The Value of Laboratory Diagnostics in the Clinical Setting

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The Value of Laboratory Diagnostics in the Clinical Setting

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(met een samenvatting in het Nederlands)

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Table of contents

1

General introduction and outline of the thesis

"The delivery of medical care is to do as much nothing as possible"
The House of God, Samuel Shem
Laws of the House of God, #13

Obviously, above quote requires some degree of nuancing. Still, as far back as in the seventies, this popular novel elaborated on many cases in which medical care was provided that was questionable at the least. Motivated by either the will to act (*"I never do nothing. I'm a doctor, I deliver medical care."*), need for thorough evaluation and living up to expectations (*"No one is going to say that we do sloppy work."*), fear of missing something, and often, money, many patients were subjected to unnecessary, non-medically indicated, unwanted tests or procedures, often doing more harm than good.

As physicians, the ultimate goal should be to help patients to the best of our ability, whether that is to do, or not to do, which is a topic that is becoming more important over the years in the context of ensuring high quality, yet affordable health care. In this thesis the study of unnecessary use of medical care in terms of diagnostics is addressed, ultimately aiming to increase health care quality in clinical practice.

Low-value care

In an era in which health care costs are increasing rapidly, efforts are being pursued to contain these costs while maintaining high quality. In this context, the concept of 'low-value care' has gained widespread attention over recent years. Low-value care includes the use of tests, procedures and treatments that are unlikely to provide health benefit, provide benefit against disproportionate harm or costs, are less (cost-) effective than alternative care, or do not fit patient preferences.[1] Performing serial blood counts on clinically stable patients, performing routine urine cultures in absence of clear signs and symptoms that localize to the urinary tract, and performing imaging studies for non-specific acute low back pain without red flags are a few examples of care activities that are considered to be of low value.[2] A significant proportion of health care spending is considered of low value. It is estimated that 30% of spending is wasteful, and that more than half of this is spent on inefficient care and unnecessary services.[3,4] Numbers on the volume of low-value care in the Netherlands are lacking, however, several studies targeting different services indicate that this number varies between 9% and 32%.[5] Utilizing care of low value consumes resources that could have been used for alternative, more (cost-) effective care.

Health care costs

In most countries, rapid increases in health care expenses have been observed over the past decades. Before the financial crisis around 2009, annual growth in health care expenditure fairly exceeded economic growth in many countries. Since then, the annual rise in expenditure has slowed down and follows economic growth more closely. According to the most recent

numbers, 8.8% of the gross domestic product (GDP) was spent on health care in 2018, on average, by the 36 OECD (Organisation for Economic Co-operation and Development) countries.[6] Of OECD countries, the United States spent the largest percentage of its GDP on health care. In 2000, 12.5%, around $1.3 trillion, was spent on health care. By 2018, this percentage had increased to 16.9% ($3.5 trillion). In the Netherlands, the burden of health care expenses on GDP has increased from 7.7% in 2000 to 9.9% in 2018, corresponding to an increase from approximately €34.8 billion to €76.9 billion.[6] If current trend continues, it is estimated that 20-30% of GDP will be spent on health care by 2040.[7]

Drivers of health care expenses

The annual growth in health care expenditure can be explained through several domains and developments, related to both the 'demand' side ('why more health care is needed') as well as the 'supply' side ('why more health care can be provided').

Demand-related factors

On the demand side, important factors include changing demographics, increases in chronic diseases and diseases related to unhealthy lifestyle, and income. Changing demographics traditionally refers to ageing of the population. More recent evidence proposes that the impact of ageing on increasing expenses is mostly attributable to the increased proportion of the population being close to death, as expenditures significantly rise in the years leading up to death.[8] Longer life expectancy, together with unhealthy lifestyles, have contributed to higher rates of comorbidities and chronic illness, increasing the demand for care.[7] Another important factor is income: with higher income, both individually and on the country level, there is willingness to spend a larger share on health care, which can lead to increasing demand and expectations.[8]

Supply-related factors

On the supply side, important drivers include for example medical technology and policy measures. Advances in medical technology, such as in devices, in-vitro diagnostics (IVD), imaging and pharmaceuticals, are often expensive. Although they provide the opportunity to improve quality or accessibility of care, not all technological innovations lead to better health care and innovations are often implemented in practice without sufficient evidence of effectiveness.[8,9] Policy measures also affect expenses, for example through expanded health care coverage by insurance companies and through payment structures in which providers are typically incentivized for increases in volume rather than in value.[8]

Containing costs while sustaining quality

Over the past years, many initiatives have focused on reducing low-value care in an effort to contain rising health care costs while sustaining or improving health care quality. In 2012, the

"*Choosing Wisely*" campaign was launched by the American Board of Internal Medicine (ABIM) Foundation aiming to promote conversations between care providers and their patients about unnecessary tests, treatments and procedures.[2] After this, many countries followed suit and adopted the Choosing Wisely principles.[10] Moreover, several medical journals have dedicated series to reducing overuse of medical services, such as JAMA Internal Medicine's "*Less is more*" series and the BMJs "*Too much medicine*" series.[11,12]

In the Netherlands, several projects and initiatives were launched over the recent years as well. In the context of the Choosing Wisely campaign, medical specialty societies have formulated a set of "*Wise Choices*" for their own specialty by creating lists of tests, treatments and procedures for which there is strong scientific evidence of overuse or potential for harm.[13] Other pillars of the Choosing Wisely Netherlands campaign include measuring clinical practice variation, bridging knowledge gaps by effectiveness research, and promoting shared decision making.[10] In 2015, the "*Bewustzijnsproject*" by the Medical Specialties Council (CGS), part of the Royal Dutch Medical Association (KNMG), carried out by Maastricht University, was initiated with the aim of integrating cost-effectiveness and high-value, cost-conscious care into medical residency programs. In this project, high-value, cost-conscious care is clustered around three themes: organizing cost-consciousness and effectiveness, choosing wisely to prevent excessive use, and risk management and ethics.[14] In addition, IQ healthcare has composed the "*Beter niet doen-lijst*", a list of 1,366 lower-value services identified in 193 Dutch clinical guidelines. Of these lower-value services, 30% involves the use of diagnostic testing.[15] This list was created as part of the "*Doen of laten?*" program, a nationwide program carried out by the Netherlands Federation of University Medical Centers (NFU) and the Netherlands Association of Medical Specialists (FMS) aiming to map and de-implement low-value care, and identify conditions needed for successful de-implementation, financed by the *"Citrienfonds"*. In this program the eight university medical centers in the Netherlands each carried out a project aiming to reduce low-value care. Our study group has performed the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) – project, aiming to reduce unnecessary diagnostics, mainly laboratory testing, by changing caregivers' mindset. Other projects carried out within this program target for example unnecessary measurement of vitamin B12 and vitamin D in primary care settings, unnecessary gastroscopy in patients with complaints of dyspepsia, and unnecessary use of urinary and intravenous catheters in hospital settings.[16,17]

Initiatives to reduce low-value care frequently target the use of diagnostic testing, including laboratory testing. More specifically, the Netherlands Society for Clinical Chemistry and Laboratory Medicine (NVKC) has developed a list of Wise Choices targeting the ordering of several laboratory tests, including recommendations on screening for malignancy using tumor markers and measurement of vitamins in patients with atypical complaints.[18]

Burden and consequences of unnecessary laboratory testing

For the purpose of this thesis, the focus was on overuse of clinical laboratory testing. In this context, overuse is defined as testing in the absence of a clear medical basis for use, or testing for which the benefit does not outweigh the risks.[19] Total costs spent on laboratory testing are unclear and estimates vary widely. In the Netherlands, a total of €278 million was spent on IVD in 2016 according to MedTech Europe, although this might not be accurate since over the previous years, estimates by this company were inconsistent with other sources.[20,21]

A considerable proportion of laboratory testing is viewed as unnecessary. A review addressing the appropriateness of diagnostic laboratory testing has reported a mean rate of overutilization of approximately 21% from 1997 to 2012.[22,23] Overuse is partially reflected in high interphysician variability of laboratory test orders. In a recent study among internal medicine residents, some residents ordered seven to eight times more tests compared to their peers.[24] In addition, in a study among five general practitioner groups in the Netherlands, the two groups that ordered the most laboratory tests, ordered two to three times more tests compared to the group that ordered the least.[25]

Besides the financial impact, overutilization increases the number of false-positive results leading to more, costly, sometimes invasive and potentially harmful downstream diagnostics, especially when pre-test probability for disease is low. This is mathematically explained through the Bayes' theorem, that connects the pre-test probability to the post-test probability taking into account sensitivity and specificity of a given diagnostic test. Using this theorem in the case of low pre-test probability, for example for rare diseases, the number of false-positives likely outnumbers the number of false-negatives, a concept that might be taken into account when making decisions regarding rational use of diagnostics.[26]

In addition, excessive testing can lead to less patient-friendly practice through punctures and unnecessary trips to the hospital. Diagnostic blood loss is also associated with hospital acquired anemia, which can lead to worse patient outcomes such as increased risk of hospital mortality and prolonged length of stay, although hospital acquired anemia might itself be a cause of frequent phlebotomy and therefore diagnostic blood loss.[27-29] Of note, hospital laboratories in the United States collect up to twelve times more blood than the required analytical volume, with the majority of the sample being discarded.[30] In the Netherlands, it is estimated that around 100 million blood tubes are collected annually. With each tube containing a volume of five milliliters on average, of which approximately 4.5 milliliters is discarded unused, this corresponds to a waste of almost half a million liters of blood each year.[31]

Drivers of overutilization of laboratory services

Overutilization of diagnostic testing is believed to be driven by factors related to physicians as well as patients.

The majority of physicians acknowledges unnecessary tests and procedures as a serious problem and feels responsibility to help their patients avoid unnecessary care. Nonetheless, the majority also indicates that they regularly order tests they believe are unnecessary.[32,33] In a survey conducted in the context of the Choosing Wisely campaign among 600 primary care physicians and specialists in the United States, 72% says that the average physician orders an unnecessary test or prescribes an unnecessary procedure at least once a week.[32] In a survey taken among 116 residents at a large medical center in the United States, 88.2% of internal medicine residents and 67.7% of general surgery residents reported ordering of unnecessary inpatient laboratory tests, with up to 43.5% of respondents reporting unnecessary ordering to occur daily.[33]

Physician factors

On the physician side, a commonly reported reason for unnecessary ordering is out of habit or routine. In above mentioned survey among internal medicine and general surgery residents of an academic medical center in the United States, 90.5% of residents report this learned behavior to contribute to unnecessary laboratory test ordering.[33] Another factor is physician culture, in which thoroughness is emphasized and residents' unnecessary laboratory utilization can be driven by perceived expectations from attending physicians.[33,34] Also, physicians often request unnecessary services out of uncertainty and need for reassurance; in the Choosing Wisely-survey mentioned above, around one third (30-36%) of physicians say they order unnecessary tests or procedures 'just to be safe' or because they want more information for reassurance, while in the survey among internal medicine and general surgery residents, 82.8% report that they order unnecessary tests due to diagnostic uncertainty.[32,33] Finally, another increasingly important physician-related driver for overutilization is fear of malpractice lawsuits. More than half of the physicians (52%) questioned for the Choosing Wisely-survey mentioned this as a major reason.[32] Although it is often presumed that this is more of an issue in other countries, the first large scale study on the extent of defensive medicine in the Netherlands demonstrated that one third (33%) of the 1,120 included care providers acts differently out of fear for legal or financial claims, this accounts especially for specialists (46%). According to 63% of respondents, a claim culture is also rising in the Netherlands.[35]

Patient factors

A main patient-related driver of overuse is patient request for testing. Patients sometimes feel that receiving more care, means receiving better care. In an era in which patients are increasingly involved in decisions regarding their health, their request for testing, and the

physician's desire to satisfy patients, can contribute to overutilization.[32,36] The Choosing Wisely-survey shows that although the majority (87%) of physicians always or almost always talks to patients about avoiding a perceived unnecessary test when a patient requests one, more than half (53%) of physicians ultimately does order a test upon persistence of the patient.[32] The extent to which patients actually request services differs between settings.[32,37,38]

Pressure from patients or their families is a major reason for overutilization, also in the Netherlands, where around six out of ten care providers (61%) say that this sometimes, often or very often leads to providing more care than would be optimal according to their professional opinion. The previously mentioned Dutch study states that the most important reason for care providers to give in to patient pressure is to make patients feel like every possible measure has been taken.[35]

A multifaceted approach to reduce unnecessary laboratory testing

In 2008, our study group performed a multifaceted intervention aimed at reducing unnecessary diagnostic testing at the internal medicine department of the Amsterdam University Medical Center (Amsterdam UMC), location VU University Medical Center (VUmc). Multiple interventions were implemented to increase awareness about the use of (unnecessary) tests in the routine hospital practice, associated costs and implications for patient safety.[39]

The intervention consisted of several steps. First, supervision of residents by experienced internists regarding test ordering was intensified. Second, laboratory orders were constrained by unbundling panel tests such as liver enzyme tests, electrolytes, and kidney function. Frequent discussions were held about the necessity and indications for other frequently used tests such as glucose, calcium, albumin, phosphate, etcetera. Third, the national protocols on the management of chronic diseases were included in a central electronic database, to create more awareness and to make it easier for clinicians to consult them. The physicians were instructed to follow these national guidelines created by the Netherlands Association of Internal Medicine (NIV) with regard to the recommended frequency of the various diagnostic tests in a given chronic disease state. Fourth, posters and pocket cards with the cost prices of laboratory tests were printed and distributed to physicians. Fifth, six-weekly overviews of the ordered laboratory tests were presented during the morning report. Finally, clinical meetings such as grand rounds, daily ward rounds and morning reports were used to provide feedback on the already performed tests.

Although the focus was mainly on laboratory testing, utilization of other diagnostics also declined. A 13% gross reduction in diagnostic expenditure was observed compared to the previous year, which was sustained over subsequent years.[39,40]

After this success, the interventions were successfully implemented in other departments within the VUmc, where they were tailored to the local context. At each department, focus was placed on a different diagnostic modality. For example, the Department of Pulmonary Disease focused on reducing the number of imaging investigations, while the Department of Gastroenterology and Hepatology targeted pathology investigations.

As previously mentioned, in 2015, the NFU initiated the "*Doen of laten?*" program, sponsored by the "*Citrienfonds*".[16] The aims of this program were to assess which care services are of low-value, to de-implement this low-value care, and to identify the conditions necessary for successful de-implementation.[5] In the context of this program, we performed the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) – project aiming to reduce unnecessary diagnostic testing, mainly laboratory testing, using the knowledge gained during the reduction efforts at the VUmc as a basis.

Objective and outline of this thesis

This thesis is dedicated to the study of overuse of diagnostics, focusing on laboratory testing, in clinical practice. As previously mentioned, a considerable proportion of laboratory tests ordered is unnecessary. The purpose of this thesis is to investigate strategies that can be used to de-implement (or reduce) unnecessary testing, implement these strategies in clinical settings, assess which factors should be taken into account in efforts to de-implement unnecessary testing, and assess which factors are of influence to their success.

We start this thesis by presenting a narrative review of published studies aiming to reduce unnecessary laboratory testing in clinical settings, in **Chapter 2**. In this review, we map the current knowledge on strategies in use, their effectiveness on both short- and long-term, and their possible effects on quality of care. Besides providing a clear overview of different strategies, this chapter points out several elements that will be addressed in the following chapters: lack of detailed description of interventions, lack of follow-up data needed to assess long-term sustainability, and heterogeneity in reporting of outcomes.

Chapter 3 introduces the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) – project, in which we performed a multifaceted intervention aiming to reduce unnecessary testing, focusing on laboratory testing, by changing caregivers' mindset, in the internal medicine department of four large teaching hospitals. In this chapter, we describe, in detail, the steps and actions performed at each clinic, allowing for replication of our intervention. This chapter also describes our approach to assessing the factors of influence to successful de-implementation. In **Chapter 4**, the results of this project are presented, together with the encountered facilitators and barriers. Since long-term sustainability of efforts to

reduce unnecessary testing remains understudied, we present the long-term results of the project carried out at the internal medicine department of the VUmc, that was described earlier, in **Chapter 5**. In this chapter we describe the elements we believe led to a sustainable reduction in diagnostic testing.

As we learned in our review, the outcome measures used and their way of reporting in studies aiming to reduce unnecessary testing are heterogeneous. In **Chapter 6**, we discuss the pros and cons of possible measures to study the reduction of unnecessary laboratory testing in a letter in which we report our difficulties with a claim made by other authors on providing evidence-based guidelines for eliminating repetitive laboratory testing.

As highlighted in an earlier section of this introductory chapter, de-implementation of low-value (or in this case, unnecessary) care is being studied extensively. The de-implementation process itself has been conceptualized in several frameworks and models, which are applicable to a wide range of services.[41] **Chapter 7** provides a step-by-step action plan appropriate for direct use to specifically reduce unnecessary laboratory testing, following the stages of de-implementation, and complemented with our own experiences and feedback from physicians participating in the RODEO project.

One of the actions we recommend in the action plan presented in **Chapter 7**, is making use of the possibilities electronic order systems have to offer. In line with this, applications such as clinical decision support systems that provide the opportunity to integrate different types of patient data into information that might aid clinicians' decision making, might also be helpful in stimulating appropriate use of laboratory services. In **Chapter 8**, we describe our efforts to take a first step in this direction by exploring the clinical usefulness of available laboratory markers to predict mortality risk.

