                                               |
| Hypotension/bradycardia (beta-blockers/diuretics/digoxin)  | 18 (27.8)                                                     | 8 (12.5)                                       | 17 (29.4)                                              |
| Delayed recovery from an infection or sustained infections<sup>b</sup> (antibiotics) | 18 (11.1)                                                     | 15 (13.3)                                      | 16 (6.3)                                               |
| Raised creatinine/renal insufficiency (antibiotics/NSAIDs/RAAS inhibitors/diuretics) | 17 (47.1)                                                     | 6 (33.3)                                       | 15 (53.3)                                              |
| Constipation or ileus (omission of laxatives while taking opiates) | 16 (6.3)                                                      | 6 (0.0)                                        | 16 (6.3)                                               |
| Hyper- and hypoglycemia (anti-diabetic drugs/corticosteroids) | 15 (6.7)                                                      | 10 (0.0)                                       | 14 (7.1)                                               |
| Raised LTs/liver insufficiency (anti-diabetic drugs/antibiotics/statins) | 15 (53.3)                                                     | 7 (85.7)                                       | 10 (60.0)                                              |
| Anemia<sup>c</sup> (omission of iron supplements) | 15 (40.0)                                                      | 4 (25.0)                                       | 13 (38.5)                                              |
| Raised INR (coumarines) | 14 (0.0)                                                      | 9 (0.0)                                        | 14 (0.0)                                               |
| Skin reactions (intra-venous antibiotics) | 10 (0.0)                                                      | 0 (0.0)                                        | 10 (0.0)                                               |
| Nausea and vomiting (antibiotics) | 9 (44.4)                                                      | 3 (33.3)                                       | 7 (28.6)                                               |

RAAS, Renin—angiotensin—aldosterone system; NSAIDs, non-steroidal anti-inflammatory drugs; LTs, liver transaminases; INR, International Normalization Ratio; <sup>a</sup> Mainly delirium (7 ADEs), extrapyramidal symptoms (4 ADEs), falls (4 ADEs), and somnolence/drowsiness (3 ADEs); <sup>b</sup> Delayed recovery from or sustained infections were primarily caused by inappropriate empirical antibiotic therapy choice, too short treatment regimes, or inappropriate route of antibiotic administration (oral where intravenous was indicated); <sup>c</sup> Mainly cases of older patients with chronic cardiovascular disease who were hospitalised due to (excessive) blood loss, in whom anemia was not sufficiently corrected to decrease risks involved with low hemoglobin values.
ications as a cause of patients’ symptoms that are present at the time of admission.

Characteristics and recognition of ADEs

In our study, recognized ADEs were more often ADEs manifesting as new symptoms (p<0.001; df=1). This finding is in line with the results reported by Hohl et al.[23] who found that ED physicians were most skillful in recognizing ADEs that represented patients’ chief complaints. In a daily practice on the wards, physicians tend to focus first on new symptoms when making differential diagnoses. The most plausible causes are listed, and actions prioritized according to urgency and/or severity of the symptoms. Worsening of existing complaints, delayed recovery, or no clinical improvement are probably more often associated with progression of the underlying pathology or the frail state of an older patient than with a drug effect.

As already mentioned, the task of distinguishing between an ADE and other causes of an event in often multi-morbid, polymedicated older inpatients is challenging[6, 9]. Our results show that a strong causality between an event and a drug (nearly certain or probable ADEs) improves the ability of a physician to recognize ADEs (p=0.014, df=1). The essential distinctions between nearly certain/probable and possible drug–event causality are that in the latter case there may be another equally likely explanation for the event and/or there is no information or uncertainty regarding what has happened after the suspected medication was stopped[31]. Therefore, it is likely to assume that possible ADEs are more easily missed. Not recognizing possible ADEs can, however, have serious consequences, as illustrated by one of our cases that of a 90-year-old man, recently started on mirtazapine 15 mg once daily for depression, presented with dyspnoea, peripheral edema, and somnolence. The reported incidence of somnolence with mirtazapine use is >1–10 % and of peripheral edema >10 %. The patient was, however, diagnosed with pneumonia, and antibiotic treatment was initiated. The peripheral edema was treated with intravenous furosemide boluses; treatment with mirtazapine was continued. One day post-discharge, the patient was readmitted with increased somnolence and peripheral edema. After consulting a geriatrician, mirtazapine was discontinued, with subsequent resolution of the somnolence and peripheral edema.

In our study, CNS events, such as somnolence or delirium, as well as hypotension/bradycardia, anemia, nausea/vomiting, raised creatinine/renal insufficiency, and raised LTs/liver insufficiency were often unrecognized as being drug-related (>20 % unrecognized). These less well-recognized events are examples of symptoms mimicking the presentation of various underlying pathologies and are less specific side-effects of medications. Moreover, in our study, these types of ADEs represented 40 % of the most frequently
identified ADEs (Table 3) and have also been reported as frequent events in other ADE studies in older inpatients\cite{5, 12-22}. It would appear that sufficient pharmacotherapeutic and geriatric knowledge is necessary to be able to identify these evidently more challenging ADEs\cite{43,44}. In the hospitals participating in this study, the day-to-day care of inpatients is, however, provided by mostly junior medical residents with 1 or 2 years of clinical experience. Studies on the level of geriatric competencies of medical residents show that there are gaps in their skills and knowledge that need to be addressed to ensure that the growing group of older inpatients receive safe care\cite{46, 47}. In case of ADEs resulting in raised creatinine/renal insufficiency and raised LTs/liver insufficiency, the fact that majority of these resulted in abnormal laboratory values only (76 %) may additionally have attributed to the lower recognition of these events (p= 0.086, df=1). In the study by Hohl et al.\cite{23}, the ER physicians were also less proficient at detecting ADEs which resulted in abnormal laboratory values, i.e., the so-called “silent ADEs”.

In contrast, ADEs resulting in hemorrhage, raised INR, constipation/ileus, skin reactions, and hyper/hypoglycemia were (almost) all recognized as being drug-related. These ADEs are examples of events with clinically apparent consequences and are very common and specific side-effects of medications. For example, the INR is often closely monitored during the hospital stay in patients taking coumarines. According to CTCAEv3 criteria\cite{32}, a severely raised INR implies an INR twofold the upper limit of normal (ULN) (9/14 cases of raised INR in our study). For atrial fibrillation, the INR target range is 2.5 to 3.5, and twofold the ULN indicates an INR of >7.0. This clinically relevant rise, a known effect and side-effect of coumarines, was, therefore, easily noticed (100% recognized). The fact that the majority of these well-recognized ADEs caused severe or worse patient harm (57–100%) may also have contributed to better recognition. The unrecognized ADEs seem more likely to be ADEs of mild or moderate severity (p=0.171, df=1).

Last but not least, in our study the majority of ADEs (70%) occurring during the hospital stay were caused by medication errors. Prescribing contra-indicated medications, dosing errors, and drug omissions accounted for 70% of all errors identified. Moreover, unrecognized ADEs were significantly more often preventable ADEs (p < 0.001). Many medications used by older patients are lifelong treatments, often prescribed (previously) by other medical specialists or general practitioners for known therapy needs and conditions at that time\cite{6}. However, these conditions and needs can change, and medication once chosen could become inappropriate\cite{6}. Physicians’ reluctance to change or question drug therapies prescribed by colleagues is a well-known phenomenon\cite{48} and a possible reason why (home) medication, even with errors, was continued unjustifiably.
Limitations

Our study has a number of limitations. First, methods based on expert opinion in the identification of ADEs are known to have a low agreement between the experts involved\[49\]. Given the obvious differences in knowledge and expertise between pharmacists and physicians, such a disagreement is, however, expected \[50\]. Yet, exactly because of these differences, pharmacists and physicians are complementary experts in terms of ADE identification\[39\]. Differences between our two experts regarding their judgments on ADE causality, severity, preventability, and recognition were resolved by consensus. Moreover, the identification and assessment of ADEs by our expert team were reproducible. Second, because we identified ADEs based on a retrospective patient chart review, a registration bias may have occurred. Although a prospective ADE identification method has been shown, especially for preventable ADEs, to provide more veracious results\[51\], an unresolved dilemma remains because the prospective method can also bias results given physicians’ awareness of data collection. To use the data presented in this manuscript for an evaluation of future interventions, we determined that a retrospective method was more suitable to our needs. Third, a patient chart review method is especially useful to identify preventable ADEs due to prescribing errors and less helpful to identify preventable ADEs due to administration errors\[52\]. This may explain why administration errors accounted for only 6% of the preventable ADEs identified in this study. We were, however, mainly interested in the suboptimal care from the medical perspective and less from the nursing perspective. Although administration errors are frequent, the majority of these errors do not lead to ADEs\[3\]. Finally, the measurement of quality of care based on chart reviews is prone for documentation bias\[53\]. Actions taken and considerations regarding the choice of therapy may not be evident from what was recorded in patient charts and could, therefore, be considered inappropriate. However, it is also well-known that actions documented in patients files are not always performed\[53\]. Therefore, we collected among other things medical files, nursing files, medication charts, medical correspondence, laboratory and diagnostic findings, discharge letters, and home and discharge medication lists. Our experts considered all of these different types of sources during the structured assessment of the ADEs. Consequently, we are confident that our chart review provides veracious results for both ADEs rates and their recognition by medical teams\[54\].

Unanswered questions

Medication errors often have a complex causality and arise not only from active errors,
such as insufficient knowledge, but also from factors such as a lack of training in prescribing or insufficient supervisor’s feedback on prescribing. The opportunity to investigate these so-called error provoking and latent conditions was limited because we identified ADEs by a retrospective patient chart review. By involving the Internal Medicine staff and residents in a risk-analysis to design future interventions, we hope to gain more insight into these factors.

Future research

Our data were obtained in three different hospitals, which increases the generalizability of our results. However, because the degree of ADEs recognition may differ between medical specialties or countries, more studies are needed to confirm our findings. Strategies such as the Screening Tool of Older Persons’ potentially inappropriate Prescriptions (STOPP), Screening Tool to Alert doctors to the Right Treatment (STOP), and quality indicators for in-hospital pharmaceutical care of elderly patients have the potential to improve the recognition of ADEs by detecting inappropriate prescribing. Considering ADEs as a differential diagnosis in older patients should be a standard approach on admission and during the hospital stay. Medical education regarding ADEs, a regular and comprehensive medication review, a daily participation of clinical pharmacists in medical teams on the wards, and CDSSs specific to older in-patients’ medication risks could all be of an added value in reducing preventable ADEs and improving ADE recognition.