Finally, **Chapter 9** provides a summary and discussion of the main findings of this thesis.

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2

Reducing test utilization in hospital settings: A narrative review

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Abstract

Background

Studies addressing the appropriateness of laboratory testing have revealed approximately 20% overutilization. We conducted a narrative review to (1) describe current interventions aimed at reducing unnecessary laboratory testing, specifically in hospital settings, and (2) provide estimates of their efficacy in reducing test order volume and improving patient-related clinical outcomes.

Methods

The PubMed, Embase, Scopus, Web of Science, and Canadian Agency for Drugs and Technologies in Health-Health Technology Assessment databases were searched for studies describing the effects of interventions aimed at reducing unnecessary laboratory tests. Data on test order volume and clinical outcomes were extracted by one reviewer, while uncertainties were discussed with two other reviewers. Because of the heterogeneity of interventions and outcomes, no meta-analysis was performed.

Results

Eighty-four studies were included. Interventions were categorized into educational, (computerized) provider order entry [(C)POE], audit and feedback, or other interventions. Nearly all studies reported a reduction in test order volume. Only 15 assessed sustainability up to two years. Patient-related clinical outcomes were reported in 45 studies, two of which found negative effects.

Conclusions

Interventions from all categories have the potential to reduce unnecessary laboratory testing, although long-term sustainability is questionable. Owing to the heterogeneity of the interventions studied, it is difficult to conclude which approach was most successful, and for which tests. Most studies had methodological limitations, such as the absence of a control arm. Therefore, well-designed, controlled trials using clearly described interventions and relevant clinical outcomes are needed.

Introduction

Over the past decades, Western countries have witnessed a marked rise in health care expenditure, with annual growth rates exceeding the rise in gross domestic product.[1] The constantly expanding field of diagnostics has contributed to this exponential growth in curative health care costs. Rapid increases have been seen in the volumes and costs of different types of diagnostics, with absolute test volumes doubling every five to ten years in the United States, the United Kingdom, and Canada.[2]

Laboratory testing represents the largest volume of medical activity and is considered to influence more than 70% of decision making in medical practice.[2,3] In 2015, Kobewka et al.[4] reviewed numerous international studies to conclude that a considerable proportion of performed (laboratory) tests were unnecessary. Another review addressing the appropriateness of diagnostic laboratory testing reported a mean rate of overutilization of approximately 20%.[5] Statistically, laboratory test results will deviate from normal in 5% of healthy individuals.[6] Besides the financial impact, overutilization increases the number of false-positive results, leading to more, sometimes invasive and potentially harmful tests. In addition, excessive blood draw can result in iatrogenic anemia.[7,8] Moreover, excessive testing can lead to less patient-friendly practices. Therefore, a reduction in unnecessary laboratory testing is often targeted with the aim of improving patient safety and reducing health care expenditure. Such a reduction does not lead to adverse patient outcomes and might even reduce the length of hospital stay and the need for red cell transfusion.[8-12]

Interventions to reduce unnecessary laboratory testing, such as educational sessions or posters, pop-up reminders upon test ordering through an electronic ordering system, modification of paper order forms, or providing clinicians insight into their ordering patterns, have been implemented and studied in different clinical settings in many countries.[4,13] Although a few reviews examine the efficacy of these interventions in different settings[4,13], no recent review has considered a hospital setting. Therefore, this review aims to describe the different types of interventions implemented to reduce unnecessary laboratory testing in hospital settings as well as the overall efficacy of these interventions and their impact on patient-related clinical outcomes.

Methods

Data sources and search strategy

We initially searched the PubMed, Embase, and Canadian Agency for Drugs and Technologies in Health-Health Technology Assessment (CADTH HTA) databases from inception through

July 2016 for potentially relevant articles describing interventions to reduce unnecessary laboratory testing in hospital settings. We combined synonyms of the following terms: laboratory test, reduction, and intervention. **Appendix 1** provides an overview of all search terms used. Highly relevant papers found in this initial screening of titles and abstracts were selected and subjected to backward reference checking in Scopus. Of the papers retrieved in this round, a selection was checked backwards and forwards for references in Scopus and Web of Science. Our search was not exhaustive, as the aim of our effort was not to report and compare exact estimates of effectiveness, but merely to describe published interventions and provide crude estimates of their effectiveness.

Study selection

We selected only hospital-based studies that reported an intervention to reduce unnecessary laboratory testing and presented data on changes in test order volumes. Only articles written in English or Dutch with full text available were included. We defined unnecessary laboratory tests as those with results that did not generate added value in clinical decision making, relying on the authors' judgment. Studies were excluded when only the influence of the intervention on costs was presented or when reduction in test order volumes was given only for a subset of all tests studied. We chose to exclude the latter to avoid over-optimism that might occur when selective results are presented.

Data extraction and quality assessment

For each report included, data on the type of intervention(s) carried out were extracted. The interventions were categorized as educational interventions, (computerized) provider order entry [(C)POE] interventions, audit and feedback interventions, and others, based in part on a subdivision previously used by Kobewka et al.[4] We extracted data on the reduction in test order volume, which was expressed as the percentage change in order volume of the targeted tests before and after the intervention.

Further, we assessed the study design and characteristics of the comparators used. To get an indication of the study size, the number of participating centers was recorded along with a measure of study population, such as number of visits and admissions and number of hospital days. We assessed the number of tests targeted and the reproducibility and sustainability of the interventions (i.e., reduction in test order volume up to two years post-intervention). In addition, we noted whether the studies provided data on patient-related (clinical) outcomes that might have been affected by the modification of laboratory utilization, such as hospital length of stay, number of intensive care unit (ICU) admissions, number of readmissions, and mortality.

Data were extracted by one reviewer (RB). Uncertainties in data extraction were discussed with two other reviewers (MB, PN) until consensus was reached. Because of the anticipated heterogeneity of the tests, studied interventions, and reported outcome measures, we did not perform a meta-analysis.

Results

Search results

After backward reference checking of 20 relevant papers selected from our PubMed/Embase/CADTH HTA database search, we retrieved 603 unique papers. Of these, 61 papers met our inclusion criteria. A selection of these papers was checked for references backwards and forwards. Of the 891 papers retrieved in this search, 23 papers fulfilled our inclusion criteria. **Figure 1** illustrates our search algorithm.

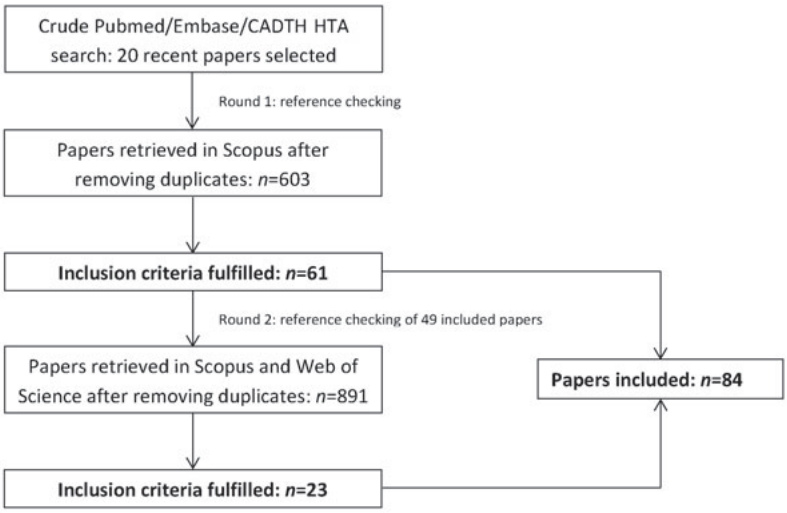

Figure 1 – Flowchart of the literature search algorithm used for identifying and selecting studies for inclusion in this review
Abbreviation: CADTH HTA, Canadian Agency for Drugs and Technologies in Health-Health Technology Assessment.

Study characteristics and quality assessment

Table 1 lists characteristics of studies included (*n*=84) in terms of design, presence and similarity of a comparator group, study size, number of tests targeted, reproducibility of the intervention, sustainability of effects, and reported effect on clinical outcomes if investigated. A more detailed overview of the individual studies can be found in **Appendix 2**.

Study design and characteristics of comparator

Of the five randomized controlled trials, randomization was performed at the patient level in two studies, at the provider level in two studies, and at the test level in one study (i.e., a test was randomized to be subject to the intervention or not). Of the non-randomized controlled trials included, six used (a subset of) other tests as a control arm (e.g., a CPOE intervention in which the intervention applied to a subset of tests and another subset was used as a comparator), six used another department within the same clinic, and in three studies, another clinic was used as the control arm.

For controlled trials, we assessed whether both the intervention group and the control group were comparable with regard to the providers subjected to the intervention as well as the patients for whom they provided. In before-after studies, we assessed whether both patient and provider groups before and after the intervention were comparable; as shown in **Table 1**, this was the case in only seven studies (8.3%).

Study population and tests

The numbers of visits and admissions analyzed ranged from 287 to 5,026,049. The number of hospital days analyzed ranged from 9,890 to 1,557,550. The majority of studies (93%) were single-center studies. In the majority of studies, more than five tests were targeted.

Reproducibility of the intervention

We assessed whether the interventions were described in sufficient detail to allow replication in another setting. This was the case in 44 studies, most of which (59%) reported (C)POE interventions. Information provided included the guidelines that were developed and screenshots of the modified order screen or form.

Sustainability

Only 15 studies (17.9%) investigated sustainability. All of these demonstrated a reduction in test order volume that was sustained for two or more years.

Table 1 – Characteristics of included studies

	***n* (%)**
Study design	56.6 (66.7)
- Before-after study	8 (9.5)
- Retrospective audit	5 (6.0)
- Randomized controlled trial	15 (17.8)
- Nonrandomized controlled trial	
Similarity of patients and providers between comparison groups	7 (8.3)
- Both patients and providers comparable between both groups	1 (1.2)
- Patients comparable, providers not comparable	1 (1.2)
- Patients and providers not comparable	21 (25.0)
- Patients comparable, no data on comparability of providers	3 (3.6)
- Patients not comparable, no data on comparability of providers	7 (8.3)
- Providers comparable, no data on comparability of patients	36 (42.9)
- No data on comparability of either patients or providers	8 (9.5)
- No comparator group	
Number of centers included	78 (92.9)
- Single center	6 (7.1)
- Multiple centers	
Number of tests studied	17 (20.2)
- 1	5 (6.0)
- 2 - 5	53 (63.1)
- > 5	9 (10.7)
- Unclear	
Reproducible intervention	44 (52.4)
- Yes	40 (47.6)
- No	
Sustainability assessed	15 (17.9)
- Yes	69 (82.1)
- No	
Data on clinical outcomes reported	45 (53.6)
- Yes	39 (46.4)
- No	

Interventions

Forty-four studies had an educational component, 49 had a (C)POE component, and 25 had an audit and feedback component. The majority of studies (55%) reported interventions in a single category. The remaining studies involved a combination of interventions from different categories. **Table 2** shows the classification of studies by category of interventions used.

Table 2 – Classification of interventions

	***n* (%)**
Studies in which a single intervention was performed	46 (54.8)
- Educational	9 (10.7)
- (C)POE	33 (39.3)
- Audit and feedback	0 (0)
- Others	4 (4.8)
Studies in which combined interventions were performed	38 (45.2)
- Educational & audit and feedback	15 (17.8)
- Educational & (C)POE	4 (4.8)
- Educational & others	3 (3.5)
- Audit and feedback & (C)POE	1 (1.2)
- (C)POE & others	2 (2.4)
- Educational & (C)POE & Others	4 (4.8)
- Educational & audit and feedback & others	4 (4.8)
- Educational & audit and feedback & (C)POE	3 (3.5)
- Educational & audit and feedback & (C)POE & others	2 (2.4)

Abbreviation: (C)POE, (computerized) provider order entry.

Table 3 provides an overview of the observed changes in test order volume in the individual studies included in this review. We classified all studies by category of intervention(s) used. A variety of outcomes are used to express the change in test order volume, e.g., "reduction in total number of tests," "reduction in the number of tests per patient per day," and "reduction in the number of tests per admission." For a more detailed description of the individual studies, see **Appendix 2**.

Interventions with educational component

Out of 84 studies, nine implemented interventions that were exclusively educational. In 35 studies, interventions combining educational efforts with other approaches were implemented.

Table 3 – Test volume reduction by category of intervention(s)

Ref	Reduction in testing
Education	
8	8.7% *
28	32.7% †
30	22.4% ‡
32	27.8% *
33	14.7% §
18	29.9% ‡
34	57% ‡
35	28.6% (I) vs 11.8% (C) ‖
36	40.6% (I) vs 21.3% (C) †
(C)POE	
Soft stop	
39	46% (pre-I) vs 14% (post-I) ¶
41	22.2 - 53.7% (I) vs 1.7 - 40.1% (C) ‖
43	16.7% ‡
45	21% ‡
46	39.8% ‡
47	19.5% ‡
49	73% (I) vs 49% (C) **
Hard stop	
19	11.2% ††
16	5.7% ‡
53	96.6% **
55	12.4% (I) vs 0.3% (C) ‡‡
57	0.56% ‡
Soft stop vs hard stop	
60	92.3% (I) vs 43.6% (C) ‡
Order form changes, display of fee	
62	44.2% ‡
64	3.9% ‡
66	25.5% (I) vs 1.3% (C) §§
67	18.6% ‖‖
69	8.6% (I) vs 5.6% (C) *
20	17.3% ‡‡
71	56.5% ‡
73	54.3 - 52.5%+ ‖
74	19.1% (I) vs 40.6%+ (C) ‡‡
76	18.5% ‖
77	32.7% ‡‡
79	4.5% ¶¶
80	23.9% ‡
Time limits on orders	
81	8.5% *
83	11.5% *
85	64.7% §
Combined (C)POE & Others	
7	33.3 - 48.5% *
88	18.0% ***
90	13.7% ‡
92	55.2% †

Ref	Reduction in testing
Others	
27	38% ‡
29	12% ‡
31	15.9% ‡
15	3.6% †
Education & Audit/Feedback	
25	5.1 - 7.0% *
24	25.5 - 42.2% (I) vs 3.7 - 22.4% (C) *
3	21% ‡
37	29.8% ‡
10	12.3 - 52.0% (I) vs 26.5 - 8.5%+ (C) ‡‡
38	14.6% *
40	12% †††
42	48.6% ‡
44	38.0 - 73.7% *
9	20.8% *
11	13.5% *
48	4.5%+ †
50	41.5% (I) vs 10.0%+ (C) *
51	24 - 32% *
52	14% †
Education & (C)POE	
54	26.7% and 36.0% ‡
56	61.5% and 100% ‡‡
58	3.1 - 58.5% (I) vs 4.1 - 33.9%+ *
59	41.9% and 44.8% ‡
Education & Others	
61	20.7 - 56.3% *
63	7.5% *
65	69.5% ‡
Audit/Feedback & (C)POE	
68	17% *
(C)POE & Others	
70	33.3 - 60% *
72	47.2%+ ‡‡‡
Education, (C)POE & Others	
75	7.1 - 8.9% *
21	66% ‡
78	80.9% (I) vs 11.8% (C) ‡
22	34.5% (I) vs 10.1 - 14.8% (C) ‖
Education, Audit/Feedback & Others	
14	5.7 - 30.4% (I) vs 1.2 - 8.8%+ (C) §
82	47.4% ‡
84	11.5% ‡‡
86	10.7% (I1) vs 52.3% (I2) vs 23.5% (I3) ‖
Education, Audit/Feedback & (C)POE	
87	20% ‡
89	95% §§§
91	19.0% (I) vs 7.6% (C) ‖‖‖
Education, Audit/Feedback, (C)POE & Others	
93	8% *
94	25.9% ‖

* Number of target tests per (in)patient day, † Number of target tests per (in)patient, ‡ Total number of target tests, § Number of tests per day, ‖ Number of tests per admission, visit or discharge, ¶ Percentage of admissions in which test was performed, ** Percentage of redundant orders cancelled, †† Number of target tests per year, ‡‡ Number of tests per month, §§ Monthly tests per patient day, ‖‖ Number of tests per 100 ED presentations, ¶¶ Fewer tests in intervention group compared to control group, *** Number of tests per week per hospitalization, ††† Percentage of patients undergoing target test, ‡‡‡ Number of tests per patient per visit, §§§ Percentage reduction in use of panel, ‖‖‖ Number of tests per 100 hospital days. Abbreviations: Ref, reference; I, intervention group; C, control group; (C)POE, (computerized) provider order entry; I1, intervention group 1; I2, intervention group 2; I3, intervention group 3.

Interventions with (C)POE component

Thirty-three studies exclusively involved modifications in the (C)POE system. In 16 studies, these modifications were combined with other approaches. In seven studies, pop-up reminders were instated upon ordering a potentially redundant test, providing the opportunity to either cancel or continue the order ("soft stop"), which in some cases required justification. Five studies used a more rigorous approach by automatically rejecting orders that appeared to be redundant ("hard stop"), with or without a direct notification of the ordering provider. Another strategy used involved the unbundling or elimination of order panels or other modifications in order forms, e.g., by grouping tests by organ or disease, or displaying fee information. This strategy was used in 13 reports. A different approach was to limit the time window for order placement, with requests scheduled to be carried out beyond this time window being cancelled, which was done in three studies.