Conclusions

By applying a comprehensive measurement strategy that included the identification of ADEs present upon admission and those occurring during the hospital stay, followed by an assessment of medical teams’ ability to recognize these ADEs, we were able to identify patient- and ADE-related factors influencing the ability of medical teams to recognize ADEs in older vulnerable patients. The medical teams involved performed best at recognizing ADEs manifesting as new or clinically apparent symptoms and those causing serious patient harm. Less specific ADEs mimicking underlying pathology, ADEs with only an abnormal laboratory value or mild to moderately severe ADEs were less well recognized. However, physicians should also aim at achieving timely recognition of such less critical and less evident ADEs to prevent future emergencies. The findings of this study suggest areas where physicians should focus their attention in order to further improve their ability to recognize ADEs.
Acknowledgments

We thank all of the staff of the Internal Medicine and Hospital Pharmacy departments of the participating hospitals for their support, and in particular Wendy van den Berg, José Popma-de Koning, Anouk Verburg-Eisma, Carla Kamp, Vera Ruijter and Jolande van der Wildt for their assistance in data collection, and Miranda Roskam for building the database for the study. We would also like to acknowledge the help of pharmacy students Kayan Tsoi and Mila Tjoa in the data entry for this study.

Collaborators

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Funding

The study was supported by an unrestricted research grant from the Netherlands Organization for Health Research and Development (ZonMW), The Hague, The Netherlands (Project number SG0000001). ZonMW had no role in the study design, data collection and analyses, interpretation of the results, or in the production of this manuscript.

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General discussion
Introduction

Pharmaceutical care is an essential component of the medical care of elderly patients. However, older patients (aged >65 years) represent a vulnerable population and suffer more from medication related problems than younger adult patients, especially during hospital stay\textsuperscript{[1-4]}.

Medication related problems can present themselves in diverse manners, as medication errors or as patient harm, and can also have very different aetiology. Consequently, there are multiple approaches to measure medication related problems. They can be measured at systems level, pointing out latent factors of for example organizational or technical nature that contribute to medication errors or ultimately to medication related patient harm; at process level, for example by counting how frequently a specific process, such as a drug administration, was conducted insufficiently or a therapeutic decision was made incorrectly; or by measuring outcomes, the actual harm that was caused to patients.

The aim of this thesis was to describe the development of three measurement methods for medication related problems in elderly hospitalised patients, each with one of the above mentioned foci, and to compare the results achieved in their application.

In this final chapter the comparison of the results of the individual studies is made and the results are placed in a broader perspective. Finally, this chapter will conclude with implications and recommendations for clinical practice and directions for future research.

Measurement of medication related problems in elderly

Medication related problems at admission and typical aspects of the elderly population

Many medication related problems originate from before hospitalisation. Besides having an increased risk for medication related problems, elderly patients present themselves more frequently than younger patients with atypical symptoms (geriatric syndromes), making it more difficult to correctly diagnose underlying disease but also to timely recognize medication related problems and adverse drug events (ADEs). Compared with younger patients, patients aged 65 years or older are at a 4-fold higher risk for ADEs\textsuperscript{[1]}. Since both geriatric syndromes (like delirium and falls) and ADEs are frequent-
ly found in acutely hospitalised elderly patients we suggested a possible association or sequential time course may exist. Therefore, in Chapter 2, we investigated whether geriatric syndromes were associated with ADEs in acutely admitted elderly patients. In this chapter we confirmed that elderly form a high-risk patient group as over 25% of the studied acutely admitted elderly had an ADE present at admission. We also underscored the importance of taking geriatric syndromes and atypical disease into account because 26% of the patients presented with delirium and 12% with a fall. ADEs were associated with a fall, with non-steroidal anti-inflammatory drugs and diuretics, but not with pre-existing functioning, delirium or older age. And, when focusing only on ADEs caused by psychoactive drugs, a fall just before hospitalisation, antipsychotics and opioids were independently associated with an ADE. To prevent elderly patients from unnecessary admissions, more proactive, preventative initiatives should be undertaken, especially in primary care. This could lead to a timely identification of ADEs revealing themselves as an atypical illness presentation, namely with a fall or delirium as a geriatric syndrome, or could even lead to the prevention of acute hospital admission. Additionally, geriatric syndromes presenting in hospital patients need a more systematic and holistic approach to recognize them in time as potential ‘atypical’ presentations of an ADE. Geriatric syndromes, especially falls, may indicate important warning signs and thus may require additional evaluations to understand potential underlying pathological processes, like the use of harmful medications.

Medication related problems during hospital stay

Three foci and their methodological aspects

Medication related problems can be measured at three levels.

1. At systems level. The goal of this approach is to point out structural risk factors (in the organisation) that can lead to medication errors or ultimately to an ADE (and hence patient harm). Prospective risk analysis methods have a systems focus and can be used for detecting ‘gaps’ in the medication-use process that contribute to medication related problems and incidents. One of the benefits of this approach is the determination of so-called ‘latent conditions’ of organizational or technical nature that contribute to an increased risk of medication related harm (for example under-staffing, ineffective safety checks or an insufficient training program for new employees). When these latent factors are resolved or improved, potentially numerous medication incidents and a large amount of patient harm can be prevented on a structural basis. In Chapter 3 we describe the adaptation of the Bow-Tie model for prospective risk analysis in medication safety in hospitals. This
model, already well-known in petrochemical and aviation industry, was applied on the medication-use process in two hospitals. We defined a recommended procedure for application of the model. By using a multidisciplinary panel, by specifying and prioritizing patient group or department specific top events and analyzing these safety issues in-depth by drawing Bow-Tie diagrams, the method was better applicable, more comprehensible, and created more awareness of latent conditions and underlying causes at a systems level. Although we did not specifically focus on elderly hospitalised patients in this chapter, multiple risk factors for medication errors and medication related harm for the hospital patient population in general were found that also apply to the elderly patient. Latent conditions in the medication-use process apply to almost all patients; it is the combination of a specific incident with the patient type and drug type that defines the consequential harm. As elderly patients are less resilient than younger patients (as mentioned earlier due to multimorbidity, pharmacokinetic and pharmacodynamic changes, polypharmacy, cognitive, social and functional limitations) and often receive complex care, extra safety barriers or strengthening of existing barriers should be considered to prevent or to mitigate harm. The Bow-Tie model can assist in this effort. Furthermore, the system is of influence on processes and outcomes. A bad organisational structure will lead to processes that are conducted wrongly and ultimately to bad outcome like patient harm. By identifying and improving these organisational weaknesses or latent conditions, many medication errors of diverse nature and bad patient outcomes like adverse drug events can be prevented. For this reason, and also because of the multidisciplinary awareness, the Bow-Tie model can be best used as a starting point in an improvement trajectory.

2. At process level. Processes can be amended and measured more easily than outcomes can. Also, in contrast to outcomes, process indicators do not need to be adjusted for potential confounders. Process indicators, consisting of a nominator and denominator, can be defined in a meticulous selection process using scientific evidence and expert opinion. These process indicators can be phrased very explicitly, thereby reducing subjective judgment when applied on medical patient information. This results in good kappa values for intrarater reliability. Furthermore, due to this aspect, several indicators can be scored in a relatively small amount of time with no necessary expert knowledge. Hence, this aspect also enables the use of non-physicians or non-pharmacists to score process indicators. Also, the principle of process indicators offers an opportunity to carefully define a comprehensive selection of different areas on which the indicators focus with no limitation on the number and content of indicators.

The ACOVE quality indicator (QI) set, developed in 2001 by RAND/UCLA,
consists of explicitly phrased IF-THEN clinical rules (indicators) with comprehensive coverage of general medical and geriatric conditions to assess the quality of care of vulnerable elderly. The ACOVE specifically addresses undertreatment, an issue often overlooked in the elderly patient population. The indicators are intended to evaluate, by measuring adherence to these rules, whether minimal standards of care are met\(^5\). In Chapter 4.1 we systematically reviewed literature to examine and analyze the various ways the ACOVE QIs have been applied in medical science since their introduction. We showed that these process indicators have formed the basis for many studies that could be categorized in two main themes: studies that applied the QIs to measure quality of care and studies that described the development and feasibility of QI sets. The ACOVE QIs inspired various applications (mostly for the assessment of quality of care) and hold promise of forming a common ground for aligning diverse research efforts.

The original ACOVE QIs were developed to assess overall quality of care of community dwelling elderly in the US healthcare setting. To be able to assess the quality of pharmaceutical care of hospitalised elderly in the Netherlands we developed a new valid and reliable QI set based upon the original ACOVE QIs (Chapter 4.2). Our QI set consisted of 87 indicators of which 49 were ACOVE and 38 were newly added. We have further improved both feasibility and reliability in comparison to the original ACOVE QIs by making patient or caretaker interviews to score the indicators of our set unnecessary. The inter-rater agreement kappa values ranged from 0.85-0.88, hence showing almost perfect agreement.

3. At outcome level. Clinical outcome measures are considered the best end point in order to measure health effects on a patient. Only by assessing what actual harm or good was done to patients one can really conclude whether a specific intervention, treatment or action has a positive or negative effect. However, as mentioned earlier, in contrast to processes, outcomes are less amendable and more difficult to measure and generally have to be adjusted for potential confounders. In the field of medication safety research adverse drug events (ADEs) are the main outcome measure. ADEs are usually defined as any injury due to the use of medication. Especially ADEs that are caused by medication errors are important because of their preventability. As opposed to unpreventable ADEs (adverse drug reactions (ADRs) or side effects), that occur during normal and correct use of medication as a result of an unavoidable pharmacological effect, preventable ADEs are associated with substantial morbidity, increased mortality, a longer length of stay in hospital and increased costs\(^6-8\).

In Chapter 5.1 we describe the research protocol of the WINGS study, a multi-
centre study to assess reduction of ADE incidence in elderly internal medicine patients by on-ward pharmacy services. We chose a clinical outcome (ADEs) as a primary endpoint because only a few studies had investigated the effect of on-ward pharmacy services on clinical outcomes\cite{9}. Furthermore, limited data exist regarding ADE incidence in elderly in the inpatient setting although elderly patients have a higher risk of experiencing an ADE.

While measuring preventable ADEs has the benefit of giving an idea of the actual preventable harm that was caused by medication related problems, it is their measurement that has its drawbacks. The golden standard for ADE detection is screening of medical records by research workers and subsequent review of suspected records by an expert panel. This expert panel usually decides by consensus whether an ADE occurred, judges on the type of ADE and estimates the severity. This strategy is laborious and due to the fact that it relies on subjective clinical judgment, it is notorious for its lack of reproducibility and its poor inter-rater agreement. However, for ADE measurement strict explicit algorithms or rules like the process indicators we used in Chapter 4 cannot be applied as strict algorithms like these process indicators hamper sensitivity in ADE measurement\cite{10}. For ADE detection clinical judgment by experienced experts is necessary, thereby accepting a more laborious and implicit method. However, a combination of both an implicit clinical judgment and an explicit decision algorithm can improve results\cite{11}. In the study method we describe in Chapter 5.1 we combined the necessary implicit clinical judgment by experts in order to achieve sufficient sensitivity with an adapted version of the explicit structured causality assessment system used for adverse drug reactions by the WHO-UMC\cite{12}.