Interventions with audit and feedback component

None of the studies included used audit and feedback methods solely. In 25 studies, audit and feedback methods, in which providers were presented with their ordering patterns, were combined with other interventions.

Other interventions

In three studies, test orders were reviewed for approval by a multidisciplinary team of specialists. In one study, the providers allowed to order tests were restricted.

Clinical patient outcomes

Possible effects of the reduction in laboratory test utilization on patient (clinical) outcomes were studied in slightly more than half (54%) of all studies evaluated. Clinical outcomes were generally not or positively affected by most of the interventions studied. Negative effects on patient outcomes were reported in only two papers. In the report by Finegan et al.[15], test selection was individualized by staff or resident anesthesiologists instead of according to surgery-specific clinical pathways by surgical staff. Significantly more complications and a higher mortality rate were found in the intervention group, although the internist reviewing the complications concluded in all cases that additional tests would not have affected these outcomes. In the report by Smit et al.[16], an electronic gatekeeping system was implemented, automatically rejecting orders not meeting specific rules. Some restored tests were evaluated after previous rejection, and the negative effects on duration of hospital stay and conducting further diagnostics were noted.

Discussion

We provided an overview of the nature and effectiveness of interventions aimed at reducing unnecessary laboratory utilization on the basis of 84 peer-reviewed studies that investigated

educational, (C)POE, audit and feedback, and other interventions. Nearly all the studied interventions had the potential to reduce unnecessary laboratory utilization without affecting patient safety. In the majority of studies, reductions in unnecessary diagnostics were achieved, which was consistent with previous findings.[4,13] Study design, type of intervention, targeted tests, and reported outcomes were heterogeneous. The positive effects reported in nearly all studies and the insufficient detail in study descriptions make it difficult to replicate the studies or to identify the exact elements underlying success. Finally, sustainability of the effects was examined in only few studies. In nearly all studies, the authors concluded that their intervention was successful; however, most studies merely reported a reduction in test order volume and no target for reduction was set at the outset, opening the way to considering the intervention successful on the basis of any positive number. In addition, publication bias may be involved, in that mainly studies with positive outcomes are reported.

Although the interventions could be subdivided into three broad categories, the study designs, interventions, and tests targeted were rather heterogeneous. Moreover, the outcomes were reported in various ways (e.g., "reduction in total number of tests," "number of tests per patient day," "number of tests per patient," "number of tests per day," and "number of tests per month"). Therefore, we conclude that it is not possible to assess the individual effectiveness of different types of interventions.

A change in test utilization requires changes in provider awareness and behavior. Knowledge and attitude are concepts regularly targeted in acquiring and sustaining behavioral change.[17] Increase of knowledge is targeted through education. Attitude can be influenced through audit and feedback methods: knowing that one is being monitored may change one's attitude towards testing, while feedback can also be a learning experience. (C)POE interventions focus directly on behavioral change, although they can contain educational elements as well. Because many interventions were not described in detail in the studies evaluated, it is difficult to identify which elements of an intervention led to success.

Although interventions from all categories seemed to be effective, most studies were relatively short and did not provide follow-up data to demonstrate the sustainability of the intervention. Another element to take into account when comparing interventions is adherence; in approximately half of the interventions, it was not clear to what extent care providers adhered to the interventions. Further, most studies did not use a control arm and had methodological limitations.

Many of the studies evaluated in this review focused on reducing repeated monitoring tests or (accidental) duplicate requests instead of focusing on assessing whether certain tests were indeed indicated. Additionally, patient-related (clinical) outcomes were studied in only slightly more than half of the studies. These outcomes, such as mortality, length of hospital

stay, and admission to the ICU, remained mostly unaffected, although they are crude and it is unclear to what extent these outcomes are linked to a reduction in laboratory testing. Further, studies might not have had sufficient power to demonstrate an effect on the reported clinical outcomes. Only a few studies have investigated consequences of reduced testing in terms of actually missing diagnosis.[18-22] This gives us the impression that reducing unnecessary testing has mostly focused on improvements in efficiency, without affecting patient outcomes.

Interventions with educational elements

Educational interventions provide an opportunity for a personal approach because physicians may be actively involved in the development and implementation of the intervention, e.g., through the development of guidelines. However, an element we did not often encounter in the studies we evaluated was to involve residents through educational sessions, flyers, e-mails, etc., which might further increase their commitment. A possible disadvantage to an educational approach is the amount of effort necessary to successfully carry out such an intervention. Here too, adherence might be a problem, as the extent to which care providers follow guidelines or algorithms, attend educational sessions, or read educational e-mails is often not clear.

Interventions with (C)POE elements

Most studies described in this review contain elements of changes in (C)POE systems. A major advantage of this type of intervention is the relatively little effort needed to carry out such an approach. While determining which modifications should be made in the order systems can be labor-intensive (e.g., how to modify order sets, how a new order form should be designed, and which time limits should be instated on which tests), once such modifications are implemented, no further action is needed. In general, provider adherence to these types of interventions is better than adherence to educational interventions since in most studies, all ordering providers receive the intervention upon ordering. Delvaux et al.[23] recently published a systematic review on the effects of computerized clinical decision support systems on laboratory test ordering and noted that in the majority of studies, a positive effect was found in compliance with recommendations made by the order system.

Interventions with audit and feedback elements

In some studies, audits were performed to assess test order volume, while other studies also assessed test appropriateness. Providers were subsequently presented with data on their ordering patterns. The amount of effort this approach requires differs depending on the content and frequency of auditing and feedback. As was described in these studies, feedback can be provided about the entire study population or on an individual basis, with or without comparison to peers, and, in some cases, anonymously. The level of feedback might influence the extent of commitment.[24,25]

Comparison with the literature

In line with findings in other reviews on de-implementation, we found that most interventions were successful.[4,13] Because of the heterogeneity in the interventions studied and the outcomes reported, we found it difficult to compare effectiveness and to draw conclusions as to which intervention(s) is/are most successful. This difficulty was also encountered by Delvaux et al.[23] However, previous reviews stated that combined interventions appear to be more successful than single interventions.[4,13]

Kobewka et al.[4] reviewed 109 studies on interventions to reduce test utilization in both primary care facilities and hospital settings. In line with our findings, they found interventions from all categories to be successful. Further, they found that combined interventions were more effective than single interventions. To express median relative reduction, different outcome measures were combined. We found this approach questionable, even more so because the authors also found the effects of interventions to be different when these were expressed using a different outcome measure (e.g., Kumwilaisak et al.[9] reported a 21% reduction in number of tests per patient per day, while the total number of tests decreased by 36% in the same study). Solomon et al.[13] reviewed 49 studies on interventions aiming to improve physicians' testing practices and assessed methodological quality and efficacy of the interventions. Of 21 interventions using a single approach, 62% reported success, while 86% of 28 interventions using a combinatorial approach were successful.

Strengths and limitations

This review and the studies included have a number of strengths and limitations. A strength of this review is that it considered a variety of interventions and approaches to reduce unnecessary laboratory testing. In addition to assessing the reduction in test order volume, we were also interested in the effects of these interventions on patient-related clinical outcomes.

A limitation is our exclusive focus on studies on reducing unnecessary testing in hospital settings, although we found that interventions carried out in primary care facilities were broadly similar to those we described.[4,26] Further, we only included studies that reported a reduction in test order volume of all, not just a subset, of studied tests. In addition, we did not perform an exhaustive literature search; we concluded our search when we had, in our opinion, reached theoretical saturation and no new domains of interventions were found. Thus, we might have missed relevant articles. Finally, we did not assess the costs of development and implementation of interventions and the cost-benefit reducing laboratory testing yields.

Conclusions and implications for future research

In conclusion, there are various interventions to reduce unnecessary laboratory testing in the hospital setting. While the majority seems to be effective, the generalizability of the data is questionable and the data are not comparable. An important step in changing test-ordering behavior is changing the mindset of providers and for this purpose, even a few test items can be used to introduce the concepts related to unnecessary diagnostics. We do, however, believe that not all interventions are equally suitable in every setting and for every test targeted, e.g., instating time limits might be more suitable for tests that are (unnecessarily) ordered in high frequency, while education might be more suitable when aiming to reduce unnecessary arterial blood gas requests. Thus, investigators should consider the clinical setting, the providers, and the tests targeted when developing or implementing strategies for reduction. Reporting on interventions can be improved if articles share more details about the study design and interventions to allow replication. In addition, we recommend performing studies with relevant patient-related outcomes and the investigation of sustainability of the effect of interventions.

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Appendices

Appendix 1 – Search terms

Search terms and combinations thereof used to find relevant articles describing interventions aimed at reducing unnecessary laboratory testing in the hospital setting in the PubMed, Embase, and Canadian Agency for Drugs and Technologies in Health-Health Technology Assessment databases

'laboratory test*' OR 'laboratory request*' OR 'laboratory order*' OR 'laboratory utilization', OR 'laboratory test utilization'

AND

'inappropriate' OR 'appropriate' OR 'reduce' OR 'reduction' OR 'improve' OR 'improving' OR 'improvement'

AND

'intervention*' OR 'strategy' OR 'strategies' OR 'education*' OR 'feedback'

Appendix 2 – Overview of individual studies

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
Education													
8	Presentations, discussions, flyers, e-mail communication		X	X	X					Y	N	N	N
28	Team discussion during rounds		X							Y	N	N	Y
30	Implementation of a guideline		X							Y	N	N	Y
32	Range of educational efforts		X	X	X				X	Y	N	N	N
33	Implementation of standard operating protocols								X	N	N	N	N
18	Implementation of algorithm		X							Y	N	N	N
34	Implementation of guidelines		X							Y	N	N	N
35	Sessions on predictive value vs. sessions on economic issues and cost control	X								Y	Y	N	N
36	Implementation of guideline and review of medical records vs. no intervention		X	X						N	N	N	N
(C)POE													
Soft stop interventions													
39	Pop-up upon ordering second ionized test within 72 hours after normal test		X							Y	Y	Y	Y
41	Pop-up upon repeat order within specific time interval vs. no intervention		X							Y	Y	N	Y
43	Pop-up upon ordering of potentially inappropriate test		X				X	X	X	N	Y	N	Y
45	Pop-up upon ordering if previous result within same hospital stay		X							N	Y	Y	Y
46	Pop-up if most recent result is less than 90 days old								X	Y	Y	N	Y
47	Pop-up upon potentially redundant ordering of test								X	N	Y	Y	Y

Appendix 2 – Continued

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
49	Pop-up upon ordering within time specific interval vs. determination of redundancy and suppression of pop-up		X		X	X			X	Y	Y	N	N
Hard stop interventions													
19	Rejection if not ordered according to order frequency rule	X								Y	Y	Y	Y
16	Rejection if ordering within minimum retesting interval or if not meeting rules		X					X		Y	Y	N	Y
53	Pop-up upon ordering same-day duplicate test, rejection of unnecessary order	X								Y	Y	Y	Y
55	Rejection of order if previous result within 48 hours vs. no intervention		X							N	Y	N	Y
57	Rejection of order if requested within certain time interval after previous test		X			X	X	X	X	N	Y	Y	Y
Hard stop vs. soft stop interventions													
60	Blocking of tests deemed unnecessary more than once per day vs. pop-up upon ordering of tests deemed unnecessary more than once per day	X								N	Y	N	Y
Order form changes, display of fee													
62	Redesign of order form through re-categorization of target test		X							N	Y	N	Y
64	Revision of test panels, reducing the number from 171 to 60	X								N	Y	N	Y
66	Display of charge and turn-around-time upon ordering test vs. no intervention								X	N	Y	N	Y
67	Limiting range of laboratory tests allowed to order by changing paper request form	X								N	Y	N	Y

Appendix 2 – Continued

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
69	Display of charge upon ordering vs. no intervention		X	X	X	X	X	X	X	N	Y	N	Y
20	Redesign of order form: removing tickbox for target test, requiring written request						X			Y	Y	N	Y
71	Change in order form indicating appropriateness (overruling of recommendation by providing reason on sheet) and display of charge of tumor marker requests on order form						X			N	Y	Y	N
73	Display of charge on order form		X	X	X	X				Y	Y	N	Y
74	Redesign of order form displaying only boxes for clinical conditions instead of individual tests vs. no intervention							X		N	N	Y	N
76	Unbundling and translocation of test panels, grouping tests, implementation of algorithms		X	X		X		X	X	N	Y	N	N
77	Elimination of predefined multitest panels		X							N	Y	N	N
79	Computerized display of charge upon ordering vs. no intervention	X								Y	N	N	Y
80	Change in order form indicating appropriateness of request						X			N	Y	N	Y
Time limits on orders													
81	Elimination of ability to order daily recurrent tests		X	X	X					Y	Y	N	Y
83	Expiration of any laboratory order at 24 hours	X								N	Y	N	Y
85	Elimination of standing orders for laboratory studies	X								Y	N	N	N
Combined (C)POE & Others													
7	Time-limit on ordering, daily order set for appraisal of tests ordered daily, patient summary tab to permit rapid review of active orders		X	X	X					Y	Y	N	Y

Appendix 2 – Continued

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
88	Implementation of inpatient electronic health record with CPOE	X								Y	Y	N	N
90	Order form change through listing organs/diagnoses which directed to the test that could be requested, changing regulations for requests						X			N	Y	N	Y
92	Time-limit on ordering, display of previous test result upon ordering, display of testing guidelines		X							N	Y	Y	Y
Others													
27	Review of microbiology send-out test requests								X	N	Y	N	Y
29	Review of reference test requests before approval								X	N	Y	N	Y
31	Review of reference test requests								X	N	Y	N	Y
15	Change of providers allowed to order tests, ordering individualized instead of through surgery-specific pathway	X								Y	Y	N	Y
Education & Audit/Feedback													
25	Information on charges, weekly feedback on mean volume and charges	X								N	N	N	Y
24	Presentations and flyers on high value care principles, pocket cards with charges, weekly feedback with peer comparison vs. no intervention		X	X						Y	N	N	Y
3	Educational seminars on overutilization, weekly feedback reports on ordering habits		X	X	X				X	N	N	N	N
37	Implementation of guidelines, audit and feedback method not further specified		X							Y	N	N	N
10	Implementation of guidelines, lectures on use of laboratory tests, reminder letters, feedback on test use vs. no intervention		X						X	N	N	Y	N

Appendix 2 – Continued

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
38	E-mails with recommendations on laboratory ordering, monthly feedback		X	X						Y	N	N	N
40	Education regarding indications for target test ordering, physicians informed of results of previous audit on ordering behavior		X							N	N	N	N
42	Discussions of related literature, feedback on previous 3 years, feedback on first months after intervention		X							N	N	N	N
44	Guide with ordering rules and test costs, educational sessions, monthly feedback		X	X						Y	N	N	N
9	Implementation of ordering guidelines, monthly update on outcome	X								Y	Y	N	Y
11	Feedback on previous audit of appropriateness of testing, review of literature, discussion on strategies for reducing unnecessary testing		X	X						Y	Y	N	Y
48	Educational information, feedback on blood loss from phlebotomy	X								N	N	N	N
50	Implementation of guidelines, teaching sessions, monthly feedback on adherence and impact of guidelines vs. no intervention		X							Y	Y	N	N
51	Teaching rounds, weekly review of cost data	X								Y	N	N	N
52	Discussing cost issues and unnecessary testing, feedback on ordering patterns relative to peers, implementation of guidelines		X	X	X	X				Y	N	N	Y
Education & (C)POE													
54	Revision of protocols, lectures, omission of tests from standard panels, implementation of presets	X								N	Y	N	N
56	Alert upon ordering in specific patients, education through e-mail								X	N	N	N	N

Appendix 2 – Continued

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
58	Implementation of guidelines, incorporation into admission templates on CPOE screen, educational sessions vs. no intervention		X	X						Y	N	N	Y
59	Information campaign, clinical justification needed if more parameters ordered, implementation of algorithm							X	X	N	N	N	N
Education & Others													
61	Staff education, visual reminders, daily checklists		X	X	X					Y	N	N	N
63	Daily information for staff, reminders at bedside of test information and costs, incentive		X	X	X	X				Y	N	N	N
65	One day e-mail discussions about utility and costs of CRP testing, no CRP day with gold coin penance if ordered		X							N	N	N	N
Audit/Feedback & (C)POE													
68	Implementation of computerized protocol management system, monthly summary of investigations used as basis for regular discussions		X							Y	Y	N	Y
(C)POE & Other													
70	Checklist enabling physicians to assess necessity for testing daily, restriction on scheduling tests to 24-hour interval		X	X	X					Y	N	N	N
72	Co-payment fee for nonemergent visits, reducing the number of eligible tests to order from the Emergency Department	X								N	Y	N	N
Education, (C)POE & Other													
75	Educational sessions, item on ICU checklist regarding routine blood tests, prompt in order system that compelled provider to specify indication for test		X	X						Y	N	N	Y

Appendix 2 – Continued

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
21	Implementation of guidelines, removal of tests from order set, pop-up warning upon ordering not according to specific rules, change of providers allowed to order tests		X							Y	N	N	Y
78	Implementation of protocol, rejection if request within 24 hours of previous request, consultant only requesting vs. no intervention		X							N	N	N	N
22	Unbundling of panels, series of lectures on economic implications of excessive use of testing, supervision of ordering by senior physician vs. no intervention	X								Y	N	Y	N
Education, Audit/Feedback & Other													
14	30-minute discussion, pocket cards with charges, discussion of laboratory tests within rounds, incentive, monthly feedback of average and individual performance vs. no intervention		X	X	X					Y	N	N	N
82	Implementation of guidelines, discouragement of use of panel, monthly feedback on ordering volume, financial incentive		X							Y	N	N	Y
84	Daily discussion of need for testing, daily coaching of resident, regular feedback on volume and costs, approval of superior needed for ordering daily tests	X								N	N	Y	N
86	One hour discussion, incentive, periodic feedback on performance in relation to testing goals vs. one hour discussion, chart review sessions vs. one hour discussion		X					X	X	Y	N	N	N

Appendix 2 – Continued

Ref	Interventions	Tests studied								Clin outcome	Adherence	Sustainability	Reproducibility
		All	Chem	Hem	Coag	Urine	TM	Endo	Other				
Education, Audit/Feedback & (C)POE													
87	Monthly discussions and feedback, unbundling panel	X								N	N	N	N
89	Educational sessions, feedback on results of previous audit, implementation of algorithm, replacement of four-component panel with two-component panel on order form				X					Y	N	Y	N
91	Restricting available emergency laboratory tests and allowed frequency of repeated orders, presentation on misuse of tests and restrictive strategy, feedback of results vs. no intervention		X							Y	N	N	Y
Education, Audit/Feedback, (C)POE & Other													
93	Educational sessions and newsletters, quarterly feedback, elimination of standing daily orders, incentive		X	X	X					Y	N	Y	Y
94	Implementation of guidelines, educational campaign, feedback on individual provider level, removal of tests from quick-pick screen, pop-ups upon ordering specific tests, justification needed for requesting daily tests beyond 3 days, use of admission templates, discontinuing tests of limited usefulness	X								N	N	Y	N

Abbreviations: Clin, clinical; Ref, reference; Chem, chemistry; Hem, hematology; Coag, coagulation; TM, tumor markers; Endo, endocrinology; Y, yes; N, no.

3

A multicenter before-after study on reducing unnecessary diagnostics by changing the attitude of caregivers: Protocol for the RODEO project

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Abstract

Background

Appropriate use of diagnostic laboratory tests is challenging, and estimates of 20% for overutilization and 45% for underutilization have been reported. Introducing effective and sustainable solutions to stimulate optimal use of laboratory testing in clinical practice is a challenge. A recent pilot study from our group, focusing on increasing the awareness about appropriate laboratory testing with the aim of changing the mindset of health care workers, has shown promising results. In this project, we aim to extend this multistep intervention to the internal medicine departments of four large Dutch hospitals. We aim to reduce unnecessary laboratory testing by 5%.

Objective

Our primary objective is to determine the effect of our intervention on diagnostic laboratory test order volume. Our secondary objectives are to determine the effect of our intervention on laboratory expenditure and order volumes, expenditures for other diagnostic modalities, and clinical patient outcomes. We will also analyze the barriers and facilitators for de-implementation of unnecessary laboratory testing.

Methods

The main interventions of this before-after study will be an intensified supervision of residents by experienced physicians regarding test ordering, creating awareness through education and monthly feedback on ordering patterns, and changes in (computerized) order entry systems.

Results

At the time of publication of this protocol, the project is in the phase of data collection. We expect to present data on reduction early in the fourth quarter of 2018.

Conclusions

In this project, we aim to reduce the unnecessary diagnostic testing in the internal medicine departments of four teaching hospitals. Although the main interventions will be similar, each clinic is given the opportunity to focus on the specific facets of the interventions as deemed useful according to the local situation. If effective, the study provides a framework for a nationwide initiative for reducing inappropriate laboratory testing.

Introduction

Over the past decades, a marked rise in health care expenses has been observed in Western countries. In the Netherlands, the burden of health care on the gross domestic product has increased from 7.9% in 1998 to 10.5% in 2016, corresponding to an increase from approximately 30.9 to 73.7 billion euros. A large part of the total health care expenditure consists of hospital care, including diagnostic testing.[1,2] The volume, and consequently the costs, of performing diagnostic tests is increasing, with earlier studies reporting a doubling of the rate every five to ten years over the past decades.[3]

In 2015, Kobewka et al.[4] reviewed numerous international studies and concluded that a considerable proportion of performed (laboratory) tests were unnecessary, that is, they did not contribute to patient care. A review addressing the appropriateness of diagnostic laboratory testing, as judged by the presence of multiple appropriateness criteria (e.g., criteria based on testing frequency, choice of test compared with possible alternatives, and probability of abnormal test results), has reported a mean rate of overutilization of approximately one-fifth from 1997 to 2012.[5] Consequently, laboratory testing is often targeted in efforts to reduce health care expenditure. Besides the financial impact, overutilization increases the number of false-positive results, which leads to more, sometimes invasive and potentially harmful, tests.[6] Also, excessive blood draw can result in iatrogenic anemia and can lead to less patient-friendly practice, for example, through painful punctures and unnecessary trips to the hospital.[7]

In 2009, a multifaceted intervention focusing mainly on laboratory test reduction was implemented at the internal medicine department of the VU University Medical Center (VUmc). Utilization of other diagnostics, such as radiology, declined too. Our efforts resulted in a 13% gross reduction in diagnostic expenditure compared with that in the previous year. When extrapolating these results, nationwide implementation of these interventions could result in a potential saving of millions of euros.

In the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) – project, we will assess the effects of a multifaceted intervention aimed at improving awareness about (in)appropriate laboratory testing on the volume and costs of diagnostic testing and clinical outcomes of patients in the internal medicine departments of multiple peripheral teaching hospitals over six months. We aim to reduce (unnecessary) diagnostic testing by 5%. Our primary focus will be on laboratory testing, although we will also assess the effects of our intervention on the volume and costs of other diagnostic modalities. In addition, we will assess the sustainability of the interventions during an additional eight-month period.

We will also analyze the process of de-implementation of unnecessary laboratory testing in the participating hospitals, aiming to identify barriers and facilitators.

This project is a part of the *"To do or not to do? Reducing low-value care"* program aimed at reducing low-value care.[8] The program was initiated by the Dutch Federation of University Medical Centers.

Methods

Study design and setting

This multicenter before-after study was conducted at the internal medicine departments (inpatient, outpatient, and emergency departments) of the Zaans Medical Center (Zaandam), Meander Medical Center (Amersfoort), North-West Hospital Group (location Alkmaar), and Spaarne Gasthuis (locations Haarlem and Hoofddorp), which are all teaching hospitals in the Netherlands; in the rest of the document, we have referred to these participating hospitals anonymously as hospital 1-4.

Access to timely data on volume and costs of different diagnostic modalities (laboratory, radiology, microbiology, pathology, and nuclear medicine) for the duration of the project and for the three preceding years was a criterion for inclusion. Another criterion for inclusion was consent of the participating hospital's Board of Directors. The project protocol was assessed by the Medical Ethics Review Committee of VUmc. They determined that the Medical Research Involving Human Subjects Act does not apply to this project and that official approval by the Medical Ethics Review Committee is not required. Local feasibility was approved by the local ethics committees and Board of Directors of all participating hospitals. Data were collected anonymously.

De-implementation strategy

The study consists of three time periods: three to four months of pre-intervention, six months of intervention, and eight months of post-intervention. The study was started in August 2016; after the study period ends, we plan to continue monitoring these interventions to assess sustainability.

Before the start of the pre-intervention period, the internal medicine departments of the participating hospitals were contacted and informed about the project. Upon inclusion of a department, cooperation agreements were signed by the principle investigator of the hospital, and thereafter, a project team consisting of a senior internist (ambassador), internal medicine resident, a business intelligence collaborator, and a clinical chemist were formed.

Pre-intervention period (three to four months)

During the pre-intervention period, data on volume and costs of diagnostics as well as on patient outcomes from the previous three years were collected. Also, data on the characteristics of the participating departments such as the number and years of experience of residents and supervising physicians, methods and frequency of supervision of residents, and characteristics of ordering systems were collected. The pre-intervention period started in August 2016 at hospitals 1 and 2, in September 2016 at hospital 3, and in November 2016 at hospital 4.

Intervention period (six months)

At the start of the intervention period, a launching conference took place with the members of all the participating project teams. Each project team was requested to give a presentation on the characteristics of their department, data on their ordering patterns over the previous years, and previous projects related to this topic. In addition, each project team was requested to present interventions tailor-made for their department structure.

We also assessed foreseen barriers and facilitators for de-implementation and discussed how to tackle them, if necessary. The program of this launching conference can be found in **Appendix 1**.

Upon starting the intervention period, data collected in the pre-intervention period and planned interventions were presented by the local project teams to the caregivers working in their departments. During the intervention period, the local project teams performed the interventions and had frequent periodic progress meetings with the coordinating project team. The interventions performed and how they were developed have been described in more detail in the subsection "Description of interventions".

A second conference was organized in which the project teams presented their results from the initial months, exchanged experiences and ideas on how to proceed in the remaining months of the project, and discussed how to sustain the effects after the termination of the active intervention period. The program of this conference can be found in **Appendix 1**.

The intervention period started in November 2016 at hospitals 1 and 2, in January 2017 at hospital 3, and in March 2017 at hospital 4.

Post-intervention period (eight months)

In the post-intervention period, the sustainability of the intervention was analyzed. During this period, a third joint conference was organized with all the participating project teams in which

the project teams were requested to present their results and exchange experiences and ideas on how to further sustain the achieved effects. The program of this conference can be found in **Appendix 1**. Data on diagnostic volume and costs and patient outcomes were reanalyzed.

The post-intervention period started in May 2017 at hospitals 1 and 2, in July 2017 at hospital 3, and in September 2017 at hospital 4. The post-intervention period ended in December 2017 at hospitals 1 and 2, in February 2018 at hospital 3, and in April 2018 at hospital 4. We will continue to monitor the progress and results for 12 months.

At the time of publication of this protocol, the project is in the data collection phase.

Description of interventions

Target items for interventions were determined by the project team from different angles: tests that are known to be frequently overused, tests ordered in high frequency or generating high costs to the department, and diagnosis-related groups occurring in high frequency or generating high costs (compared with the benchmark, when available). All participating hospitals were given the opportunity to focus on the specific facets of the intervention as deemed useful in the local situation, thus, "tailoring" their interventions.

The interventions performed in this project were partly derived from previous literature[4,9] in which the interventions were divided into the following categories: education, audit and feedback methods, (computerized) provider order entry system changes, and others. To develop and classify the interventions in the RODEO project, we used slightly different categories.

The main interventions were intensified supervision, creating awareness, and modifications in (computerized) order entry systems. Intensified supervision of residents by senior physicians refers to explicitly focusing on indications for ordering laboratory tests and asking critical questions ("Does the result of this test add value for diagnostics, treatment, or prognosis?", "Is repetition of this test necessary at this moment?", "Is it necessary to order these tests combined?") during morning reports, daily supervision meetings, grand rounds, and other clinical meetings.

In addition to paying more attention to laboratory ordering, awareness was also created through educational sessions or e-mails, posters displaying recommendations and general agreements on ordering of (specific) tests, and distribution of pocket-cards containing charges for frequently ordered tests. Awareness was also created by providing feedback on (changes in) ordering patterns to the physicians working in the department.

Modifications in (computerized) order entry systems included instating time limits on ordering tests for which a repeat test is not necessary within a certain time interval and modification of existing order panels.

The coordinating project team and the local project teams held monthly meetings during the intervention period and bi- or tri-monthly meetings during the post-intervention period. In these meetings, the progress of (development of) each intervention was discussed. Also, changes in total order volume and costs were discussed using data acquired from the business intelligence or business control collaborator. If explicit focus was placed on specific tests, changes in the order volume of these tests were discussed separately.

The interventions performed in each clinic, classified by category, are displayed in **Figure 1**. Details on each intervention can be found in **Appendix 2**.

Endpoints and data collection

In the RODEO project, we aim to reduce the amount of (unnecessary) diagnostic laboratory testing. Based on previous experience from our pilot study, we decided to aim for a conservative estimate of 5% reduction in total test volume.

Primary endpoint

The primary endpoint is diagnostic laboratory test order volume in the internal medicine department (inpatient, outpatient, and emergency department).

Hospital	Intervention	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14
1	E & Aw	●●●●	●	●●		●			●	●	●	●	●●		●
	(C)POE				●	●			●●	●					
	C	●													
	Ag & P	●●		●											
	M & C	●*●	●	●	●	●		●			●			●	●
	O	●*												●	●
2	E & Aw	●●●	●●	●●●		●			●●					●	
	(C)POE		●●		●		●	●							
	C	●													
	Ag & P	●			●										
	M & C	●*	●	●	●	●●		●			●		●		●
	O	●*		●					●			●	●	●	
3	E & Aw	●●●●	●	●●	●●			●		●					
	(C)POE					●	●	●							
	C				●	●									
	Ag & P			●											
	M & C	●*	●	●	●	●	●	●	●				●●		
	O	●*●*				●									
4	E & Aw	●*●●	●	●	●●●●●	●●●	●●●●	●	●	●	●	●	●●	●●●	●●
	(C)POE						●				●		●		
	C					●									
	Ag & P														
	M & C	●*●●	●	●	●	●		●		●	●	●			
	O	●*			●							●●			

Figure 1 – Timeline of interventions

*Action took place before the intervention period. Abbreviations: M1, intervention period month 1, etcetera; E & Aw, education and awareness; (C)POE, (computerized) provider order entry; C, involvement of clinical chemist(s); Ag & P, agreements and protocols; M & C, meetings and conferences; O, others.

Laboratory test order volume will be assessed as the total number of orders for laboratory tests and will be corrected for patient census using "standardized patient units", a measure that will be calculated using the numbers of admissions, in-hospital admission days, day care admissions, and number of first outpatient consultations.[10] Order volume and data required for calculation of the number of standardized patient units will be acquired through the Department of Business Intelligence or Business Control and the Department of Clinical Chemistry.

Secondary endpoints

Secondary endpoints are laboratory expenditure, order volumes and expenditure for other diagnostic modalities, and clinical patient outcomes.

Laboratory expenditure will be assessed as total expenditure and corrected for patient census. Order volumes and expenditure (if possible) for other diagnostic modalities (radiology, microbiology, pathology, and nuclear medicine considered separately) will be assessed as the total number or costs of orders and will also be corrected for patient census.

To ensure that a reduction in diagnostic testing does not affect patient outcomes, we will take into account clinical patient outcomes before and after the intervention based on duration of hospital stay, 30-day readmission rate, and rate of repeated outpatient visits relative to first outpatient visits, and glycated hemoglobin.

Expenditure, order volumes, data required for calculation of the number of standardized patient units, and data on clinical outcomes will be acquired through the Department of Business Intelligence or Business Control and the Department of Clinical Chemistry.

Evaluation of barriers and facilitators

An important part of the RODEO project is evaluating the barriers and facilitators of de-implementation of unnecessary laboratory testing. To identify these factors, questionnaires (**Appendix 3**) on these topics were administered to each project team during the (pre-) intervention period. During the remainder of the project, these factors were discussed during multiple conferences.

Statistical analysis

All statistical analyses will be performed using R version 3.4.2. We will assess the volume of diagnostic tests ordered (total volume and volume of laboratory, radiology, microbiology, pathology, and nuclear medicine tests separately) during intervention period and post-intervention period and the preceding years. We will adjust for patient census using

"standardized patient units", a concept previously used by Dutch insurance companies for reimbursement purposes. The number of standardized patient units will be calculated using the following formula:

(10 × number of admissions) + (0.5 × number of patient days) +
(3.5 × number of day admissions) + (1.2 × number of first outpatient consultations)

An interrupted time series analysis will be performed to assess the effects of the intervention on test volume. We will use an autoregressive integrated moving average model to analyze whether the intervention led to a (more profound) change in the number of tests per standardized patient unit after the intervention. We will adjust for seasonal variation.

Results

We expect the study period to end in April 2018. Furthermore, we expect to be able to present data on reduction early in the fourth quarter of 2018.

Discussion

In this protocol, we have described the objective, design, de-implementation strategy, and endpoints of the RODEO project, aiming to reduce unnecessary diagnostic testing in the internal medicine departments of four large teaching hospitals in the Netherlands.

The approach used in this project was derived from an approach previously used in a pilot project within different departments of VUmc.[1] In this project, a senior physician was designated as "ambassador" or "local champion" who was responsible for coordinating and performing the interventions in the participating departments, which consisted mainly of intensified supervision, education, and feedback. During this pilot project, no modifications were made in the (computerized) order entry system. Although commitment of a supervisor has been shown to play a crucial role in the success of a project, the VUmc project identified a prominent role for residents as one of the key success factors. Furthermore, the VUmc study team found that the clinical chemistry department played an important role in the pilot project. Therefore, we appointed a central project team at each participating department consisting of an internal medicine supervisor and a resident, a clinical chemist, and a collaborator from the Department of Business Intelligence or Business Control.