**General comparison of results of three measurement methods**

At systems level

The application of the Bow-Tie model for prospective risk analysis in the medication-use process in two hospitals gave insight into many hospital wide risks that affect all patients (Chapter 3). As mentioned earlier, those general risks impose potentially more danger for elderly patients due to their vulnerability and lesser resilience compared to younger patients. Prescription errors, prescribing the wrong drug for the indication but also prescribing the wrong dosage, were considered to be one of the main risks in the medication-use process. Compared to younger patients, prescribing the correct indicated drug for elderly is more challenging due to multi-morbidity and sometimes conflicting guidelines and therapy for co-morbidities. Furthermore, prescribing the correct dose
Chapter 6

is more complex because of the need to frequently adjust the dose due to organ function loss (kidney, liver) or increased effect by pharmacodynamic sensitivity. Pro-active on-ward participation of a hospital pharmacist was considered an important safety barrier that should be implemented in the future. The effect of that future safety barrier on ADEs in elderly was examined in the WINGS study. In this thesis we describe the research method of the WINGS study (Chapter 5.1) and the results of the baseline measurement (Chapter 5.2).

Another large risk form patient transfers (between different care settings, admission and discharge, between care takers) and information exchange about medication. Continuity of care and continuity of information is very important in order to provide safe and correct pharmaceutical care. It is well-known that patient transfers pose a great risk for error and information loss[13-14]. For this aspect too, elderly are at higher risk due to polypharmacy, their complex care, due to multiple treating medical specialists and sometimes multiple care institutions that concurrently or consecutively care for a patient. Furthermore, elderly sometimes have to cope with cognitive impairment and social isolation making it more difficult for the patient to manage his/her medication use. Hence, all the more reason for healthcare providers to address this issue, especially since the elderly patient group will continue to grow. The importance of continuity of care is further underscored by the fact that it forms one of the four main domains of care on which our quality indicator set focuses (Chapter 4.2 and 4.4.).

At process level

ACOVE QIs formed the starting point for many studies in which quality of care for elderly was assessed. In those studies the original ACOVE QIs or adaptations thereof were used to gauge whether the minimally accepted care for one or more specific conditions was delivered. Our systematic review (Chapter 4.3) showed that in 17 studies published after the development of the ACOVE criteria measured quality of care for elderly was still relatively low. Also, when we applied our ACOVE-based QI set in a Dutch elderly patient population we showed that the quality of in-hospital pharmaceutical care for elderly was insufficient (Chapter 4.4). Patients received an average of 42.9% of the care recommended by the indicators. Especially, in order of magnitude, in the domains of continuity of care (median pass rate of only 20.3%), monitoring of drug therapy (median pass rate of 37.3%), and prescription of indicated medication (median pass rate of 63.6%) we showed that there is a strong need to improve the quality of care. These results are worrisome as the ACOVE and our criteria represent the minimal standard of care. The findings about continuity of care and prescribing indicated medication correspond to the main risks found in Chapter 3.
At outcome level

In Chapter 5.2 the results of the baseline measurement of the WINGS study are described. In 250 elderly patients 269 ADEs were found. Of those ADEs 50.2% (135 ADEs) was considered preventable, i.e. caused by medication errors. Underlying medication errors were most often identified as omissions in prescribing an indicated drug, prescribing the incorrect dose, prescribing contra-indicated medication, and prescribing the wrong drug for the indication. These findings are in line with the main risk found in our study focusing on the medication-use process in Chapter 3 (prescribing the wrong drug and dose), and one of the three out of four domains in pharmaceutical care that our QI set pointed out as insufficient and needing improvement in Chapter 4.4. However, whereas the QI set gave insight into specific therapy that was omitted (calcium and bisphosphonates for osteoporosis; secondary prophylaxis of a transient ischemic attack with thrombocyte aggregation inhibitors) the screening of patient records for ADEs pointed out apparent ‘harm’ that a patient suffered from. Most frequent were electrolyte disturbances, hemorrhage, central nervous system effects (like delirium), hypotension/bradycardia, delayed recovery after an infection or sustained infection, and renal insufficiency/raised creatinin. This difference in findings can be explained by the focus of each measurement method. The QIs of Chapter 4 tested whether a clinical rule was followed, thus whether the process was conducted correctly or erroneous. The results of such a method will give insight into medication related process errors. This in contrast to screening records for ADEs where one will get insight into harmful medication related outcomes and less about the underlying preventable errors, unless one specifically examines causality and preventability. Causality and preventability, however, were part of our screening method described in Chapter 5. Hence, our ADE measurement method of the WINGS study made it possible to define the medication that was related to an ADE and its underlying medication error. For the earlier mentioned ADEs that had the highest incidence, the most involved medication was: diuretics/RAAS inhibitors causing electrolyte disturbances; coumarins, anti-platelet medication and omissions of gastroprotective medication causing hemorrhage; opiates, benzodiazepines and beta-blockers causing central nervous system effects; betablockers, diuretics and digoxin causing hypotension/bradycardia; the omission of antibiotics causing delayed recovery after an infection or sustained infection; and antibiotics, NSAIDs, RAAS inhibitors and diuretics causing renal insufficiency/raised creatinin. Therapy of elderly with these drugs should therefore receive extra attention and should be monitored carefully.
Conclusion

Elderly hospitalised patients are indeed a patient group that is at higher risk compared to younger patients for medication related problems. In order to measure their medication related problems and ultimately improve the quality and safety of pharmaceutical care we examined three levels of measurement focus. These three levels of focus (systems, process and outcome level) were practiced in three measurement methods. We did not only describe the development and characteristics of the three measurement methods, but also the results found.

With respect to the aim of this thesis we can conclude that each focus of measurement has its unique characteristics. This is reflected in the general results obtained with each method and the indications for improvement one obtains. Therefore it is necessary to choose a measurement method bearing the aim of a quality improvement project or research study in mind. Furthermore, the use of two or more methods could also be an option, as the methods can be complementary. It can be said that the best and most complete picture of the quality of pharmaceutical care can be obtained using aspects of the three approaches. However, based on our studies recommendations on applying the individual measurement methods can be given. As a starting point in an improvement trajectory a systems approach using the prospective risk analysis method of the Bow-Tie model is recommended. For periodical quality of care measurement and less resource intensive research it is best to use explicit process measures like our QIs (or the original ACOVE QIs). The QIs can be applied at low cost and because of the explicit phrasing no experts are needed to conduct the measurements. Furthermore, by using process measures one will acquire insight into tangible parts of processes that need improvement which thereafter can be amended swiftly. For research in which resources and time are not scarce and measuring actual patient harm in detail is of importance (such as in a study that examines the effect of a specific intervention on patient outcomes), the ADE measurement method of our WINGS study is the best choice. Whereas explicit process measures like our indicators facilitate comparison of results of other studies using the same or comparable indicators, results of studies reporting ADEs should be compared with utmost caution due to differences in applied criteria and definitions.

Despite the differences in characteristics of each applied measurement method, the results of the three methods were in concordance regarding the fact that the quality of (pharmaceutical) care for elderly patients is still poor and needs improvement.

Based on the results discussed in this thesis, we summarize implications for clinical
practice and provide suggestions for future research, all in order to improve quality of pharmaceutical care of the elderly and to reduce medication related problems.

Implications for clinical practice and medication related problems research in elderly

- Elderly patients are a patient group at higher risk for medication related problems. Due to the growing number of elderly and their increasing age healthcare should focus on safer care for these patients.

- To prevent elderly patients from unnecessary admissions more proactive, preventative initiatives should be undertaken, starting in primary care. This could lead to a timely identification of ADEs revealing themselves as an atypical illness presentation, namely a fall or a delirium as a geriatric syndrome, or even to prevention of an acute hospital admission.

- As geriatric syndromes, especially falls, may indicate important warning signs for underlying problems with medication, they need a more systematic and holistic approach to recognize them in time as an atypical presentation of an ADE.

- (Internist-) geriatricians and hospital pharmacists are the obvious professionals to deliver this care. Collaboration between these two groups is necessary.

- When an elderly patient presents his or herself with atypical disease during acute admissions, ADEs should be considered as a differential diagnosis.

- In measurement of medication related problems in elderly patients and the subsequent definition of improvement strategies there are three options for focus: at systems level, at process level, and at outcome level.

- Use prospective risk analysis utilizing the Bow-Tie method as a starting point to align/focus improvement projects in a multidisciplinary fashion (systems level).

- For periodical quality of care measurement and relatively less laborious quality of care measurement as part of studies QIs are well suited. Due to their explicit phrasing, ACOVE like QIs could be automated using IT making their application even less resource intensive (process level).

- Due to the laborious nature of ADE measurement it is more suitable for research
purposes than for general periodical quality measurements. It is the most clinical relevant measure as it reflects actual patient harm due to medication. The lack of reliability in ADE measurement and judgment, however, forms an important drawback (outcome level).

- There is an opportunity to use ACOVE(-based) QIs pro-actively to steer health-care professionals to deliver the right care at the right time; for example by incorporating the QIs in clinical decision support tools.

- Pharmaceutical in-hospital care for elderly in the Netherlands, as measured with our QI set, but also the care for elderly in general internationally, is insufficient. Continuity of care, medication monitoring and prescribing indicated medication should be improved.

- ADEs occur frequently in Dutch elderly inpatients. On-ward pharmacy services and a collaborative approach by hospital pharmacist and geriatrician can possibly reduce the preventable ADEs.

- ADE measurement suffers from poor reliability. Much depends on the ADE screening method used and subjective judgments, based on clinical opinion, of experts. Therefore comparison of results between studies should be done with caution.

- All three measurement methods, with each a different focus, point out that especially prescribing indicated medication in the correct dose and continuity of care for elderly patients need improvement.

Future Research

- Study the proactive application of QIs to directly improve care, for example in clinical decision support systems to influence and support physicians. It is worthwhile to shift focus from assessment to improvement in the application of QIs.

- Study the application of our QI set in one or more larger cohorts of elderly hospitalised patients for further validation. This can possibly result in further selection (and thus also discarding) of indicators based on eligibility. Furthermore, a more reliable image can be gained about the quality of in-hospital pharmaceutical care of the Dutch elderly patient.
• Study the effect of collaborative hospital-pharmacist and (internist-)geriatrician lead improvement initiatives on the quality of care for elderly, especially focusing on continuity of care, prescribing medication, medication monitoring, and acute admissions.

• Study the effect of interventions to increase the awareness of doctors, both in and outside of the hospital, that medication related problems and ADEs can present with atypical symptoms. The effect can be measured by the number of acute admissions due to medication.

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7.1 Summary
Summary

Medical care has the danger of causing unintended harm besides serving the patient. Application of medication is one of the most commonly applied medical interventions and has contributed significantly to the increase of quality of medical practice, of life expectancy, and health of people. However, the application of medication can also cause problems, can be erroneous, and cause harm. Among medical errors, medication errors make up the largest part. Of the medical adverse events (harmful events), adverse drug events (ADEs) are the most frequent type in hospitalised patients. ADEs may occur during the normal use of medication as a result of an unavoidable pharmacological effect (side effects or Adverse Drug Reactions (ADRs)), or as a result of a medication error (preventable ADEs). ADEs are associated with extra length of hospital stay, increased morbidity and mortality, and considerable extra costs. Furthermore, a considerable part of hospital admissions are related to ADEs.

Pharmaceutical care is an essential component of the total medical care of elderly patients. However, older patients (aged >65 years) represent a vulnerable population and suffer more from medication related problems than younger adult patients, especially during hospital stay. Older patients are at a higher risk for several reasons: the coexistence of multiple morbidities and often complex care; the presence of pre-existent cognitive, social and functional limitations; altered pharmacokinetics and pharmacodynamics; the use of multiple drugs (polypharmacy) and, consequently, the risk of over- and undertreatment. Furthermore, elderly often transfer from one care setting to the other (hospital-nursing home, hospital-home) thereby increasing the risk for medication errors and adverse drug events. Continuity of care is an important point of attention.

Medication related problems can present themselves in diverse manners, as medication errors or as patient harm, and can also have very different aetiology. Consequently, there are multiple approaches to measure medication related problems and thus quality and safety of pharmaceutical care.

Medication related problems can be measured at systems level, pointing out latent factors of, for example, organisational or technical nature that contribute to medication errors or ultimately to medication related patient harm. Medication related problems can be measured at process level, for example by counting how frequent a specific process, such as a drug administration was conducted insufficiently or a therapeutic decision was made incorrectly. Finally, medication related problems can be gauged by measuring outcomes, the actual harm that was caused to patients.
The aim of this thesis was to describe the development of three measurement methods for medication related problems in elderly hospitalised patients, each with one of the three foci mentioned above and to compare the results achieved in their application.

Elderly patients, besides having an increased risk for medication related problems, present more frequently than younger patients with atypical symptoms (geriatric syndromes), making it more difficult to correctly diagnose a disease but also to timely recognize medication related problems and adverse drug events (ADEs). Compared with younger patients, patients aged 65 years or older are at a 4-fold higher risk for ADEs. Since both geriatric syndromes (like delirium and falls) and ADEs are frequently found in acutely hospitalised elderly patients we suggested a possible association or sequential time course may exist. In Chapter 2 we investigated in a prospective cohort study whether geriatric syndromes were associated with ADEs in acutely admitted elderly patients. Of the total of 641 included patients over 25% had an ADE present at admission, 26% presented with delirium and 12% with a fall. Delirium was associated with the use of antidepressants, antipsychotics and antiepileptics. In all ADEs (n=167), ADEs were associated with a fall, with non-steroidal anti-inflammatory drugs and diuretics, but not with pre-existing functioning, delirium or older age. For ADEs involving psychoactive medication (n = 35), an association was found between delirium, falls, opioids and antipsychotics in bivariate analyses. A fall just before hospitalisation (odds ratio [OR] 3.69 [95% CI: 1.41-9.67]), antipsychotics (OR 3.70 [95% CI: 1.19-11.60]) and opioids (OR 14.57 [95% CI: 2.02-105.30]) remained independently associated with an ADE involving psychoactive medication. The study demonstrated that, in a cohort of elderly hospitalised patients, a fall before admission and prevalent delirium are associated with several pharmacological groups and/or with ADE-related hospital admission.

Systems level

In an exploratory study in Chapter 3 we adapted the Bow-Tie model, a prospective risk analysis method already well-known and used in petrochemical and aviation industries, to the clinical setting for medication safety risk analysis. This model integrates causes, errors, preventive and recovery measures, and consequences and gives insight into the magnitude and causes of existing safety risks. The model was consecutively applied on the medication-use process in two hospitals (a large tertiary academic hospital and a large general teaching hospital). Multiple risk factors for medication errors and medication related harm for the hospital patient population in general were found. Based on the findings in both hospitals we defined a recommended feasible procedure for application of the model. By using a multidisciplinary panel, by specifying and prioritizing patient group or department or ward specific top events and analyzing these
safety issues in-depth by drawing Bow-Tie diagrams, the method was better applicable, more comprehensible and created more awareness of latent conditions and underlying causes at a systems level.

Process level

In Chapter 4 we describe four studies concerning process indicators. The ACOVE quality indicator (QI) set, developed in 2001 by RAND/UCLA, consists of explicitly phrased IF-THEN clinical rules (indicators) with comprehensive coverage of general medical and geriatric conditions to assess the quality of care of vulnerable elderly. The ACOVE specifically addresses undertreatment, an issue often overlooked in the elderly patient population. The indicators are intended to evaluate, by measuring adherence to these rules, whether minimal standards of care are met. In Chapter 4.1 we systematically reviewed literature to examine and analyze the various ways the ACOVE QIs have been applied in medical science since their introduction. We aimed to describe the studies within a comprehensive thematic model that reflected how the indicators were used. A total of 41 articles met our selection criteria. Studies were classified into the themes ‘Application of indicators’ (32 studies) and ‘Analysis and development of indicators’ (13 studies). ‘Application’ studies included assessing quality of care, influencing behavior of health professionals and examining the association of quality of care with other factors. ‘Analysis and development’ included studies developing new indicator sets, and those adapting and validating the original quality indicators to new settings. The ACOVE indicators were used in a wide range of applications with two main foci: the assessment of quality of care for elderly patients and investigating the feasibility of similar indicators and their adaptation to new settings. Very few of the included studies had addressed the goal of care improvement.

The original ACOVE QI set was mainly developed to assess the overall quality of care of community-dwelling vulnerable elders (as opposed to hospitalised elderly). Therefore, they need to be adapted when used in a non-US hospital setting. In addition, the ACOVE QIs depend on patient and caretaker interviews to assess the quality of care. In Chapter 4.2 we aimed to develop and validate a set of explicitly phrased QIs to measure (without the need for interviews) the quality of pharmaceutical care of elderly hospitalised patients in the Netherlands. The developed QI set was based on the ACOVE QIs, Dutch national guidelines, evidence from the literature, and expert opinion. The QI set focused on in-hospital pharmaceutical care and we evaluated whether the QIs were able to assess the quality of care using medical records and a hospital information system. In three review rounds, the QI set was adapted and judged valid on face and content validity. An 87-item QI set was accepted by the expert panel.
Of this set, 49 QIs were based on ACOVE QIs and 38 QIs were newly added. The QI set demonstrated excellent inter-rater reliability (Fleiss’ kappa values for three raters: 0.87 (95% CI: 0.67-1.00); 0.85 (95% CI: 0.70-1.00); 0.88 (95% CI: 0.75-1.00) for respectively determination of condition, drug (class) and quality indicator passed/not passed; intra-class correlation coefficient for two raters: 0.80 (95% CI : 0.63-0.90) for quality indicator passed/not passed for the QIs that were scored by only two raters and good feasibility.

In Chapter 4.3 we aimed to systematically review literature to summarize studies that assess the quality of care using QIs from or based on ACOVE, in order to evaluate the state of quality of care for the reported conditions. Seventeen studies were included with 278 QIs (original, adapted or newly developed). The quality scores showed large variation between and within conditions. Only a few conditions showed a stable pass rate range over multiple studies. Overall, pass rates for dementia (interquartile range (IQR): 11%–35%), depression (IQR: 27%–41%), osteoporosis (IQR: 34%–43%), and osteoarthritis (IQR: 29–41%) were notably low. Medication management and use (range: 81%–90%), hearing loss (77%–79%), and continuity of care (76%–80%) scored higher than other conditions. Out of the 278 QIs, 141 (50%) had mean pass rates below 50% and 121 QIs (44%) had pass rates above 50%. Twenty-three percent of the QIs scored above 75%, and 16% scored below 25%. Although much effort has been put in improving the care for elderly patients in the last years, the reported quality of care according to the ACOVE indicators used in the included studies is still relatively low.

In a retrospective cohort study in Chapter 4.4 we aimed to assess the quality of pharmaceutical care provided to elderly patients admitted to an internal medicine ward (n=200) applying the 87-item set we developed in Chapter 4.2. A secondary objective was to examine the association between the assessed quality of pharmaceutical care and 500 day survival after discharge and readmission rate within 90 days. The study showed that improvements in 3 out of 4 domains of pharmaceutical care are needed. The median pass rates for the four domains ‘Using indicated medication’, ‘Avoiding inappropriate medication’, ‘Continuity and documentation’, and ‘Medication monitoring’ were 63.6%, 100%, 20.3% and 37.3%, respectively. The 200 participating patients had a mean quality score of 42.9%, SD 13.4%. After adjustment for potential confounders no difference was found in survival 500 days after discharge between patients with a low and high quality score (hazard ratio=1.351, p= 0.237). A difference in readmission rate and mortality 90 days after discharge was not found either (p= 0.516). According to the indicators a better quality of pharmaceutical care was not associated with an improved 500-day survival and fewer readmissions within 90 days.
Outcome level

Clinical outcome measures are considered the best end point in order to measure health effects on a patient. Only by assessing what actual harm or good was done to patients one can really conclude whether a specific intervention, treatment, or action has a positive or negative effect. In the field of medication safety research adverse drug events (ADEs) are the main outcome measure. ADEs are usually defined as any injury due to the use of medication. In Chapter 5.1 we described the research protocol of the WINGS study, a multicentre interrupted time series study to assess the reduction of preventable ADE incidence in elderly internal medicine patients by on-ward pharmacy services. The WINGS study consists of a pre-intervention measurement period of ADE incidence, after which ward-oriented pharmacy services are introduced. Thereafter the effects of these services are assessed during a post-intervention measurement period. The ADEs are detected and assessed by a method with a combination of explicit and implicit elements. A structured trigger tool enhanced implicit retrospective chart review by the expert panel consisting of a pharmacist and a physician. The pharmacist and physician knowledge was meant to be complementary. Furthermore, causality and severity assessment of ADEs was structured using a 3 point scale based on the WHO-UMC system and a 5 point scale of the CTCCAEv3 criteria.

In Chapter 5.2 the results of the pre-measurement of the WINGS study are described. In 250 elderly patients 269 ADEs were found. Of those ADEs 50.2% (135 ADEs) was considered preventable, i.e. caused by medication errors. Underlying medication errors were most often identified as omissions in prescribing an indicated drug, prescribing the incorrect dose (for example by not taking renal function loss into account), prescribing contra-indicated medication, and prescribing the wrong drug for the indication. Most frequently encountered drug induced harm was electrolyte disturbances, hemorrhage, central nervous system effects (like delirium), hypotension/bradycardia, delayed recovery after an infection or sustained infection, and renal insufficiency/raised creatinin. The drugs causing electrolyte disturbances were mostly diuretics/RAAS inhibitors; causing hemorrhage were coumarins, anti-platelet medication and omissions of gastroprotective medication; causing central nervous system effects were opiates, benzodiazepines, and beta-blockers; causing hypotension/bradycardia were betablockers diuretics and digoxin; causing delayed recovery after an infection or sustained infection were antibiotics; and causing renal insufficiency/raised creatinin were antibiotics, NSAIDs, RAAS inhibitors, and diuretics.