Although the main interventions were intensified supervision, creating awareness through education and feedback, and changes in (computerized) order entry systems, each hospital

was given the opportunity to focus on the specific facets of the interventions as deemed useful in the local situation. Each clinic, thus, had the opportunity to "tailor" its interventions as deemed fit, which can be considered a strength of our approach. Another strength of our project is the inclusion of four relatively large teaching hospitals. A potential limitation of our approach is the nonexistence of a control group. Also, it was not possible to determine the effect of individual aspects of this multistep intervention due to the limited time available for this project. Furthermore, we did not include patients in our efforts to reduce laboratory testing. We expect the study period to end in April 2018. If effective, this study will provide a framework for a nationwide initiative for reducing inappropriate laboratory testing.

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Appendices

Appendix 1 – Program conferences

Program launching conference RODEO project
Thursday September 29th, 2016
Location: Olympic Stadium Amsterdam

12.00 – 13.00	*Lunch*
13.00 – 13.30	Introduction by coordinating project team
13.30 – 14.15	Introductory presentation by participating project teams (5 – 6 minutes per project team)
14.15 – 14.45	Brainstorm by project team members within their own discipline: assessment of foreseen barriers and facilitators
14.45 – 15.15	Developing a plan for reduction by each project team
15.15 – 15.45	*Coffee break*
15.45 – 16.45	Presentation of developed plan for reduction by each project team (8 minutes per project team)
16.45 – 18.00	Discussion

Program second launching conference RODEO project
Wednesday March 22th, 2017
Location: VU University Medical Center

17.30 – 18.00	*Dinner*
18.00 – 18.10	Introduction
18.10 – 18.50	Presentation of current situation by participating project teams (10 minutes per project team)
18.50 – 19.00	Presentation on national initiative aiming to integrate cost-consciousness into resident training programs ('Bewustzijnsproject')
19.00 – 19.10	*Coffee break*
19.10 – 19.40	Brainstorm by project team members within their own discipline: • Do's and Don'ts • Points of concern for sustainability
19.45 – 20.00	Follow-up agreements
20.00	Discussion

Program third launching conference RODEO project
Wednesday December 13th, 2017
Location: VU University Medical Center

17.30 – 18.00	*Dinner*
18.00 – 18.10	Introduction
18.10 – 19.10	Presentation of current situation by participating project teams (10 minutes per project team)
19.10 – 19.30	*Coffee break*
19.30 – 20.30	Learned lessons: what works, what doesn't work? • Education • Time limits, protocols and agreements • Preliminary conclusions
20.30 – 20.45	Publication of results and experiences Discussion

Appendix 2 – Interventions by hospital

Interventions – Hospital 1

Education and awareness

November 2016:

- Presentation: Introduction of project and diagnostic test ordering patterns (volume and costs)
- Educational session: Antinuclear Antibody (ANA) testing
- Brainstorm meeting on possible targets for interventions
- Distribution of mouse pad with questions to keep in mind when ordering laboratory tests: "Does the result of this test have added value for diagnostics, treatment of prognosis?", "Is repetition of this test necessary at this moment?", "Is it necessary to order these tests combined?"

December 2016:

- Educational session: Amylase and lipase

January 2017:

- Educational session: Blood cultures
- Presentation: Feedback on diagnostic test ordering patterns (volume, costs, number of phlebotomies)

March 2017:

- Distribution of pocket-cards containing charges for commonly used tests

June 2017:

- Educational session: Liver biochemistry

July 2017:

- Educational session: Kidney function panel

August 2017:

- Educational session: Fecal cultures

September 2017:

- Presentation: Feedback on diagnostic test ordering patterns (volume, costs, number of phlebotomies) to Internal Medicine staff

October 2017:

- Educational session: Analysis of anemia
- Presentation: Principles of project to residents and interns from all departments

December 2017:

- Educational session: Cardiac enzymes in patients with chest pain at the inpatient department

Order system changes

February 2017:

- Modification of 'Geriatrics' order panel

March 2017:

- Instatement of time limits on test orders: repetitive order within prespecified time frame is automatically rejected, can only be overruled after direct contact with the laboratory

June 2017:

- Abolishment of amylase testing by the laboratory
- Modification to order system ensuring fast display of performed blood culture tests while awaiting result

July 2017:

- Introduction of 'kidney function' panels WITH or WITHOUT urea

Clinical chemist

November 2016:

- Introduction of presence and participation in 1-2 grand rounds a week by clinical chemist

Agreements and protocols

November 2016:

- Introduction of general agreement: Limit the frequency of laboratory testing to two times a week in clinically stable patients
- Introduction of general agreement: Limit the frequency of CRP testing to three times a week

January 2017:

- Introduction of general agreement: Instruction to care providers to clearly indicate which tests are to be requested by medical secretaries (e.g., list tests to be requested individually instead of ordering 'kidney panel')

Meetings and conferences

September 2016:

- Launching conference with project teams of all participating departments and coordinating project team

November 2016:

- Monthly progress meeting (1) project team and coordinating project team

December 2016:

- Monthly progress meeting (2) project team and coordinating project team

January 2017:

- Monthly progress meeting (3) project team and coordinating project team

February 2017:

- Monthly progress meeting (4) project team and coordinating project team

March 2017:

- Monthly progress meeting (5) project team and coordinating project team
- Conference with project teams of all participating departments and coordinating project team

May 2017:

- Monthly progress meeting (6) project team and coordinating project team

August 2017:

- Progress meeting (7) project team and coordinating project team

November 2017:

- Progress meeting (8) project team and coordinating project team

December 2017:

- Conference with project teams of all participating departments and coordinating project team

Others

October 2016:

- Presentation: Introduction of project to Board of Directors

November 2017:

- Display of posters in workspaces stating important RODEO principles

December 2017:

- Introduction of e-mail to inform new employees of the RODEO project and its main principles

Interventions – Hospital 2

Education and awareness

November 2016:

- Presentation: Introduction of project and diagnostic test ordering patterns (volume and costs)
- Distribution of pocket-cards containing charges for commonly used tests
- Distribution of mouse pad with questions to keep in mind when ordering laboratory tests: "Does the result of this test have added value for diagnostics, treatment of prognosis?", "Is repetition of this test necessary at this moment?", "Is it necessary to order these tests combined?"

December 2016:

- Educational session: Local guideline on 'Chronic fatigue'
- Newsletter: Frequency of CRP testing, combining liver panel tests

January 2017:

- Newsletter: Sodium testing
- Educational session: Amylase and lipase
- Educational session: Value of routine hemoglobin measurement after kidney biopsy

March 2017:

- Educational session: 'Standard Internal Medicine' order panel

June 2017:

- Presentation: Principles of project at hospital-wide meeting
- Presentation: Principles of project to residents and interns from all departments

November 2017:

- Presentation: Feedback on diagnostic test ordering patterns (volumes and costs) to Internal Medicine staff

Order system changes

December 2016:

- Sequential ordering, pop-up upon ordering TSH: FT4 value will automatically be determined if TSH value deviates from normal (this pop-up was deleted in February 2017 due to provider complaints)
- Sequential ordering: Anti-IA2 will only be performed when anti-GAD is negative

February 2017:

- Instatement of time limits on test orders: repetitive order within prespecified time frame is automatically rejected, can only be overruled after direct contact with the laboratory

April 2017:
- Modification to order system ensuring fast display of performed blood culture tests while awaiting result

May 2017:
- Modification of 'Emergency Department' order panel

Clinical chemist

November 2016:
- Introduction of presence and participation in 1-2 grand rounds a week by clinical chemist

Agreements and protocols

November 2016:
- Introduction of general agreement: Limit the frequency of laboratory testing to two times a week in clinically stable patients

February 2017:
- Modification of local guideline for laboratory diagnostics in hemodialysis patients

Meetings and conferences

September 2016:
- Launching conference with project teams of all participating departments and coordinating project team

December 2016:
- Monthly progress meeting (1) project team and coordinating project team

January 2017:
- Monthly progress meeting (2) project team and coordinating project team

February 2017:
- Monthly progress meeting (3) project team and coordinating project team

March 2017:
- Monthly progress meeting (4) project team and coordinating project team
- Conference with project teams of all participating departments and coordinating project team

May 2017:
- Monthly progress meeting (5) project team and coordinating project team

August 2017:
- Progress meeting (6) project team and coordinating project team

October 2017:
- Progress meeting (7) project team and coordinating project team

December 2017:

- Conference with project teams of all participating departments and coordinating project team

Others

October 2016:

- Presentation: Introduction of project to Board of Directors

January 2017:

- Involvement of specialists representing internal medicine sub-specialisms (Nephrology, Oncology) within project team

June 2017:

- Presentation: Feedback on diagnostic test ordering patterns (volumes and costs) to Board of Directors

September 2017:

- Involvement of second resident within project team

October 2017:

- Display of posters in workspaces stating important RODEO principles

November 2017:

- Presentation: Feedback on diagnostic test ordering patterns (volumes and costs) to Board of Directors

Interventions – Hospital 3

Education and awareness

January 2017:

- Presentation: Introduction of project and diagnostic test ordering patterns (volume and costs)
- Educational session: Blood cultures
- Newsletter: Costs for laboratory diagnostics at hospital 3, Amylase and lipase
- Distribution of mouse pad with questions to keep in mind when ordering laboratory tests: "Does the result of this test have added value for diagnostics, treatment of prognosis?", "Is repetition of this test necessary at this moment?", "Is it necessary to order these tests combined?"

February 2017:

- Newsletter: Arterial versus venous blood gas analysis, D-dimer, Choosing Wisely campaign, Urine testing

March 2017:

- Newsletter: Creatinine and urea, Costs for diagnostic testing at hospital 3
- Newsletter: ASAT and ALAT, Importance of input from specialists for RODEO

April 2017:

- Presentation: Feedback on diagnostic test ordering patterns (volume and costs)
- Newsletter: Volume and costs of diagnostic testing at hospital 3, Abdominal X-ray, Imaging for diverticulitis

July 2017:

- Newsletter: Charges per laboratory order, Volume and costs of 25 most frequently requested laboratory tests

September 2017:

- Presentation: Feedback on diagnostic test ordering patterns (volume and costs)

Order system changes

May 2017:

- Modification of 'Pulmonary Medicine' and 'Internal Medicine' order panels

June 2017:

- Instatement of time limits on test orders: repetitive order within prespecified time frame is automatically rejected, can only be overruled after direct contact with the laboratory

July 2017:

- Adjustment of previously instated time limits due to complaints

Clinical chemist

April 2017:
- Introduction of presence and participation in 1-2 grand rounds a week by clinical chemist

May 2017:
- Involvement of second clinical chemist within project team

Agreements and protocols

March 2017:
- Introduction of working agreement: Tests to be performed after patient discharge are to be requested by treating physician instead of by medical secretaries

Meetings and conferences

September 2016:
- Launching conference with project teams of all participating departments and coordinating project team

February 2017:
- Monthly progress meeting (1) project team and coordinating project team

March 2017:
- Conference with project teams of all participating departments and coordinating project team

April 2017:
- Monthly progress meeting (2) project team and coordinating project team

May 2017:
- Monthly progress meeting (3) project team and coordinating project team

June 2017:
- Monthly progress meeting (4) project team and coordinating project team

July 2017:
- Monthly progress meeting (5) project team and coordinating project team

August 2017:
- Progress meeting (6) project team and coordinating project team

December 2017:
- Progress meeting (7) project team and coordinating project team
- Conference with project teams of all participating departments and coordinating project team

Others

November 2016:
- Presentation: Introduction of project to Board of Directors
- Presentation: Introduction of project to internal medicine specialists within department

May 2017:
- Involvement of specialists representing internal medicine sub-specialisms (Nephrology, Oncology, Gastro-Enterology), no active role in project team

Interventions – Hospital 4

Education and awareness

September 2016:

- Presentation: Introduction of project

March 2017:

- Distribution of pocket-cards containing charges for commonly used tests
- Distribution of mouse pad with questions to keep in mind when ordering laboratory tests: "Does the result of this test have added value for diagnostics, treatment of prognosis?", "Is repetition of this test necessary at this moment?", "Is it necessary to order these tests combined?"

April 2017:

- Educational session: Health care costs in the Netherlands, ASAT testing

May 2017:

- Educational session: Urea

June 2017:

- Educational session: Arterial blood gas analysis
- Educational session: ASAT
- Educational session: Blood cultures
- Educational session: Amylase and lipase
- Newsletter: Information on RODEO project in department newsletter

July 2017:

- Educational session: Iron, ferritin, transferrin
- Educational session: Abdominal X-ray
- Educational session: Vitamins

August 2017:

- Educational session: Urine testing
- Educational session: CRP
- Educational session: Blood products
- Educational session: MLPA

September 2017:

- Educational session: (NT-pro)BNP

October 2017:

- Educational session: Actual deviation or natural fluctuation?

November 2017:

- Educational session: Rheumatoid factor and anti-CCP

December 2017:

- Educational session: Urine antigen test

January 2018:
- Educational session: Erythrocyte Sedimentation Rate

February 2018:
- Educational session: Previously discussed subject
- Educational session: Previously discussed subject

March 2018:
- Educational session: Previously discussed subject
- Educational session: Previously discussed subject
- Educational session with ED personnel: Indications for arterial blood gas analysis

April 2018:
- Educational session: Troponin
- Educational session: Previously discussed subject

Order system changes

August 2017:
- Removal of order panels that are infrequently used: 'Deep Venous Thrombosis' and 'Sepsis'

December 2017:
- Modification of 'Hematologic IC' order panel

February 2018:
- Instatement of time limits on test orders: repetitive order within prespecified time frame triggers an alert on redundancy

Clinical chemist

July 2017:
- Introduction of presence and participation in 1 grand round a week by clinical chemist

Meetings and conferences

September 2016:
- Launching conference with project teams of all participating departments and coordinating project team

March 2017:
- Monthly progress meeting (1) project team and coordinating project team
- Conference with project teams of all participating departments and coordinating project team

April 2017:
- Monthly progress meeting (2) project team and coordinating project team

May 2017:
- Monthly progress meeting (3) project team and coordinating project team

June 2017:
- Monthly progress meeting (4) project team and coordinating project team

July 2017:
- Monthly progress meeting (5) project team and coordinating project team

September 2017:
- Progress meeting (6) project team and coordinating project team

November 2017:
- Progress meeting (7) project team and coordinating project team

December 2017:
- Conference with project teams of all participating departments and coordinating project team

January 2018:
- Progress meeting (8) project team and coordinating project team

Others

September 2016:
- Presentation: Introduction of project to Board of Directors

June 2017:
- Involvement of nephrologist and Nephrology resident within project team

January 2018:
- Addition of the RODEO project and its main principles as topic in introductory meetings for new employees

Display of posters in workspaces stating important RODEO principles

Appendix 3 - Questionnaire 'Willingness to change'

As you know, carrying out the RODEO project means changing work habits. The success of the project is partly determined by employees' willingness to change. To acquire insight in which factors determine the willingness to change we ask you to fill in this questionnaire. We also ask you for possible barriers and facilitators for the change process. We kindly ask you to return the filled out questionnaire to us before **Thursday September 22th 2016**.

Hospital:	**Fully agree**	**Somewhat agree**	**Neither agree nor disagree**	**Somewhat disagree**	**Disagree**	**Comments**
WORK RELATED CONSEQUENCES						
1. Reducing unnecessary diagnostics will increase the quality of care.						
EMOTIONS						
2. Senior physicians and junior physicians find reducing unnecessary diagnostics challenging.						
3. Senior physicians and junior physicians find reducing unnecessary diagnostics risky.						
EMOTIONAL INVOLVEMENT						
4. Senior physicians and junior physicians experience involvement with the RODEO project.						
ATTITUDES						
5. The Board of Directors fully supports the RODEO project.						
6. Senior physicians fully support the RODEO project.						
PREVIOUS EXPERIENCE WITH CHANGE						
7. Senior physicians are able to contribute to the success of the RODEO project with their knowledge on the subjects.						
8. Senior physicians have had successful experiences with similar projects.						
TIME						
9. Senior physicians and junior physicians have sufficient time to pay attention to reducing unnecessary diagnostics.						

Appendix 3 - Continued

Hospital:	Fully agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Disagree	Comments
MANAGEMENT OF THE CHANGE PROCESS						
10. The RODEO project has a clear underlying phasing.						
COMPLEXITY OF THE CHANGE PROCESS						
11. The RODEO project can be introduced with the current means and manpower.						
TEAMS' WILLINGNESS TO CHANGE						
12. In your opinion, are senior physicians and junior physicians willing to commit to the process of change?						
13. In your opinion, are senior physicians and junior physicians willing to overcome possible resistance against the process of change?						
BARRIERS AND FACILITATORS FOR CHANGE						
14. Please name the three, in your opinion most important facilitators of the change process. - ... - ... - ...						
15. Please name the three, in your opinion most important barriers of the change process. - ... - ... - ...						

4

Association of a multifaceted intervention with ordering of unnecessary laboratory tests among caregivers in internal medicine departments

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Abstract

Importance

Inappropriate use of laboratory testing is a challenging problem. Estimated overuse rates of approximately 20% have been reported. Effective, sustainable solutions to stimulate optimal use are needed.

Objective

To determine the association of a multifaceted intervention with laboratory test volume.

Design, setting and participants

A before-after quality improvement study was performed between August 1, 2016, and April 30, 2018, in the internal medicine departments of four teaching hospitals in the Netherlands. Data on laboratory order volumes from nineteen comparable hospitals were used as controls. The participants were clinicians ordering laboratory tests.