In the general discussion in Chapter 6 the results of the previous mentioned chapters are discussed in a broader context. In this chapter we focus on:
1. The three foci of measuring medication-related problems and their methodological aspects.

2. General comparison of the results obtained with the three measurement methods.

3. Implications for clinical practice and recommendations for future research.

In conclusion, elderly hospitalised patients form a patient group that is at higher risk for medication related problems compared to younger patients. In order to measure medication related problems in hospitalised elderly and to ultimately improve their pharmaceutical care we examined three possible levels of measurement one can choose. These three levels of focus (systems, process, and outcome level) were practiced in three measurement methods. As a starting point in an improvement trajectory a systems approach using the prospective risk analysis method with the Bow-Tie model is recommended. For periodical quality of care measurement and less resource intensive research it is best to use explicit process measures like our QIs (or the original ACOVE QIs). For research in which resources and time are not scarce and measuring actual patient harm is of importance, the ADE measurement method of our WINGS study is the best choice. Whereas explicit process measures, like our indicators, facilitate comparison of results of other studies using the same or comparable indicators, results of studies reporting ADEs should be compared with utmost caution. Based on the results from all three measurement methods in this thesis it can, however, be concluded that the quality of pharmaceutical care for elderly patients is still poor and needs improvement.
7.2 Samenvatting
Samenvatting

Medische zorg kan naast het verbeteren van de gezondheid van de patiënt, juist ook onbedoelde schade veroorzaken. Farmacotherapie is een van de meest toegepaste medische interventies en heeft in belangrijke mate bijgedragen aan de toename van de kwaliteit van de medische zorg in algemene zin, aan de toename van de levensverwachting en de verbeterde gezondheid van patiënten. De toepassing van medicatie kan echter ook problemen veroorzaken, er kunnen medicatiefouten optreden en de medicatie kan de patiënt schade berokkenen. Van alle voorkomende medische fouten vormen medicatiefouten het grootste aandeel. Daarnaast zijn adverse drug events (ADE’s) het meest voorkomende subtype van medisch onbedoelde schadelijke uitkomsten bij in het ziekenhuis opgenomen patiënten (‘adverse events’ genoemd in het gebied van patiëntveiligheid). ADE’s kunnen optreden tijdens normaal gebruik van medicijnen als gevolg van een onvermijdelijk farmacologisch effect (een bijwerking ofwel adverse drug reaction, ADR) of als gevolg van een medicatiefout (een voorkombare ADE). ADE’s worden geassocieerd met een verlengde opnameduur in het ziekenhuis, met een verhoogde morbiditeit en mortaliteit, en met aanzienlijke extra kosten. Bovendien is groot deel van de ziekenhuisopnames medicatiegerelateerd.

Farmaceutische zorg is een essentieel onderdeel van de gehele medische zorg die oudere patiënten krijgen. Echter, oudere patiënten (leeftijd> 65 jaar) vertegenwoordigen een kwetsbare groep die vergeleken met jongere volwassen patiënten meer medicatiegerelateerde problemen ondervinden, vooral tijdens verblijf in het ziekenhuis. Oudere patiënten lopen meer risico om verschillende redenen: de aanwezigheid van verscheidene co-morbiditeiten, vaak complexere zorg die deze patiëntengroep nodig heeft, de aanwezigheid van pre-existentie cognitieve, sociale en functionele beperkingen, veranderde farmacokinetiek en -dynamiek, het gebruik van meerdere geneesmiddelen (polyfarmacie) en, dientengevolge, het risico op over-en onderbehandeling. Bovendien bewegen ouderen zich frequent tussen verschillende zorgomgevingen (ziekenhuis-verpleeghuis, ziekenhuis-thuis, verschillende specialisten) waardoor het risico op medicatiefouten en adverse drug events toeneemt. Continuïteit van zorg is daarom een belangrijk punt van aandacht.

Medicatie gerelateerde problemen kunnen zich op verschillende wijze presenteren, bijvoorbeeld als een medicatiefout of als letsel aan de patiënt, en kunnen een zeer diverse etiologie hebben. Daarom zijn er meerdere benaderingen om medicatie gerelateerde problemen en de kwaliteit en veiligheid van de farmaceutische zorg te meten.

Medicatiegerelateerde problemen kunnen worden gemeten op systeem niveau, door
te zoeken naar latente factoren van bijvoorbeeld organisatorische of technische aard die bijdragen aan de kans op medicatiefouten en uiteindelijk aan medicatie gerelateerd letsel voor de patiënt. Medicatiegerelateerde problemen kunnen worden gemeten op procesniveau, bijvoorbeeld door te tellen hoe vaak een bepaalde proces correct is uitgevoerd (hoe vaak is een medische handeling onvoldoende uitgevoerd of hoe vaak is een verkeerde therapeutische beslissing genomen). Ten slotte kunnen medicatiegerelateerde problemen worden gemeten door het meten van patiënten uitkomsten, de werkelijke schade die is veroorzaakt aan patiënten.

Het doel van dit proefschrift was om de ontwikkeling van drie meetmethoden voor medicatiegerelateerde problemen bij in het ziekenhuis opgenomen oudere patiënten te beschrijven, waarbij elke meetmethode afzonderlijk een focus heeft die valt onder de drie bovengenoemden (systeem, proces, uitkomst). Daarnaast was het doel om de bij de toepassing van de drie methodes verkregen resultaten te vergelijken.

Naast het hebben van een verhoogd risico voor medicatie gerelateerde problemen, hebben oudere patiënten een ander kenmerk waar rekening mee dient te worden gehouden. Ze vertonen vaker dan jongere patiënten atypische symptomen (‘geriatrische syndromen’), waardoor het moeilijker wordt om volledig en juist te kunnen diagnosticeren, maar ook om tijdig medicatie gerelateerde problemen en ADE’s te herkennen. In vergelijking met jongere patiënten hebben patiënten van 65 jaar of ouder een vier maal zo hoog risico op ADE’s. Aangezien zowel geriatrische syndromen (zoals delier en valincidenten) als ADE’s regelmatig voorkomen bij acuut in het ziekenhuis opgenomen oudere patiënten, achten wij het mogelijk dat er een associatie of een sequentiële tijdsverloop zou kunnen bestaan. In hoofdstuk 2 hebben we in een prospectief cohort onderzoek onderzoek onderzocht of geriatrische syndromen geassocieerd waren met ADE’s bij acuut opgenomen oudere patiënten. Van de in totaal 641 opgenomen patiënten had meer dan 25% een ADE bij opname, presenteerde 26% zich met een delier en 12% had een valincident doorgemaakt. Een delier bleek geassocieerd met het gebruik van antidepressiva, antipsychotica en anti-epileptica. Bij analyse van alle ADE’s (n=167) bleek een ADE geassocieerd te zijn met een val, met NSAID’s en diuretica, maar niet met dagelijks functioneren, delier of oudere leeftijd. Voor ADE’s ten gevolge van psychoactieve medicatie (n=35), werd een verband gevonden met delier, vallen, opioiden en antipsychotica in bi-variante analyses. Een val vlak voor opname in een ziekenhuis (odds ratio [OR] 3.69 [95% CI: 1.41-9.67]), antipsychotica (OR 3.70 [95% CI: 1.19-11.60]) en opioiden (OR 14.57 [95% CI: 2.02-105.30]) bleven onafhankelijk geassocieerd met ADE met psychiatrische medicatie. De studie toonde aan dat, in een cohort van oudere ziekenhuispatiënten, een val vlak voor de opname en delier geassocieerd zijn met verschillende farmacologische groepen en / of met een ADE-gerelateerde ziekenhuisopname.
Systeem niveau

In een verkennend onderzoek in hoofdstuk 3 hebben we het Bow-Tie model, een prospectieve risico-analyse methode waar reeds ervaring mee was in de petrochemische en luchtvaartindustrie, aangepast aan de klinische setting om toegepast te kunnen worden voor risicoanalyses op het gebied van medicatieveiligheid. Dit model integreert oorzaken, preventie- en herstelmaatregelen en gevolgen. Daarnaast geeft het model inzicht in de omvang en de oorzaken van bestaande veiligheidsrisico's. Het model werd achtereenvolgens toegepast voor een risicoanalyse van het medicatieproces in twee ziekenhuizen (een groot academisch ziekenhuis en een groot algemeen opleidingsziekenhuis). Meerdere risicofactoren voor medicatiefouten en medicatiegerelateerde schade voor de algemene patiëntenpopulatie werden gevonden. Op basis van de bevindingen in beide ziekenhuizen definieerden we een aanbevolen werkwijze voor de toepassing van het Bow-Tie model. De methode bleek beter toepasbaar, begrijpelijker en creëerde meer bewustzijn over de veiligheidsrisico's bij deelnemers door de volgende werkwijze te kiezen: een multidisciplinair panel voor de risicoanalyse, het specificeren van patiëntengroep of verpleegafdeling waarvoor de analyse zal worden in tegenstelling tot het gehele ziekenhuis, het prioriteren van voor de verpleegafdeling of patiëntengroep specifieke top-events en alleen deze diepgaand analyseren door het tekenen van Bow-Tie diagrammen. Deelnemers werden op deze wijze beter bewust van latente factoren en onderliggende oorzaken op systeem niveau waardoor, die het mogelijk maken dat medicatiefouten en onbedoelde schade optreden.

Proces niveau

In hoofdstuk 4 beschrijven we vier onderzoeken met betrekking tot procesindicatoren. De ACOVE kwaliteitsindicator (KI) set, ontwikkeld in 2001 door RAND / UCLA, bestaat uit expliciet geformuleerde IF-THEN (‘ALS-DAN’) klinische beslissingsregels met uitgebreide dekking van de algemene medische en geriatrische ziektebeelden bedoeld om de kwaliteit van de zorg voor kwetsbare ouderen te beoordelen. De ACOVE KI meten specifiek ook onderbehandeling; een aspect dat vaak over het hoofd wordt gezien in de oudere patiëntenpopulatie die juist al veel medicatie gebruikt. De indicatoren reflecteren de minimale normen voor de verwachte kwaliteit van zorg. Aan de hand van de naleving van deze beslisregels kan de kwaliteit van zorg worden bepaald.

In hoofdstuk 4.1 hebben we wetenschappelijke literatuur systematisch beoordeeld om te onderzoeken en analyseren op welke verschillende manieren de ACOVE KI sinds hun invoering in de medische wetenschap zijn toegepast. We beoogden de gevonden
onderzoeksartikelen te beschrijven binnen een uitgebreid thematische model dat de verschillende wijzen waarop de indicatoren werden gebruikt tot uitdrukking bracht. In totaal voldeden 41 artikelen aan onze selectiecriteria. De artikelen werden ingedeeld in de thema’s ‘Toepassing van indicatoren’ (32 artikelen) en ‘Analyse en ontwikkeling van indicatoren’ (13 artikelen). ‘Toepassing’ artikelen omvatten het beoordelen van de kwaliteit van de zorg, het beïnvloeden van het gedrag van medisch personeel en het onderzoeken van de associatie tussen de kwaliteit van zorg en andere factoren. Onderzoeken behorend tot ‘Analyse en ontwikkeling’ omvatten het ontwikkelen van nieuwe indicator sets en het aanpassen van de oorspronkelijke ACOVE KIs naar een nieuwe zorgsetting en validatie van de KI set aldaar. De ACOVE indicatoren werden op diverse manieren toegepast in de onderzoek, waarvan er twee manieren duidelijk naar voren kwamen: de inzet voor de beoordeling van de kwaliteit van zorg voor oudere patiënten en de beschrijving van de aanpassing van de KI aan een nieuwe zorgsetting en het onderzoeken van de uitvoerbaarheid van de toepassing van de KI set. Zeer weinig van de geïncludeerde studies hadden de verbetering van de kwaliteit van de zorg tot doel.

De oorspronkelijke ACOVE KI set was vooral ontwikkeld om de algemene kwaliteit van de zorg van thuiswonende kwetsbare ouderen in de Verenigde Staten (in tegenstelling tot het ziekenhuis opgenomen ouderen) te beoordelen. Om deze KI te kunnen gebruiken in een niet-Amerikaans ziekenhuis dienen de ACOVE KI te worden aangepast. Daarnaast zijn voor een meting gebruikmakend van de originele ACOVE KI interviews van patiënten en medisch personeel noodzakelijk om de kwaliteit van de zorg goed te kunnen beoordelen. Dit bemoeilijkt de uitvoerbaarheid. In hoofdstuk 4.2 beoogden we een set van expliciet gedefinieerde KI te ontwikkelen en te valideren. Deze KI set was gericht op het beoordelen van de kwaliteit van de farmaceutische zorg van in het ziekenhuis genomen oudere patiënten in Nederland. Daarnaast zouden er voor de beoordeling van de KI geen interviews met patiënten en medisch personeel meer nodig moeten zijn. De uiteindelijk ontwikkelde KI set werd gebaseerd op de originele ACOVE KI, op Nederlandse nationale richtlijnen, op bewijslast uit de medisch-wetenschappelijke literatuur en op kennis van deskundigen. In drie beoordelingsrondes is de KI set aangepast tot de definitieve samenstelling en als valide beoordeeld op aangezichts-en inhoudsvaliditeit. Uiteindelijk werd een definitieve set van 87 indicatoren vastgesteld door het panel van deskundigen. Van de definitieve set waren 49 indicatoren gebaseerd op ACOVE KI en 38 indicatoren waren nieuw toegevoegd. De KI set toonde een goede uitvoerbaarheid en een uitstekende interbeoordelaarsbetrouwbaarheid (Fleiss kamma waarden voor drie beoordelaars: 0,87 (95% CI: 0.67-1.00), 0,85 (95% CI: 0.70-1.00); 0,88 (95%-CI: 0.75-1.00) voor respectievelijk de bepaling van de voor de patiënt van toepassing zijnde ziektebeelden, de voor de patiënt van toepassing zijnde geneesmiddelen of geneesmiddellkasses en het wel of niet voldoen aan de “ALS-DAN” voorwaarde van de indicator. Voor de KI die werden gescoord door slechts twee beoordelaars
was de intraclass correlatiecoëfficiënt 0,80 (95% CI: 0,63 tot 0,90) voor het wel of niet voldoen aan de “ALS-DAN” voorwaarde van de indicator.

In hoofdstuk 4.3 hebben we systematisch de medisch-wetenschappelijke literatuur onderzocht naar wetenschappelijke onderzoeken die de kwaliteit van de zorg met behulp van ACOVE of daarop gebaseerde indicatoren bepaald hadden. Door de gevonden artikelen te analyseren beoogden we de staat van de kwaliteit van de zorg te evalueren voor alle gerapporteerd ziektebeelden. Zeventien studies konden worden geïncludeerd die in totaal 278 KI beschreven (originele ACOVE, aangepaste of nieuw ontwikkelde KI). De kwaliteitscores (gebaseerd op scores op indicatoren die betrekking hadden op zorg voor een bepaald ziektebeeld) vertoonden grote variatie tussen en binnen de ziektebeelden. Slechts voor een paar ziektebeelden toonde de geleverde zorg een stabiel slagerspercentage bezien over meerdere studies. Met name waren de slagerspercentages voor de zorg voor dementie (interkwartielbereik (IQR): 11% -35%), depressie (IQR: 27% -41%), osteoporose (IQR: 34% -43%) en artrose (IQR: 29-41%) laag. Medicatiebeheer en gebruik (bereik: 81% -90%), zorg bij gehoorverlies (77% -79%) en de continuïteit van de zorg (76% -80%) vertoonden juist een hogere score dan de zorg voor andere ziektebeelden. Van de 278 KI, hadden 141 (50%) een gemiddeld slagerspercentage onder de 50% en 121 KI (44%) hadden een gemiddeld slagerspercentage boven de 50%. Drieëntwintig procent van de KI scoorde hoger dan 75%, en 16% scoorde onder de 25%. Ondanks dat er de laatste jaren veel moeite is gestoken in het verbeteren van de zorg voor oudere patiënten, blijkt dat de gerapporteerde kwaliteit van de zorg in de geïncludeerde studies is nog steeds relatief laag is.

In een retrospectief cohort onderzoek in hoofdstuk 4.4 hebben we geprobeerd om de kwaliteit van de farmaceutische zorg voor oudere patiënten die opgenomen waren op verpleegafdelingen interne geneeskunde (n = 200) te bepalen door gebruik te maken van de door ons ontwikkelde KI set uit hoofdstuk 4.2. Een tweede doelstelling was om de associatie tussen de beoordeelde kwaliteit van de farmaceutische zorg en de overleving 500 dagen na ontslag en heropnames binnen 90 dagen te onderzoeken. Ons onderzoek toonde aan dat verbeteringen in 3 van de 4 domeinen van de farmaceutische zorg nodig zijn. De mediane slagerspercentages voor de vier domeinen ‘Voorschrijven van geïndiceerde medicatie’, ‘Vermijden van ongepaste medicatie’, ‘Continuïteit en documentatie’ en ‘Monitoren van mediatie’ waren respectievelijk 63,6%, 100%, 20,3% en 37,3%. De 200 geïncludeerde patiënten hadden een gemiddelde kwaliteitsscore van 42,9%, SD 13,4%. Na correctie voor potentiële confounders werd geen verschil gevonden wat betreft overleving 500 dagen na ontslag tussen patiënten met een lage en een hoge kwaliteitsscore (hazard ratio=1,351, p=0,237). Een verschil in heropname of dood 90 dagen na ontslag werd ook niet gevonden tussen beide groepen (p=0,516). Volgens de indicatoren was een betere farmaceutische zorg niet geassocieerd met een verbeterde
overleving 500 dagen na ontslag of met minder heropnames binnen 90 dagen.

**Uitkomsten niveau**

Klinische uitkomstmaten worden beschouwd als het beste eindpunt om effecten op de gezondheid van een patiënt te meten. Alleen door te beoordelen welke schade of welk voordeel de patiënt heeft ondervonden, kan men echt concluderen of een bepaalde interventie, behandeling of actie een positief of een negatief effect heeft. Op het gebied van medicatieveiligheidsonderzoek zijn adverse drug events (ADE's) de belangrijkste uitkomstmaat. Een ADE wordt gewoonlijk gedefinieerd als de schade door het toepassen van medicatie. In *hoofdstuk 5.1* hebben we het onderzoeksprotocol van het WINGS onderzoek beschreven, een multicenter interrupted time series onderzoek om de vermindering van de incidentie van vermijdbare ADE's bij oudere patiënten op interne geneeskunde door klinisch-farmaceutische activiteiten op de verpleegafdeling te bepalen. Het WINGS onderzoek bestond uit een pre-interventie periode waarin de ADE incidentie werd gemeten. Vervolgens werden de klinisch-farmaceutische activiteiten op de verpleegafdeling geïntroduceerd. Daarna werden de effecten van deze interventie gemeten in een post-interventie meetperiode. De ADE's werden gemeten met behulp van een methode die bestaat uit een combinatie van expliciete en impliciete elementen. Een expliciete gestructureerde “trigger-tool” werd ingezet om het impliciete statusonderzoek van het expert panel te verbeteren. Daarnaast werd de beoordeling van de causaliteit en de ernst van de ADE's verder gestructureerd door het gebruik van een 3-punts schaal gebaseerd op het WHO-UMC systeem (causaliteit) en een 5-punts schaal van de CTCAEv3 criteria (ernst). Het expert panel bestond uit een ervaren arts en apotheker. De bedoeling was dat de kennis van de apotheker complementair was aan die van de arts.

In *hoofdstuk 5.2* hebben we de resultaten van de pre-interventie periode van het WINGS onderzoek beschreven. In 250 oudere patiënten werden 269 ADE's gevonden. Van deze ADE's werd 50,2% (135 ADE's) als vermijdbaar beoordeeld, dat wil zeggen dat een medicatiefout er aan ten grondslag ligt. De onderliggende medicatiefouten die het frequentst voorkwamen waren omissies in het voorschrijven van een medicijn, het voorschrijven van de onjuiste dosis (bijvoorbeeld door geen rekening te houden nierfunctieverlies), het voorschrijven gecontra-indiceerde medicatie en het voorschrijven van het verkeerde geneesmiddel voor de betreffende indicatie. De meest voorkomende schade ten gevolge van medicatie waren elektrolytenstoornissen, bloedingen, effecten op het centrale zenuwstelsel (zoals delier), hypotensie / bradycardie, een vertraagd herstel na een infectie of aanhoudende infectie en nierinsufficiëntie / verhoogd creatinine. De geneesmiddelen die het frequentst verantwoordelijk waren voor verstoringen

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van de elektrolytenbalans waren diuretica / RAAS-remmers; voor bloedingen waren dit coumarines, trombocyten-aggregatieremmers en het achterwege laten van het geven van maagprotectie door middel van protonpompremmer; voor de effecten op het centrale zenuwstelsel opiaten, benzodiazepinen en bètablokkers; voor hypotensie / bradycardie bètablokkers, diuretica en digoxine; voor vertraagd herstel na een infectie of aanhoudende infectie waren dit antibiotica en als laatste, voor nierinsufficiëntie / verhoogd creatinine waren dit antibiotica, NSAID’s, RAAS-remmers en diuretica.