Interventions

The intervention included creating awareness through education and feedback, intensified supervision of residents, and changes in order entry systems. Interventions were performed by local project teams and guided by a central project team during a six-month period. Sustainability was investigated during an eight-month follow-up period.

Main outcomes and measures

The primary outcome was the change in slope for laboratory test volume. Secondary outcomes were change in slope for laboratory expenditure, order volumes and expenditure for other diagnostic procedures, and clinical outcomes. Data were collected on duration of hospital stay, rate of repeated outpatient visits, 30-day readmission rate, and rate of unexpected prolonged duration of hospital stay for patients admitted for pneumonia.

Results

The numbers of internists and residents ordering tests in hospitals 1 to 4 were 16 and 30, 18 and 20, 13 and 17, and 21 and 60, respectively. Statistically significant changes in slope for laboratory test volume per patient contact were found at hospital 1 (change in slope, −1.55; 95% CI, −1.98 to −1.11; $P < .001$), hospital 3 (change in slope, −0.74; 95% CI, −1.42 to −0.07; $P = .03$), and hospital 4 (change in slope, −2.18; 95% CI, −3.27 to −1.08; $P < .001$). At hospital 2, the change in slope was not statistically significant (−0.34; 95% CI, −2.27 to 1.58; $P = .73$). Laboratory test volume per patient contact decreased by 11.4%, whereas the volume increased by 2.4% in nineteen comparable hospitals. Statistically significant changes in

slopes for laboratory costs and volumes and costs for other diagnostic procedures were also observed. Clinical outcomes were not associated with negative changes. Important facilitators were education, continuous attention for overuse, feedback, and residents' involvement. Important barriers were difficulties in data retrieval, difficulty in incorporation of principles in daily practice, and high resident turnover.

Conclusions and relevance

A set of interventions aimed at changing caregivers' mindset was associated with a reduction in the laboratory test volume in all departments, whereas the volume increased in comparable hospitals in the Netherlands. This study provides a framework for nationwide implementation of interventions to reduce unnecessary laboratory testing.

Introduction

In recent years, the concept of low-value care has gained attention, and international campaigns have been launched to discourage the unnecessary use of tests and procedures. In the United Kingdom, *"Do Not Do"* recommendations were formulated, and in the United States, the *"Choosing Wisely"* campaign was introduced.[1,2] Thereafter, many other countries, including the Netherlands, followed suit with programs aimed at de-implementing unnecessary care.[3]

Inappropriate use of laboratory tests is a well-recognized phenomenon, and estimated overuse rates of approximately 20% have been reported.[4] Overuse is also reflected in high interphysician variability of test orders. In a recent study among internal medicine residents, some residents ordered seven to eight times more tests than their peers.[5] Many interventions have proven effective in reducing unnecessary laboratory testing.[6-8] In addition to financial consequences, overuse is less patient-friendly and may increase the number of false-positive results, which leads to more, potentially harmful tests.[9]

In 2012, our study group published the findings of a multifaceted intervention begun in 2008 aimed at reducing unnecessary diagnostic testing through increasing awareness at the internal medicine department of the Vrije Universiteit Medical Center in Amsterdam, the Netherlands.[10] Although we mainly focused on laboratory testing, the use of other diagnostic procedures also decreased. A 13% gross reduction in diagnostic expenditure was observed compared with the previous year and was sustained over subsequent years.[11]

In the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) – project, we implemented this same multifaceted intervention in the internal medicine departments of four large teaching hospitals in the Netherlands. The goal of this project was to reduce total laboratory testing by 5%. Our primary focus was on laboratory testing, although associations with other diagnostic procedures were also assessed. Furthermore, we assessed the facilitators and barriers to de-implementation of unnecessary testing.

Methods

This project is a part of the *"To Do or Not to Do? Reducing Low-Value Care"* program, a national program initiated by the Dutch Federation of University Medical Centers. The study protocol providing a detailed description of the methods has been published previously.[12,13] Therefore, we provide only a brief overview of the methods here.

This report follows the Standards for Quality Improvement Reporting Excellence (SQUIRE) reporting guideline for quality improvement studies. The medical ethics review committee of Vrije Universiteit Medical Center assessed the project protocol, determined that official approval by the committee was not required, and waived the need for informed consent because data were collected anonymously. Local ethics committees and boards of directors of all participating hospitals approved the study.[13]

Study design and setting

We conducted a before-after quality improvement study at the departments of internal medicine of four teaching hospitals in the Netherlands. The study was performed by a coordinating project team together with a local project team at each hospital (**Appendix 1**). The inclusion criteria were previously described.[13]

Characteristics of participating departments

Table 1 shows the characteristics of participating departments at initiation of the project. The departments differ mainly in annual patient load and in number of physicians working at the departments. In the remainder of this article, the participating hospitals are referred to as hospitals 1 to 4. Numbers were selected randomly.

Outcomes, data sources, and measurements

Our primary outcome was change in slope for laboratory test volume per patient contact. Secondary outcomes were change in slope for laboratory test costs; order volumes and costs for radiology, microbiology, and nuclear medicine tests per patient contact; and clinical outcomes. Orders placed for the internal medicine specialty by inpatient and outpatient departments and the emergency department were included.

To investigate whether our intervention influenced patient care, we assessed the mean duration of hospital stay, rate of repeated outpatient visits, 30-day readmission rate, and rate of unexpected prolonged duration of hospital stay for patients admitted for pneumonia. The last two outcomes are quality indicators assessed yearly by the Healthcare Inspectorate in the Netherlands.[14]

In addition, we collected data on laboratory order volumes from nineteen comparable hospitals in the Netherlands. Most of these were large peripheral hospitals, reflecting the national mix of hospital type. The criterion for inclusion was availability of data for the duration of the project. The benchmark data used in this study are based on standardized and validated production data of these nineteen hospitals. These data were acquired through Performation, a Dutch data-driven consultancy firm.[15]

Table 1 – Characteristics of participating departments at initiation of the project

	Zaans Medical Center	North-West Hospital Group, location Alkmaar	Spaarne Gasthuis, locations Haarlem and Hoofddorp	Meander Medical Center
Annual number of ED visits for internal medicine	3,000	3,800	6,000	4,400
Annual number of OPD visits for internal medicine	25,000	36,900	54,200	37,600
Annual number of inpatient admissions for internal medicine	1,800	3,000	4,248	2,900
Number of internists	13	18	21	16
Number of residents	17	20	60	30
Involvement of clinical chemist	Participation in clinical meetings once a month, available on call	No participation in clinical meetings, available on call	Participation in several clinical meetings, available on call	Participation in clinical meetings including daily morning report, available on call
Laboratory ordering system	Electronic	Electronic at ED and inpatient clinic, paper forms at OPD	Electronic	Electronic at ED and inpatient clinic, electronic and paper forms at outpatient clinic
Comments	In the preceding years the ZMC already actively focused on reducing unnecessary care through several projects and initiatives.	The Medical Center Alkmaar and the Gemini Hospital in Den Helder merged in 2015.	The Kennemer Gasthuis in Haarlem and Spaarne Hospital merged in 2015.	Send-out test requests are discussed with providers before approval.

Assessment of facilitators and barriers

Facilitators and barriers were identified through questionnaires with the project teams[13] at initiation, during joint conferences, and through a questionnaire filled out by all physicians at participating departments at the end of the project (**Appendix 2**).

De-implementation strategy

A timeline of the project is shown in **Figure 1**. After consent by the Board of Directors of each hospital, cooperation agreements were signed. Thereafter, project teams consisting of one or more internists, residents, and clinical chemists and a business intelligence or control specialist were formed.

Pre-intervention period

Ordering patterns from the preceding years were analyzed with the aim of recognizing patterns in test use. A joint conference was organized with all members of the project teams to exchange ideas and experiences and to discuss target laboratory items for reduction. In addition, anticipated facilitators and barriers were discussed. Each department was encouraged to develop interventions specifically for their department, in addition to the generic intervention that is described in this article.

Intervention period

The local project teams performed the interventions and had monthly meetings with the coordinating project team, during which the progress of the study and ordering patterns were discussed. A second joint conference was organized with all project teams to discuss interim results, facilitators and barriers, and ideas and experiences.

Post-intervention period

A third joint conference was organized, during which the main goal was to discuss sustainability. The local project teams continued the actions introduced earlier, performed new actions, and had two to three monthly progress meetings with the coordinating project team.

Description of interventions

The intervention consisted of several items. Education and feedback were used to create awareness and were provided through, for example, presentations and newsletters. In addition, supervision of residents by experienced physicians regarding test ordering was intensified. This entailed explicitly focusing on indications for tests and asking critical questions during morning reports and other clinical meetings. In addition, modifications were made to order entry systems, for example by enacting time limits on repeated orders.

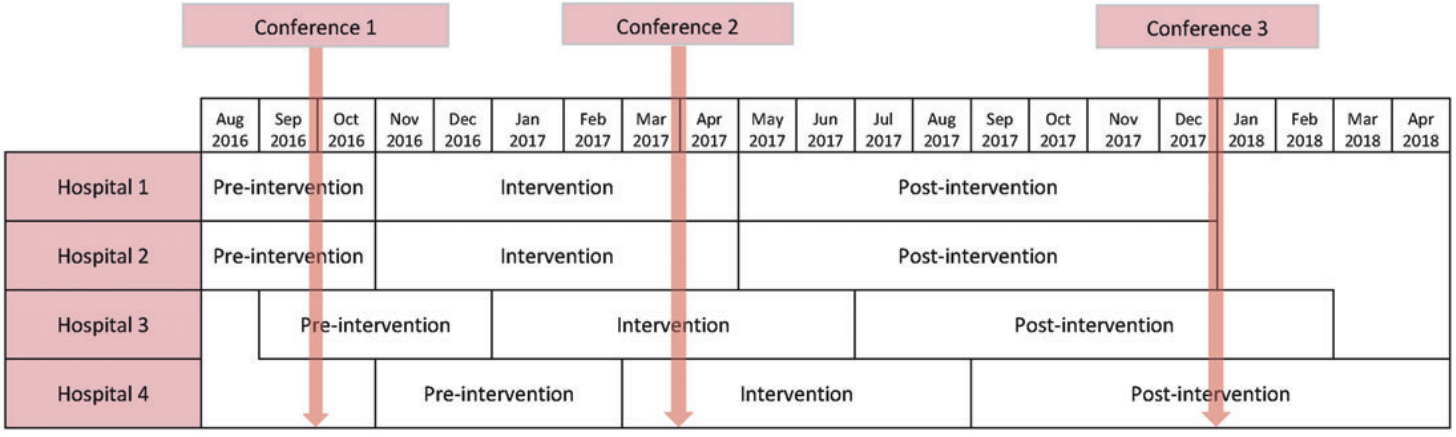


Figure 1 – Project timeline at four hospitals in the Netherlands, August 1, 2016 through April 30, 2018

The actions performed in each clinic are displayed in **Appendix 3**. Details on specific actions are published in the study protocol.[13] An overview of the modifications made to the order entry systems is provided in **Appendix 4**.

The project teams placed specific focus on a set of tests that are known to be frequently overused: blood urea nitrogen, creatinine, amylase, aspartate aminotransferase, alanine aminotransferase, C-reactive protein, and erythrocyte sedimentation rate. These were used to create a change in physician mindset, which we believed would lead to greater awareness when requesting diagnostic procedures in general. A more-detailed description of the de-implementation strategy is published in the protocol.[13]

Statistical analysis

Volumes and costs of diagnostic procedures

For our primary outcome, we collected the weekly number of tests performed during the intervention and post-intervention period and the two preceding years. Secondary outcomes were reported by the hospitals per month. We adjusted volumes and costs for patient load using the number of patient contacts, defined as the sum of the number of visits, day admissions, and patient days for the internal medicine department. We decided against using standardized patient units to adjust for patient load, which we previously described in the study protocol, because we observed that a large proportion of diagnostic procedures were ordered during repeated outpatient visits that were not included in the calculation of standardized patient units.[13]

Clinical outcomes

The mean duration of hospital stay and rate of repeated outpatient visits were assessed monthly. The 30-day readmission rate and the rate of unexpected prolonged duration of hospital stay for patients admitted for pneumonia were assessed yearly for 2015, 2016, and 2017.

Analysis

All statistical analyses were performed using the forecast package in R statistical software version 3.4.3 (R Project for Statistical Computing). Interrupted time series analyses were performed using the weekly or monthly data to assess the associations of the intervention with volumes and costs. We used an autoregressive integrated moving average model to analyze whether a (more profound) change in the number or costs of tests per patient contact was observed after starting the intervention. We adjusted for seasonal variation using autocorrelations with a yearly period. The trend in mean was modeled using a regression model with separate parameters for slope before and after implementation of the intervention and allowing for a direct change in the period after the start of the intervention. The autocorrelation

and moving average parameters were selected using the automated auto.arima function in R, minimizing the corrected Akaike information criterion statistic. Outcomes are expressed as the difference in slope between the two years before the intervention started and the fourteen months after the intervention started (six-month intervention period plus eight-month post-intervention period).We used a *z* test to determine whether regression coefficients in the autoregressive integrated moving average model differed from 0. All *P* values refer to two-sided tests. $P < .05$ was considered statistically significant. The percentage change in laboratory test volume per patient contact was calculated using the mean number of laboratory tests per patient contact during the final six months of the project and the mean number during the same six months of the previous year.

Results

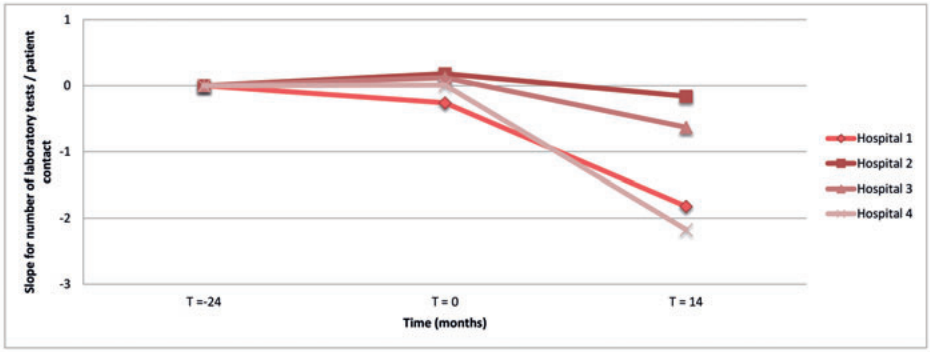
The numbers of internists and residents ordering tests in hospitals 1 to 4 were 16 and 30, 18 and 20, 13 and 17, and 21 and 60, respectively.

Laboratory test volume

Our main goal was to assess the association of our multifaceted intervention with laboratory test volume. Slopes and changes in slopes for laboratory test volume per patient contact per year are presented in **Figure 2** and **Table 2.** Changes in slope were statistically significant at hospital 1 (−1.55; 95% CI, −1.98 to −1.11; $P < .001$), hospital 3 (−0.74; 95% CI, −1.42 to −0.07; $P = .03$), and hospital 4 (−2.18; 95% CI, −3.27 to −1.08; $P < .001$). At hospital 2, the change in slope was not statistically significant (−0.34; 95% CI, −2.27 to 1.58; $P = .73$). For hospitals 1 to 4, reductions in numbers of tests per patient contact in the last six months of the intervention were 11.5%, 5.9%, 8.3%, and 14.7%, respectively, compared with the same period in the year before, yielding an overall decrease of 11.4%. In **Appendices 5-8**, we present the changes in laboratory test volumes relative to the same months in the preceding year during the fourteen months, along with the interventions performed.

Control group

In the Departments of Internal Medicine of nineteen comparable hospitals, we saw a significant increase of 0.32 laboratory tests per patient contact per year (95%CI, 0.21-0.42; $P < .001$) between January 1, 2015, until our intervention started in the first two hospitals on November 1, 2016, and a comparable increase (0.33; 95%CI, 0.20-0.47; $P < .001$) between November 1, 2016, and April 30, 2018, which was when the project was concluded. The number of laboratory tests per patient contact increased by 2.4% in the last six months of the project compared with the same period in the year before.



	0 months	14 months	Difference in slope
Hospital 1	-0,26	-1,82	-1,55
Hospital 2	0,18	-0,16	-0,34
Hospital 3	0,12	-0,63	-0,74
Hospital 4	0,01	-2,17	-2,18

Figure 2 – Slopes and differences in slope for laboratory test volume before and after the start of the intervention
Effect is expressed as slope for number of tests per patient contact per year.

Specific tests

The departments targeted all tests described in the Methods section, except for hospital 2, which did not focus on blood urea nitrogen and creatinine. Significant changes in slope for number of requests were observed for blood urea nitrogen and creatinine (hospitals 1 and 4), amylase (hospitals 1, 2, and 3), aspartate aminotransferase (hospitals 3 and 4), and alanine aminotransferase (hospital 4). Full data are shown in **Appendix 9**. The associations of the multifaceted intervention with costs of laboratory tests, and with volumes and costs of radiology, microbiology, and nuclear medicine tests are presented in **Table 2**.