In de algemene discussie in Hoofdstuk 6 worden de resultaten van de eerder genoemde hoofdstukken besproken in een bredere context. In Hoofdstuk 6 richten we ons op:

1. De drie foci van het meten van medicatie-gerelateerde problemen en hun methodologische aspecten

2. Algemene vergelijking van de resultaten verkregen met de drie meetmethoden

3. Implicaties voor de klinische praktijk en aanbevelingen voor toekomstig onderzoek

Concluderend kan worden gezegd dat in het ziekenhuis opgenomen ouderen een patiëntengroep zijn met een een verhoogd risico op medicatiegerelateerde problemen in vergelijking met jongere patiënten. Om medicatiegerelateerde problemen bij in het ziekenhuis opgenomen ouderen in kaart te brengen en uiteindelijk hun farmaceutische zorg te verbeteren hebben we drie niveaus onderzocht waarop kan worden gemeten. Deze drie verschillende niveaus met elk een unieke focus (systeem, proces en uitkomsten niveau) kwamen tot uiting in drie meetmethoden waarvan we de principes en verkregen resultaten hebben beschreven in de hoofdstukken van dit proefschrift. Deze drie meetmethoden beschouwend kan het volgende worden gesteld: als startpunt in een verbetertraject kan het beste een benadering worden gekozen met een systeem focus zoals een prospectieve risicoadalyse methode met het Bow-Tie model. Wanneer periodiek de kwaliteit van de zorg gemeten moet worden en wanneer een arbeidsintensieve methode ongewenst is, dan kan het beste een expliciete meetmethode worden gebruikt zoals door ons ontwikkelde set van kwaliteits indicatoren (of de oorspronkelijke ACOVE KI). Voor een onderzoek waarbij middelen en tijd niet schaars zijn en wanneer het meten van de werkelijke door geneesmiddelen aan de patiënt toegebrachte van belang is, kan het beste gebruik gemaakt worden van de ADE meetmethode van onze WINGS studie. Expliciete methoden die op proces niveau meten, zoals onze indicatorset, maken een vergelijking tussen studies met dezelfde of vergelijkbare expliciete metingen zeer eenvoudig. Echter, de resultaten van onderzoeken die ADE incidenties rapporteren moeten met de grootst mogelijke voorzichtigheid met elkaar vergeleken. De reden is het impliciete karakter van de ADE meetmethodes en de
daaruit volgende subjectiviteit van de ADE beoordelingen. Op basis van de resultaten van alle drie de meetmethoden in dit proefschrift kan bovendien worden geconcludeerd dat de kwaliteit van de farmaceutische zorg voor oudere patiënten nog steeds onvoldoende is en moet worden verbeterd.
7.3 Dankwoord
7.4 List of publications
7.5 Curriculum vitae
7.6 Portfolio
Dankwoord

Ik heb lang zitten denken over de inhoud van juist dit onderdeel van het proefschrift. Want eerlijk gezegd verbaasde ik me soms over dankwoorden die ik in enkele proefschriften voorbij heb zien komen. Dankwoorden die zich uitspanden over ettelijke pagina’s waarbij enkele dozijnen mensen persoonlijk werden bedankt en geknuffeld. Zou dat komen door de blinde euforie waarin de promovendus verkeert zo vlak voor de eindstreep? Of komt het doordat, wanneer je eenmaal begint met bedanken van personen en het opschrijven van namen, je uiteindelijk maar doorgaat omdat je niemand wil vergeten of tegen de schenen wilt schoppen?

Nee, ik probeer het nu op een iets andere wijze. Ik wil niet een uitputtende lijst met namen op papier zetten, maar toch ieder de eer doen toekomen die hij of zij verdient. Want ook al is de promotie een bewijs van bekwaamheid in het zelfstandig uitvoeren van wetenschappelijk onderzoek, uiteraard had deze klus nooit geklaard kunnen worden door de directe of indirecte bijdrage van zeer veel mensen die mijn pad hebben gekruist de afgelopen jaren. Daarom: allen, stuk voor stuk, van collega’s die kritisch meedachten met een onderzoeksoopzet en de interpretatie van resultaten tot collega’s die het mogelijk maakten dat ik kon promoveren tijdens het reguliere werk en de opleiding, van begeleiders (promotor, co-promotores, en professoren waarmee is samengewerkt) tot onderzoeksstudenten, van collega onderzoekers tot onderzoeksverpleegkundigen, van AMC-ers tot de medewerkers van andere ziekenhuizen waar mijn onderzoek deels is uitgevoerd, van geïnteresseerde vrienden tot mijn directe familie, oprecht bedankt daarvoor!

Bovenstaande genoemd hebbende, wil ik toch vanzelfsprekend enkele mensen persoonlijk of met nadruk in enkele zinnen bedanken.

Mijn opleider en promotor Loraine, gekoppeld aan jouw start in het AMC kreeg ik van jou de kans promotieonderzoek te combineren met mijn opleiding tot ziekenhuisapotheker (ZAPIKO). Een kans die ik met beide handen aangreep. Ik kijk terug op een zeer leerzame periode, want op een rijdende trein kon ik niet stappen. Sterker nog, de trein stond niet alleen stil maar moest nog door ons worden gebouwd. En die ervaring van het opzetten van een onderzoekslijn, het leggen van contacten en het aanvragen van subsidies neemt niemand me meer af. Eigenlijk is dat nog het meest leerzame van de hele promotie geweest, ook al ging het soms ook gepaard met onzekerheden. Loraine, ik heb respect voor de wijze waarop je afgelopen jaren alle grote klussen die er in het AMC lagen naast de wetenschappelijke activiteiten hebt geklaard of nu nog steeds hard aan werkt. Dank voor de steun en het vertrouwen
en ik vind het prachtig dat ik nu als eerste promovendus van jou dit proefschrift mag afleveren. En gelukkig volgen er volgend jaar waarschijnlijk nog meer!

Mijn co-promotor Susanne werd ons eigenlijk in de schoot geworpen nadat zij namens het CBO een presentatie gaf en kwam meedenken over onze onderzoekslijn. Binnen de kortste keren werkte Susanne in de ziekenhuisapotheek. Ik heb veel van haar geleerd door samen te brainstormen over ideeën voor onderzoek en samen succesvol te werken aan enkele grote subsidieaanvragen. Susanne, dank voor de energieke motor die je bent geweest voor het opzetten van onderzoek van de apotheek en je kritische blik wat betreft artikelen in de latere fase toen je inmiddels elders werkte.

Mijn tweede co-promotor Sophia, dank je voor de samenwerking en de mogelijkheden die je hebt geboden om bij ‘jouw’ patiëntengroep mijn onderzoek te doen. Dank voor het laatste duwtje dat je in eindfase hebt gegeven waardoor ik nu hier vandaag kan staan. Inmiddels heb jij al weer een grote stap gemaakt nu je professor bent geworden en 29 november je oratie hebt. Veel succes gewenst en ik hoop op een samenwerking in toekomstig onderzoek.

Natuurlijk wil ik Joanna, collega promovendus, bedanken voor het vele werk dat we samen hebben verzet en al aardig wat artikelen heeft opgeleverd. Het is fijn als je op elkaar kan terugvallen en gezamenlijk voor dezelfde klus staat. Ook Marjan, collega onderzoeker bij de MIK, bedankt voor het de gezellige samenwerking aan de twee grote review artikelen. Beiden veel succes met de afronding van jullie promoties! Wat betreft de MIK wil ik ook Ameen bedanken voor de fijne samenwerking en prettige, rustige begeleiding die hem zo kenmerkt.

Beste collega’s van het AMC, omdat ik al vanaf 2004 in het AMC heb rondgelopen, heb ik een groot aantal van jullie meegemaakt. Ik kan me geen fijnere en gezelliger plek voorstellen om mijn opleiding te hebben gehad en promotieonderzoek uit te voeren. Ik blijf altijd een beetje AMC-er en heb ontzettend veel meegemaakt in de jaren dat ik er werkte. Ik prijs me gelukkig dat zovelen van jullie niet alleen collega’s waren, maar tot aan vandaag vrienden zijn waarmee ik regelmatig een borreltje kan doen (of borreltjes tijdens de inmiddels legendarische jaarlijkse APO-ski)

Wat betreft afdeling Klinische Farmacie van het Deventer Ziekenhuis wil ik Frank Jansman en mijn overige collega’s bedanken voor de ruimte die jullie me hebben geboden om mijn promotieonderzoek voor een deel tijdens mijn werkzaamheden af te ronden. Ik voel me ontzettend thuis bij jullie. Ik ben trots op onze teamgeest, de manier waarop we elkaar aanvullen en alle bijzondere mijlpalen die we met onze relatief kleinere groep telkens weten te realiseren.
Alexander en Dimitri, dank dat jullie deze dag er voor me willen zijn als mijn paranimfen. Ik ben blij dat we elkaar al zoveel jaren kennen en dat jullie zulke goede vrienden zijn, waarmee ik zeker de laatste jaren veel heb gedeeld. Het regelen van deze dag en zeker het feestje zijn bij jullie in goede handen!

Paula en Marjolein, dank voor de ondersteuning bij het tot stand komen van dit proef- schrift.

Lieve Yuma, dank voor de liefde en de ongelooflijke steun die je me geeft. Het is fijn om iemand te hebben waarop ik zo kan terugvallen en waarbij ik mezelf zo op mijn gemak voel. Prachtige Noor, jij hebt iets in mij losgemaakt waardoor al het andere waarover ik me vroeger druk maakte, onbelangrijk is geworden. Ik geniet van je enthoudisme en je handjes in mijn nek als ik je optil. Ik kan me niets mooiers wensen.

Lieve pap en mam, dank voor het immer meeleven en de onvoorwaardelijke wijze waarop jullie altijd voor me klaar staan. Ik prijs mezelf gelukkig met jullie en ik hoop dat jullie ook voelen dat datgene wat ik bereik voor een groot deel aan jullie te danken is.
List of publications

- Klopotowska JE, Wierenga PC, Stuijt CCM, et al. (2013) Adverse Drug Events in Older Hospitalised Patients: Results and Reliability of a Comprehensive and Structured Identification Strategy. PLoS One. 2013 Aug 5; 8(8): e71045. doi: 10.1371/journal.pone.0071045

- Klopotowska JE, Wierenga PC, Smorenburg SM, et al. PW Wetenschappelijk Platform 2013; 7(2): a1305

- Askari M, Eslami S, Louws M, Wierenga PC, et al. Frequency and nature of drug-drug interactions in the intensive care unit. Pharmacoepidemiol Drug Saf. 2013 Apr; 22(4): 430-7. doi: 10.1002/pds.3415

- Klopotowska JE, Wierenga PC, Smorenburg SM, et al. Recognition of adverse drug events in older hospitalised medical patients. Eur J Clin Pharmacol. 2013 Jan; 69(1): 75-85. doi: 10.1007/s00228-012-1316-4

- Askari M, Eslami S, Louws M, Dongelmans D, Wierenga P, et al. Relevance of drug-drug interaction in the ICU - perceptions of intensivists and pharmacists. Stud Health Technol Inform. 2012; 180: 716-20

- Wierenga PC, Buurman BM, Parlevliet JL, et al. Association between Acute Geriatric Syndromes and Medication-Related Hospital Admissions. Drugs Aging. 2012 Aug 1; 29(8): 691-9. doi: 10.2165/11632510-000000000-00000

- Wildenbeest JG, Van den Broek P, Benschop KS, Koen G, Wierenga PC, Vossen AC, Kuijpers TW, Wolthers KC. Pleconaril revisited: clinical course of chronic enteroviral meningoencephalitis after treatment correlates with in vitro susceptibility. Antivir Ther. 2012; 17(3): 459-66. doi: 10.3851/IMPI936

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- Askari M, Wierenga PC, Eslami S, et al. Assessing quality of care of elderly patients using the ACOVE quality indicator set: a systematic review. PLoS One. 2011; 6(12): e28631. doi: 10.1371/journal.pone.0028631
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- Wierenga PC, Klopotowska JE, Smorenburg SM, et al. Quality Indicators for In-Hospital Pharmaceutical Care of Dutch Elderly Patients: Development and Validation of an ACOVE-Based Quality Indicator Set. Drugs Aging. 2011 Apr 1;28(4):295-304. doi: 10.2165/11587700-000000000-00000

- Khajouei R, Wierenga PC, Hasman A, et al. Clinicians satisfaction with CPOE ease of use and effect on clinicians’ workflow, efficiency and medication safety. Int J Med Inform. 2011 May; 80(5): 297-309. doi: 10.1016/j.ijmedinf.2011.02.009

- Medlock S, Opondo D, Eslami S, Askari M, Wierenga P, de Rooij SE, Abu-Hanna A. LERM (Logical Elements Rule Method): A method for assessing and formalizing clinical rules for decision support. Int J Med Inform. 2011 Apr; 80(4): 286-95. doi: 10.1016/j.ijmedinf.2011.01.014

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- Khajouei R, Peek N, Wierenga PC, et al. Effect of predefined order sets and usability problems on efficiency of computerized medication ordering. Int J Med Inform. 2010 Oct; 79(10): 690-8. doi: 10.1016/j.ijmedinf.2010.08.001

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- Bijleveld YA, Wierenga PC, Klopotowska JE, et al. Gebruik van procesindicatoren voor kwaliteitsmeting van farmacotherapeutische ouderenzorg bij polyfarmacie. PW Wetenschappelijk Platform 2009 (nr. 3/3): 53-55

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- Wösten YB, Wierenga PC, Smorenburg SM, et al. Gereedschap voor de ziekenhuis-apothekers. Toolkit risicoanalyse NVZA. Pharm Weekbl 2007 (nr. 2): 36-37

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- van den Bemt P, Graatsma B, Lie-A-Huen L, Wierenga P, Tijink H. (2006) Medicatieveiligheid. In: Praktijkboek Patiëntveiligheid (Hoofdstuk 14, p187-199) Houten, uitgeverij Bohn Stafleu Van Loghum
Curriculum vitae

Peter Christiaan Wierenga was born on November 30 1978, in Hengelo (Ov.), the Netherlands. In 1996 he completed secondary school (Gymnasium, cum laude) at the OSG Bataafse Kamp in Hengelo (Ov.). Subsequently he studied Pharmacy at the University of Groningen. He obtained his Master’s degree in 2001, followed by his PharmD in 2003.

Thereafter, in May 2003, he started working as a pharmacist at the Department of Clinical Pharmacy at the Hofpoort Hospital in Woerden. In February 2004 he started as a pharmacist at the Department of Clinical Pharmacy at the Academic Medical Center in Amsterdam. In February 2005 he initiated in the prior mentioned department his training to become a hospital pharmacist. He combined this training with the PhD research described in this thesis. During his PhD research he collaborated with the Department of Internal and Geriatric Medicine, the Department of Medical Informatics and the Department of Quality and Process Innovation at the Academic Medical Center in Amsterdam.

From February 2011 he holds a position as a registered hospital pharmacist at the Department of Clinical Pharmacy at the Deventer Hospital in Deventer.
Portfolio PhD student – selection of activities related to PhD and corresponding workload

Name PhD student: Peter Wierenga
PhD period: 2005-2013
Name PhD supervisor: Prof. dr. L. Lie-A-Huen

| I. PhD training | Year | Workload (ECTS) |
|-----------------|------|----------------|
| **General courses** |      |                |
| Clinical Data management (AMC Science Education) | 2006 | 0.2 |
| Practical Biostatistics (AMC Science Education) | 2005 | 1.4 |
| Systematic Reviews and meta-analysis; Theory en practice (EMGO) | 2005 | 0.6 |
| Epidemiology (AMC Science Education) | 2005 | 0.6 |
| Systematic Reviews (Dutch Cochrane Center) | 2005 | 0.3 |
| Evidence Based Medicine in clinical practice (Dutch Cochrane Center) | 2006 | 0.8 |
| PhD General Introduction Course UvA (LAC) | 2005 | 0.3 |
| Expert Management of Medical Literature (Pubmed, Ref Manager, Ovid, Searching databases for systematic reviews, citation analysis and impact factors, evidence based searching) | 2005-2006 | 0.5 |
| Time Management (Postgrade) | 2005 | 0.3 |
| Clinical drug research and GCP (PAO Pharmacy) | 2009 | 0.3 |

| **Specific courses** |      |                |
| ZonMw training in applying for grants (Netherlands Organisation for Health Research and Development) | 2005 | 0.2 |
| Basic course Hospital Management (Stichting Managementscholing Medische Specialisten) | 2007 | 0.6 |

**Seminars, workshops and master classes**

| Masterclass Research Brugge (CWZO) | 2005 | 0.6 |
## Presentations

### Oral presentations

| Title                                                                 | Location                                      | Year  | Value |
|----------------------------------------------------------------------|-----------------------------------------------|-------|-------|
| Risk Analysis in Clinical Pharmacy. ViP Symposium AMC, Amsterdam     |                                               | 2005  | 0.5   |
| Risk Analysis in Clinical Pharmacy. EAHP (European Association of Hospital Pharmacy) Congress, Geneva, Switzerland |                                               | 2006  | 0.5   |
| Medication Safety at the AMC. National Congress 'Managing Patient Safety', Rotterdam |                                               | 2006  | 0.5   |
| Risk Analysis using the Bow-Tie method. Starting Conference of the National Patient Safety Week, Rotterdam |                                               | 2006  | 0.5   |
| Risico's, breng ze in kaart. Workshop at symposium “Patientveiligheid, topsport of diplomazwemmen”, AMC, Amsterdam |                                               | 2007  | 0.5   |
| Medication Safety in Pediatrics. NVK Conference, Veldhoven           |                                               | 2007  | 0.5   |

### Poster presentations

| Title                                                                 | Location                                      | Year   | Value |
|----------------------------------------------------------------------|-----------------------------------------------|--------|-------|
| Risk Assessment in Clinical Pharmacy: The AMC Pharmacy Risk model. ISQua (The International Society for Quality in Health Care) Congress, Vancouver, Canada |                                               | 2005   | 0.5   |
| Risk Assessment in Clinical Pharmacy. EAHP (European Association of Hospital Pharmacy) Congress, Geneva, Switzerland |                                               | 2006   | 0.5   |
| Incidence of parenteral drug preparation and administration errors on an internal and a pediatric ward of an university hospital (a baseline measurement). Nederlandse Ziekenhuisfarmacie Dag, Nijmegen |                                               | 2006   | 0.5   |
| Incidence of parenteral drug preparation and administration errors on an internal and a paediatric ward of an university hospital (a baseline measurement). Patient Safety Research Conference, Porto; Portugal |                                               | 2007   | 0.5   |
| A hospital admission due to a fall in elderly medical patients is often medication related. Nederlandse Ziekenhuisfarmacie Dag, Leiden and Geriatriedagen, Rotterdam |                                               | 2007-2008 | 1.0   |
| The quality of in-hospital pharmaceutical care of elderly patients assessed by a newly developed set of explicit indicators based on the ACOVE criteria. International Forum on Quality and Safety in Healthcare, Berlin, Germany |                                               | 2009   | 0.5   |

### (Inter)national conferences

| Title                                                                 | Location                                      | Year  | Value |
|----------------------------------------------------------------------|-----------------------------------------------|-------|-------|
| ISQua (The International Society for Quality in Health Care) Congress, Amsterdam |                                               | 2004  | 0.75  |
2. Teaching

Lecturing

| Lecturer Amstel Academy — ICU and CCU specialization for nurses — Pharmacotherapy in Ischemic Cardiac Disease, Antitrombotics | Year       | Workload (ECTS) |
|-------------------------------------------------------------|------------|-----------------|
| Lecturer pharmacotherapy (senior nurses AMC)                | 2007       | 0.1             |
| Lecturer at a 3 day evening-symposium in Paramaribo, Surinam: Risk Management and Risk Analysis in healthcare for medical specialists, general physicians, pharmacists (KWF) | 2007       | 0.4             |
| Lecturing in Patient Safety course medical students         | 2007       | 0.1             |
| Lecturing in ‘Medicatiebegeleiding’ course for hospital pharmacists in training | 2007 & 2009 | 0.3             |

Tutoring, Mentoring

| Clinical tutor at Evidence Based Medicine course of the Dutch Cochrane Center | Year | Workload (ECTS) |
|-------------------------------------------------------------------------------|------|-----------------|
| Tutor Pharmacotherapy at pre-intern education medical students               | 2008-2009 | 0.3            |

Supervising

| Research projects of several students | Year       | Workload (ECTS) |
|---------------------------------------|------------|-----------------|
| Klopotowska, Handbook Injectable Drugs, Dept Clinical Pharmacy AMC | 2005       | 1               |
| Wöstien, Risk Analysis, Dept Clinical Pharmacy AMC                    | 2006       | 1               |
3. Parameters of Esteem

| Grants                                                                 | Year |
|----------------------------------------------------------------------|------|
| Bow-Tie method' in risk analysis for the improvement of medication safety. Netherlands Organisation for Health Research and Development (ZonMw), Patient Safety Program. Project leader | 2006 |
| Development of an evidence based handbook for the preparing and administering injectable drugs. AMC grant for guideline projects. Project leader | 2006 |
| pharmacy Coordinated ADE Reducing Efforts For Use in all Levels of healthcare (CAREFUL). Netherlands Organisation for Health Research and Development (ZonMw), Patient Safety Program. Project member of and contribution to WINGS study AMC (part of CAREFUL) | 2008 |
| The clinical and economic impact of a clinical pharmacy team on surgical patients; a randomised cost-effectiveness study (SUREPILL). Netherlands Organisation for Health Research and Development (ZonMw). Co-author of grant application | 2007 |

Other

Chairman at symposium '25 years of incident reporting in the AMC', Amsterdam | 2009 | 0.3