Clinical outcomes

Clinical outcomes are shown in **Table 3**. For mean duration of hospital stay, no significant changes in slope were observed. For rate of repeated outpatient visits, a significant decreasing change in slope was found at hospital 1. The 30-day readmission rates remained unchanged. The rate of unexpected prolonged duration of hospital stay for patients admitted with pneumonia increased in all departments, which was consistent with the national trend and presumably was attributable to the severe influenza epidemic in 2017.

Table 2 – Changes in volumes and costs for diagnostics following the intervention*

	Hospital 1		Hospital 2		Hospital 3		Hospital 4	
Variable	**Change (95% CI)**	***P* value**	**Change (95% CI)**	***P* value**	**Change (95% CI)**	***P* value**	**Change (95% CI)**	***P value***
Volume								
Laboratory	-1.55 (-1.98, -1.11)	<.001	-0.34 (-2.27, 1.58)	.73	-0.74 (-1.42, -0.07)	.03	-2.18 (-3.27, -1.08)	< .001
Radiology	-0.03 (-0.05, -0.01)	.005	0.01 (-0.02, 0.03)	.57	0.00 (-0.02, 0.03)	.80		
Microbiology	-0.02 (-0.07, 0.11)	.617	0.15 (0.02, 0.28)	.02	-0.16 (-0.28, -0.03)	.02		
Nuclear medicine	0.00 (-0.02, 0.02)	.986	-0.04 (-0.05, -0.02)	< .001	-0.02 (-0.03, -0.01)	< .001		
Costs								
Laboratory	-4.13 (-9.26, 1.01)	.115	-0.90 (-4.17, 2.37)	.59	-1.88 (-4.4, 0.67)	.14	-8.60 (-12.94, -4.25)	< .001
Radiology	4.57 (1.61, 7.53)	.002	1.42 (-0.72, 3.56)	.20	1.49 (-0.19, 3.17)	.08		
Microbiology	-0.08 (-1.41, 1.26)	.909	0.66 (-0.66, 1.98)	.33	-1.91 (-4.53, 0.71)	.14		
Nuclear medicine	-4.96 (-9.11, -0.81)	.019	-14.26 (-21.19, -7.33)	< .001	-0.35 (-3.27, 2.57)	.81		

* Expressed as change in slope for number of tests per patient contact per year (for volume), or costs for tests in euros per patient contact per year (for costs). For hospital 4, data on radiology, microbiology and nuclear medicine were not available.

Table 3 – Clinical outcomes

	Hospital 1		Hospital 2		Hospital 3		Hospital 4	
Outcome	**Value**	***P* value**	**Value**	***P* value**	**Value**	***P* value**	**Value**	***P* value**
LOS, mean*	-0.60 (-1.57, 0.36)	.22	0.23 (-0.49, 0.96)	.53	-0.13 (-1.20, 0.94)	.81	0.44 (-0.19, 1.06)	.17
Repeat frequency*	-0.40 (-0.72, 0.09)	.01	-0.38 (-0.90, 0.14)	.15	-0.09 (-0.40, 0.22)	.58	0.07 (-1.03, 1.16)	.90
30-day readmissions†								
2015	12%		97		104		110	
2016	13%		98		107		117	
2017	13%		100		90		111	
Unexpected prolonged LOS‡								
2015	87		11.6%		16.7%		14.6%	
2016	93		12.9%		15.2%		13.1%	
2017	97		15.8%		18.9%		15.2%	

Abbreviation: LOS, length of stay. * Expressed as change in slope (95% CI). † Thirty-day readmissions are expressed as either the percentage of total admissions that were readmissions within 30 days, or as a ratio (total number of 30-day readmissions/expected number of 30-day readmissions according to case mix).
‡ Unexpected prolonged LOS is expressed as either a percentage of total admissions for pneumonia with a LOS greater than or equal to 150% than the mean LOS during the previous year, or as a ratio (number of admissions for pneumonia with LOS greater than or equal to 150% than the mean LOS during the previous year/ number of admissions for pneumonia with LOS greater than or equal to 150% than the mean LOS during the previous year, expected according to case mix).

Facilitators and barriers to de-implementation

The factors identified through the initial questionnaire and first and second conference, categorized into different levels as proposed by Grol and Wensing,[16] were used as input to adjust our strategy (**Appendix 10**). During the final conference and through the final questionnaire, we evaluated which factors were of greatest influence (**Appendices 11-13**).

Important facilitators were education, continuous attention for diagnostic testing, and feedback. Involvement of clinical chemists and establishing clear working agreements were also considered important. During the project, the teams were expanded with physicians representing internal medicine subspecialties. This facilitated our efforts to obtain widespread support, which was a crucial element in the RODEO project. Having enthusiastic internists and residents function as role models was considered a strong facilitating factor. Members of the coordinating project team viewed the involvement of residents as the main factor contributing to the success of the project.

Although the teams aimed to establish clear working agreements, incorporation in daily practice was impeded by the high rate of turnover of residents, which required regular repetition of RODEO principles. The most important barrier was obtaining reliable data on order volumes and costs, which made it difficult to monitor progress in some clinics. In addition, it took several months before reduction efforts translated into consistent changes in ordering patterns (**Appendices 5-8**). It was challenging to maintain the efforts needed for the project, especially when only one resident was included in the project team and that resident changed rotation. Moreover, we noticed that lessening attention was associated with an almost immediate change in ordering patterns (**Appendices 5-8**). Although modifying order systems was an important facilitator, their rigidness was seen as a barrier in one hospital, because clinicians were not immediately informed when a test was not performed and the time limits for repeated requests were considered too strict.

Discussion

In this project, we aimed to reduce inappropriate laboratory testing by implementing interventions aimed at changing the mindset of health care professionals. In three of four departments, a significant decrease in slope was found for laboratory test volume, whereas an increase in slope was observed in nineteen comparable hospitals in the Netherlands. The laboratory test volume per patient contact decreased by 11.4% overall. Although every department performed interventions from all categories, nuances were different. In hospital 1, the role of the clinical chemist in the project team was substantial, whereas hospital 3 mainly focused on order system changes by instituting time limits for repeat orders, and hospital 4 placed emphasis on educating physicians.

For other diagnostic procedures, significant changes in slopes were also found. At hospital 1, statistically significant changes in slope were found for volume and/or costs of laboratory, radiology, and nuclear medicine tests. At hospital 2, although a 5.9% reduction in volume of laboratory tests per patient contact was achieved, the change in slope was not statistically significant. For nuclear medicine, we did find statistically significant decreasing changes in slope for volume and costs, which we think are a result of the departments' increased focus on indications for positron emission tomography scans during the intervention period. At hospital 3, the decreases in slope for order volumes of microbiology and nuclear medicine tests were statistically significant, together with laboratory test volume. For hospital 4, data on diagnostic procedures other than laboratory tests were not available. The observed changes in ordering patterns for diagnostic procedures on which little focus was placed suggest that the intervention led to a change in caregivers' mindset for ordering diagnostic procedures in general. Clinical outcomes were not associated with negative changes following the reduction in diagnostic testing.

Overall, important facilitators to de-implementation were education, feedback, continuous attention for diagnostic testing, and involvement of residents. In contrast to hospitals 3 and 4, only one resident was included in the project team at hospital 2. In addition, this resident changed rotation during the project. Also, the outpatient department at hospital 2 was not as emphatically targeted, although we observed that in all participating hospitals, a large number of orders were placed at the outpatient department. We believe that this finding, in part, reflects the importance of obtaining widespread support for the success of the project. This knowledge was used as input for performing the project at hospitals 3 and 4, where several residents were included in the local project team from initiation, and much attention was paid to orders placed at the outpatient department. The most important barriers were difficulties in data collection, difficulties in incorporation of working agreements in daily practice, and a high rate of resident turnover.

The total cost for performing the project was approximately €250,000. The largest part of this amount was spent on the personnel who coordinated the project (€200,000). At the end of the project, the intervention was integrated into daily routine without hiring extra staff. As for potential cost reduction through reducing laboratory testing, an estimated reduction of approximately €1.2 million could be made. This yields an 11.4% reduction of the total €10.9 million spent on laboratory testing in 2017 by all four departments. Because of the fixed costs for personnel and laboratory equipment, the actual cost reduction will be lower. Cost reduction through the reduction of other diagnostic procedures as well as downstream costs were not included in this calculation.

Comparison with previous literature

In line with previous literature, a multifaceted intervention was associated with a reduction in laboratory testing.[6-8] Contrary to most other studies, we used a multicenter approach, introducing our intervention in four large hospitals. Data were collected during the six-month intervention period and, unlike most other studies, we also assessed sustainability during an additional eight-month period. Furthermore, we collected clinical data to investigate patient-related outcomes. This study is one of the first to investigate all these aspects, to our knowledge, and we further demonstrate that with the help of local teams, these interventions can be implemented successfully in daily practice. Previous literature does not show that any particular intervention is the most effective, and combined interventions are advocated.[6-8] However, in the questionnaires conducted at the end of the project, the physicians in our project reported perceiving the educational sessions to be the most effective intervention, followed by modifications in order systems.

Strengths and limitations

The intervention used in this study was originated and first applied in an academic medical center in Amsterdam.[10,11] In the current study, we have shown that it is feasible to implement this intervention in four large peripheral teaching hospitals. The positive and sustained changes observed in different settings suggest that our approach may also be effective in other hospitals and for other services. By assessing facilitators and barriers, we point out specific issues to take into account in future studies. Another strength entails assessment of sustainability. Although we investigated short-term sustainability, long-term sustainability can be expected through our approach, as we have previously shown.[11] Measures to ensure sustainability include, for example, repeated education, modifications in ordering systems, posters stating important principles regarding test ordering displayed in work spaces, mouse pads with reminders regarding test ordering, and inclusion of these principles in the introductory program for new employees. Another strength of this project is the study of clinical outcomes. Another strength involves the intervention itself. By providing departments the liberty to place focus on different elements of the standard intervention, we ensured that the actions suited the departmental structure.

This project has several limitations. First, because multiple interventions were performed at once, it was not possible to assess the effectiveness of individual interventions. Second, data collection was difficult and incomplete for one hospital. Also, it was not possible to assess the numbers of blood samples obtained at all clinics, which would be a desirable end point in future studies in the context of delivering patient-friendly care. The lack of patient involvement in this project is another limitation.

Conclusions

A set of interventions aimed at changing caregivers' mindset was associated with a reduction in the laboratory test volume in all departments, whereas the volume increased in comparable hospitals in the Netherlands. In three of four departments, the change in slope was significant. Laboratory costs and other diagnostic procedures were also reduced following the intervention, and clinical outcomes were unchanged. Furthermore, we identified facilitators and barriers to de-implementation. The approach used in this study can be extended to other types of services and clinics. This study provides a framework for nationwide implementation of these interventions and might be complemented with involving patients and emphasizing patient-friendly care in future efforts.

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Appendices

Appendix 1 – Project teams

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Appendix 2 – RODEO project evaluation

Male / Female
Resident / Internist
Number of years of experience within this function
For how long have you been employed at this department?
Have you contributed to the project? If yes, how did you contribute?

During the past months, we have carried out the RODEO project within your department, in which we aimed to reduce the amount of unnecessary diagnostics without affecting quality of care. Through this questionnaire we would like to assess your thoughts on the RODEO project. We ask for your opinion on and experiences with unnecessary diagnostics, and specifically, we ask questions regarding aspects that were addressed in this project. Please return the filled in questionnaire to us before February 28th 2018.

Fully agree, agree, neutral, disagree, fully disagree, not applicable

1. The importance of reducing unnecessary diagnostics was clear.
2. The aim of the project was clear.
3. Enough attention was paid to the importance for patients of reducing unnecessary diagnostics.
4. The environment at the department was such that I felt free to ask questions regarding the usefulness of test requests.
5. The amount of questions colleagues have asked me regarding the usefulness of test requests was sufficient.
6. Internists have asked me, as resident, a sufficient amount of questions regarding the usefulness of test requests.
7. As internist, I have asked residents a sufficient amount of questions regarding the usefulness of test requests.
8. I have been sufficiently informed about the progress of the project.
9. (Changes in) ordering patterns at department level have been made sufficiently transparent.
10. Reducing unnecessary testing has been sufficiently supported by scientific evidence.
11. There was sufficient space to bring in ideas for the project.
12. I have gained new knowledge on diagnostics.
13. Novel working agreements have been sufficiently embedded into daily practice.
14. Reducing unnecessary diagnostics leads to higher quality care.
15. Reducing unnecessary diagnostics leads to more patient friendly care.
16. I fear to miss clinically relevant information by performing less diagnostic tests.
17. During the past month, I have received negative feedback for performing less diagnostic tests.

Never, <1x/month, 1x/month, 1x/3 weeks, 1x/2 weeks, 1x/week, >1x/week

18. Before the project, how often did you see examples of unnecessary use of diagnostics?
19. After the project, how often do you see examples of unnecessary use of diagnostics?
20. How often was unnecessary use of diagnostics addressed during morning or afternoon reports?
21. How often was unnecessary use of diagnostics addressed during grand rounds?
22. How often was unnecessary use of diagnostics addressed during other clinical discussions?
23. How often has time been reserved explicitly for discussion of unnecessary use of diagnostics?

Open-ended questions

24. Which interventions (addressing unnecessary use during clinical meetings, education, changes in order entry systems, feedback on ordering patterns, involvement of clinical chemist, etc.) did you find most effective?
25. Which factors were facilitators of the project?
26. Which factors were barriers to the project?
27. How could the agreements made in this project be sustained?
28. Do you have any further tips or comments?

Appendix 3 – Interventions divided by category

Hospital	Intervention	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14
1	E & Aw	●●●●	●	●●		●			●	●	●	●	●●		●
	(C)POE				●	●			●●	●					
	C	●													
	Ag & P	●●		●											
	M & C	●*●	●	●	●	●		●			●			●	●
	O	●*												●	●
2	E & Aw	●●●	●●	●●●		●			●●					●	
	(C)POE		●●		●		●	●							
	C	●													
	Ag & P	●			●										
	M & C	●*	●	●	●	●●		●			●		●		●
	O	●*		●					●			●	●	●	
3	E & Aw	●●●●	●	●●	●●			●		●					
	(C)POE					●	●	●							
	C				●	●									
	Ag & P			●											
	M & C	●*	●	●	●	●	●	●	●				●●		
	O	●*●*				●									
4	E & Aw	●*●●	●	●	●●●●●	●●●	●●●●	●	●	●	●	●	●●	●●●	●●
	(C)POE						●				●		●		
	C					●									
	Ag & P														
	M & C	●*●●	●	●	●	●		●		●	●	●			
	O	●*			●							●●			

*Action took place before the intervention period. Abbreviations: M1, intervention period month 1, etcetera; E & Aw, education and awareness; (C)POE, (computerized) provider order entry; C, involvement of clinical chemist(s); Ag & P, agreements and protocols; M & C, meetings and conferences; O, others.

Appendix 4 – Redundancy checks

Laboratory test	Hospital 1		Hospital 2		Hospital 3		Hospital 4	
	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion
1,25-hydroxy vitamin D	21 days	21 days						
25-OH vitamin D	21 days	28 days						
Alkaline phosphatase						Inp. 1 day; Outp. 2 days*		
ALT						Inp. 1 day; Outp. 2 days*		
AST						Inp. 1 day; Outp. 2 days*		5 days
Amylase						Inp. 1 day; Outp. 7 days*		Pop-up upon request†
Anti-phospholipid antibodies	56 days	56 days						
Alpha-1-antitrypsin						Once*		
Alpha-1-antitrypsine in feces	14 days	14 days						
ANA			30 days	30 days				
Anti-cardiolipin			70 days	70 days				
Anti-CCP			150 days	150 days		365 days		
Apolipoprotein A1	14 days	14 days						
Apolipoprotein B	14 days	14 days						
Bilirubin						Inp. 1 day; Outp. 2 days*		
BNP	5 days	5 days	7 days	7 days				
CDT	14 days	14 days						
Chromosome test	Once	Once						
Creatinin						Inp. 1 day; Outp. 3 days*		
CRP						Inp. 1 day; Outp. 5 days*		2 days
ESR		4 days	1 day	< 18 y, 1 day; >18 y, 7 days		7 days*		
Ferritin				7 days		14 days*		
Folic acid		28 days		20 days		30 days*		
Free protein S	30 days	30 days						
FT4				> 18 y, 5 days		30 days		

Appendix 4 – Continued

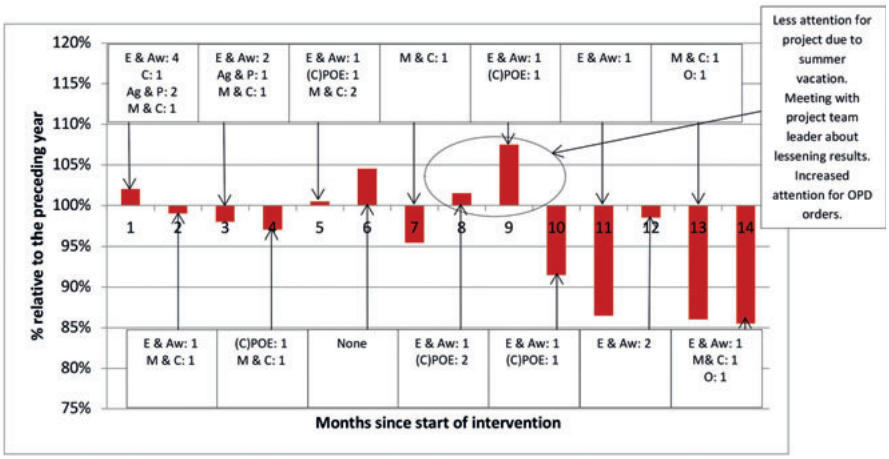
Laboratory test	Hospital 1		Hospital 2		Hospital 3		Hospital 4	
	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion
GGT						Inp. 1 day; Outp. 2 days*		
HbA1c	21 days	21 days	40 days	40 days		30 days		
HDL cholesterol				14 days		30 days*		
IgA								
IgG						1 year, unless abnormal		
IgM						1 year, unless abnormal		
Iron						14 days*		
Iron-binding capacity						14 days*		
Iron saturation						14 days*		
Irregular antibodies	3 days	3 days						
Lactate dehydrogenase						Inp. 7 days; Outp. 14 days		
LDL cholesterol				14 days		30 days*		
Leukocyte differential count		1 day	1 day	1 day			3 days	3 days
Lipoprotein (a)	14 days	14 days						
Lupus anticoagulans			70 days	70 days				
NT-proBNP						30 days		
p-Elastase in feces	30 days	30 days						
Protein C Activity	30 days	30 days						
Protein C Antigen	30 days	Abolished						
Protein S Antigen	30 days	Abolished						
Rheumatoid factor			30 days	30 days				
Serum protein	30 days	7 days	5 days	20 days				
Total cholesterol						30 days*		
Triglycerides						Inp. 5 days; Outp. 30 days*		

Appendix 4 – Continued

Laboratory test	Hospital 1		Hospital 2		Hospital 3		Hospital 4	
	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion	Present at initiation	Present at conclusion
TSH				> 18 y, 5 days		30 days		
T3				> 18 y, 5 days		30 days		
Tumor markers (PSA, CEA, CA-125, CA15-3, AFP, b-HCG)						14 days*		
Urea								5 days
Viscosity	7 days	Abolished						
Vitamin A	7 days	7 days						
Vitamin B2	7 days	7 days						
Vitamin B12		28 days				30 days*		
Vitamin E	7 days	7 days						
Vitamins			7 days	14 days				
Zinc protoporphyrin	30 days	Abolished						

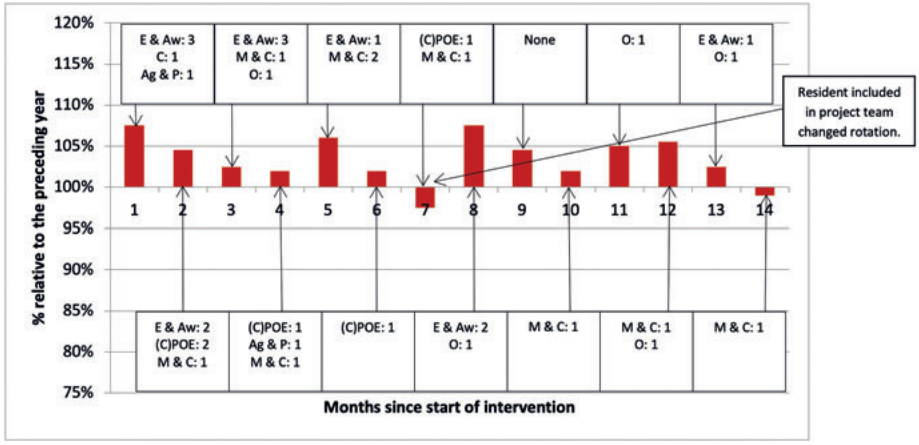
* The time limit for repetitive requesting of this test was adjusted during the project due to resistance from physicians working at the department. † Pop-up instated upon each request: For pancreatitis, amylase testing is not deemed appropriate at this hospital. Lipase is sufficient. Abbreviations: ANA, antinuclear antibodies; CDT, carbohydrate deficient transferrin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FT4, free thyroxin; GGT, gamma-glutamyl transferase; TSH, thyroid stimulating hormone; PSA, prostate specific antigen; CEA, carcino-embryonic antigen; CA-125, cancer antigen-125, CA15-3, cancer antigen 15-3; AFP, alpha fetoprotein; b-HCG, beta-human chorionic gonadotropin; Inp, inpatient department; Outp, outpatient department.

Appendix 5 – Hospital 1: Interventions and laboratory test volume relative to preceding year



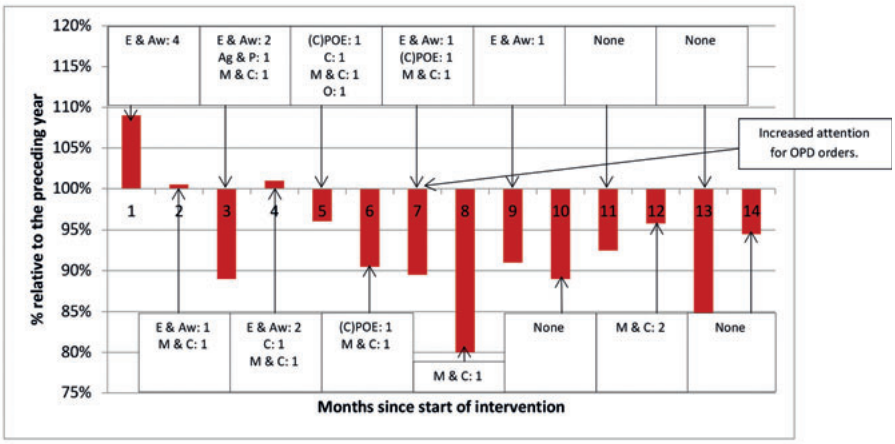
Abbreviations: E & Aw, education and awareness; C, involvement of clinical chemist(s); Ag & P, agreements and protocols; M & C, meetings and conferences; O, others; (C)POE, (computerized) provider order entry.

Appendix 6 – Hospital 2: Interventions and laboratory test volume relative to preceding year



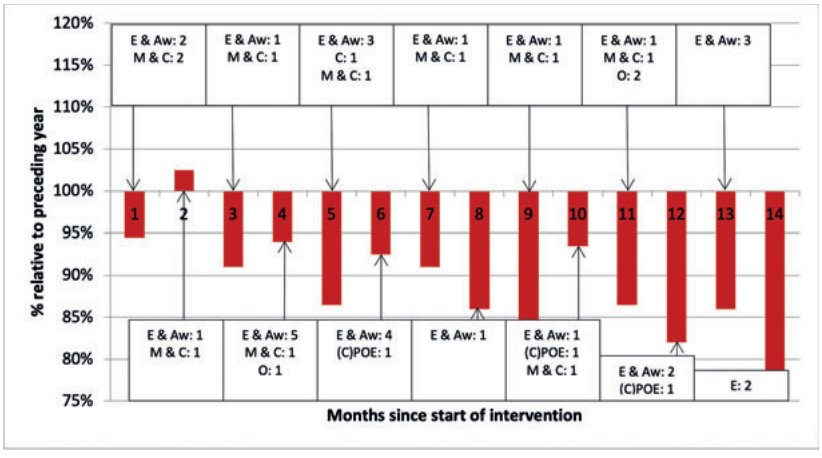
Abbreviations: E & Aw, education and awareness; C, involvement of clinical chemist(s); Ag & P, agreements and protocols; M & C, meetings and conferences; O, others; (C)POE, (computerized) provider order entry.

Appendix 7 – Hospital 3: Interventions and laboratory test volume relative to preceding year



Abbreviations: E & Aw, education and awareness; C, involvement of clinical chemist(s); Ag & P, agreements and protocols; M & C, meetings and conferences; O, others; (C)POE, (computerized) provider order entry.

Appendix 8 – Hospital 4: Interventions and laboratory test volume relative to preceding year



Abbreviations: E & Aw, education and awareness; C, involvement of clinical chemist(s); Ag & P, agreements and protocols; M & C, meetings and conferences; O, others; (C)POE, (computerized) provider order entry.

Appendix 9 – Effect of interventions on ordering of specific tests*

	Hospital 1		Hospital 2		Hospital 3		Hospital 4	
Test	**Change (95% CI)**	***P* value**	**Change (95% CI)**	***P* value**	**Change (95% CI)**	***P* value**	**Change (95% CI)**	***P* value**
BUN	-0.08 (-0.11, -0.05)	< .001	0.00 (-0.01, 0.02)	.69	0.00 (-0.03, 0.04)	.84	-0.07 (-0.12, -0.02)	.01
Creatinin	-0.07 (-0.12, -0.02)	.01	+0.01 (-0.02, 0.04)	.41	-0.02 (-0.07, 0.03)	.40	-0.13 (-0.20, -0.06)	< .001
Amylase	-0.01 (-0.02, -0.01)	< .001	-0.05 (-0.07, -0.04)	< .001	+0.05 (0.04, 0.06)	< .001	+0.01 (-0.03, 0.05)	.62
AST	-0.02 (-0.03, 0.002)	.07	+0.01 (-0.003, 0.02)	.14	-0.13 (-0.17, -0.10)	< .001	-0.07 (-0.10, -0.05)	< .001
ALT	-0.01 (-0.02, 0.01)	.58	+0.01 (-0.001, 0.02)	.07	-0.02 (-0.05, 0.01)	.27	-0.07 (-0.09, -0.04)	< .001
CRP	0.00 (-0.02, 0.03)	.72			+0.03 (-0.002, 0.06)	.07	-0.03 (-0.06, 0.01)	.09
ESR					-0.01 (-0.02, 0.002)	.1	0.00 (-0.01, 0.02)	.46

* Expressed as change in slope for number of tests per patient contact per year. Abbreviations: BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate. For hospitals 1 and 2, not all data was available.

Appendix 10 – Facilitators and barriers: Questionnaire 'Willingness to change', first and second conference

	Facilitators	Barriers
Individual factors: caregivers	- Educational efforts, supported by scientific evidence - Continuous attention for overuse, repetition - Enthusiasm caregivers and project teams - Importance for health care and resident training - Focusing on quality and safety	- Fear of missing clinically relevant information, insecurity - Fear of prolongation of length of stay - Ambiguity about what overuse reduction efforts yield - Difficult to change working habits or routine behavior - Costs are negligible and remain vague
Individual factors: patients	- Involvement of patients in efforts to reduce overuse	
Social factors	- Making use of morning reports, grand rounds, etc. to discuss ordering behavior - Role models, local champions - Providing insight into ordering patterns and costs - Feedback on progress and changes in ordering patterns - Establishing clear agreements on ordering diagnostics - Involvement of subspecialties to broaden support - Involvement of clinical chemists and controllers	- Lack of role models - Physicians don't feel personally responsible for making changes - Difficulty in establishing clear agreements on ordering diagnostics - Lack of consensus among specialists - Unwillingness of specialists
Organizational factors	- Changes in ordering systems - In-depth evaluation of ordering patterns - Simple dataset for follow-up - Feasibility within department - Sustainability of results - Incorporation of RODEO and its principles into introduction programs for new employees - Support by coordinating project team - Hospital-wide introduction of RODEO	- Lack of time and availability of physicians, clinical chemists and controllers to dedicate to the project - High rate of turnover of residents - Convenience of standard ordering panels - Difficulties in obtaining correct utilization data - Long lead time to implement changes in ordering systems - Changes in ordering systems can often only be made for the entire hospital, thus requiring consensus between specialties - Fear Department of Clinical Chemistry for an increase in the number of afterwards requested tests
Environmental factors	- Reducing overuse is currently a hot topic	- Focusing on euros reduction instead of on quality and safety - Willingness of diagnostics departments might be affected by negative effects on their income

Appendix 11 – Facilitators and barriers: third conference

	Facilitators	Barriers
Individual factors: caregivers	- Educational efforts, supported by scientific evidence - Continuous attention for overuse, repetition - Enthusiasm caregivers and project teams	
Individual factors: patients	- Involvement of patients in efforts to reduce overuse	
Social factors	- Making use of morning reports, grand rounds, etc. to discuss ordering behavior - Role models, local champions - Involvement of subspecialties to broaden support	- Lack of communication
Organizational factors	- Changes in ordering systems - Simple dataset for follow-up - Incorporation of RODEO and its principles into introduction programs for new employees - Incentivize controller	- Performing too many actions at once - Placing too much focus on details
Environmental factors		- Focusing on euros instead of on quality and safety

Appendix 12 – Facilitators: Questionnaire RODEO project evaluation (*n*=75)

		Hospital 1	Hospital 2	Hospital 3	Hospital 4	Total
Individual factors: caregivers	- Educational efforts, supported by scientific evidence	8	3	1	4	16
	- Continuous attention for overuse	6	3	2	0	11
	- Enthusiasm of caregivers and project teams	1	2	1	2	6
Social factors	- Feedback on progress and changes in ordering patterns	5	1	3	0	9
	- Involvement of clinical chemists	5	0	0	0	5
	- Involvement of residents	0	3	1	0	4
	- Results of the project	0	1	0	1	2
	- Involvement of project team	0	0	0	1	1
	- Involvement of internists	0	0	1	0	1
	- Initiating the project	0	0	1	0	1
Organizational factors	- Order system changes	4	0	0	0	4
	- Clarity about the aims of the project	1	0	0	0	1
Environmental factors	- Not focusing on cost reduction	0	0	1	0	1
	- Reducing overuse is currently a hot topic	0	1	0	0	1

Appendix 13 – Barriers: Questionnaire RODEO project evaluation (*n*=75)

		Hospital 1	Hospital 2	Hospital 3	Hospital 4	Total
Individual factors: caregivers	- Lack of attention for overuse reduction	2	0	0	0	2
	- Difficult interpretability of results	1	0	0	0	1
Social factors	- Principles and agreements not fully incorporated in day-to-day practice	3	0	0	1	4
	- Lack of feedback	1	1	0	0	2
	- Role of supervisor	2	0	0	0	2
	- Lack of involvement of clinical chemists	1	0	0	0	1
	- Lack of presence of specialists at educational sessions concerning their specialty	1	0	0	0	1
	- Lack of visibility of project	0	0	1	0	1
	- Reproachful tone of clinical chemistry department	0	0	1	0	1
Organizational factors	- High rate of turnover of residents	1	1	0	2	4
	- Rigidness of order system changes	0	0	0	4	4
	- Lack of time or other priorities	0	1	1	1	3
	- Difficulties in instatement of order system changes, not enough order system changes	0	1	0	2	3
	- Difficulties in obtaining correct utilization data	0	2	0	0	2
	- Logistics	0	0	0	1	1
Environmental factors	- Focusing on cost reduction	0	0	1	0	1

5

Long-term sustainability of a multi-step intervention to reduce unnecessary diagnostic testing

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In recent years, many initiatives have been introduced in clinical practice to reduce unnecessary use of care, including unnecessary diagnostics, with the aim of controlling the increasing costs of health care and improving patient safety.[1] Although most initiatives demonstrate short-term success only a few studies have investigated the long-term sustainability of their interventions.[2] In 2009, we initiated a project at the internal medicine department of the VU University Medical Center in Amsterdam (VUmc), aiming to reduce the costs of unnecessary diagnostic tests. The first results of this successful project were published in 2012.[3] In this letter we present the long-term results of the project.

In 2008 and 2009, we implemented multiple interventions to increase awareness about the use of (unnecessary) tests in the routine hospital practice, associated costs and implications for patient safety. The intervention consisted of several steps as described in the publication by Vegting et al.[3] First, we intensified the supervision of young residents by introducing a mentorship system and these consultants were instructed to pay as much attention to the laboratory tests performed as to the diagnostic and therapeutic dilemmas. Second, laboratory orders were constrained by unbundling panel tests such as liver enzyme tests [alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT)], electrolytes (sodium and potassium), and kidney function (creatinine and urea/BUN). Indications for other frequently used tests such as glucose, calcium, albumin and phosphate were also strictly regulated. Third, the national protocols on the management of chronic diseases were included in a central electronic database, to create more awareness and to make it easier for clinicians to consult them. The physicians were strictly instructed to follow these national guidelines created by the Dutch Association of Internal Medicine with regard to the recommended frequency of the various diagnostic tests in a given chronic disease state. Fourth, we printed posters and pocket cards with the cost prices of the laboratory tests and distributed them to all the doctors for reference. Fifth, we presented six-weekly overviews of the ordered laboratory tests during the morning report. Finally, clinical meetings such as the grand rounds, daily ward rounds and morning reports were used to provide feedback on the already performed tests.

During the first year after implementation of the interventions a 13% reduction was observed in total expenditure on all types of diagnostic tests in the internal medicine department. The largest reduction was observed in laboratory expenses, which were reduced by 21%.[3] Although the interventions were primarily targeted at laboratory diagnostics, the expenses for other diagnostics also decreased.

In the subsequent years the intensity of the interventions was reduced as these were believed to have been incorporated in daily practice. We continued to monitor diagnostic test ordering patterns and total costs of diagnostics and presented these to the Board of Directors and the

departmental heads every three months. When unexpected increases in ordering volume or expenses were noted, the topics of overutilization and costs were brought under the attention of the caregivers again.

During the subsequent years diagnostic expenses adjusted for the total number of patients continued to decrease, as is shown in **Figure 1.** We therefore conclude that in spite of reducing the intensity of our intervention, there is a sustainable reduction in expenses on (unnecessary) diagnostics.

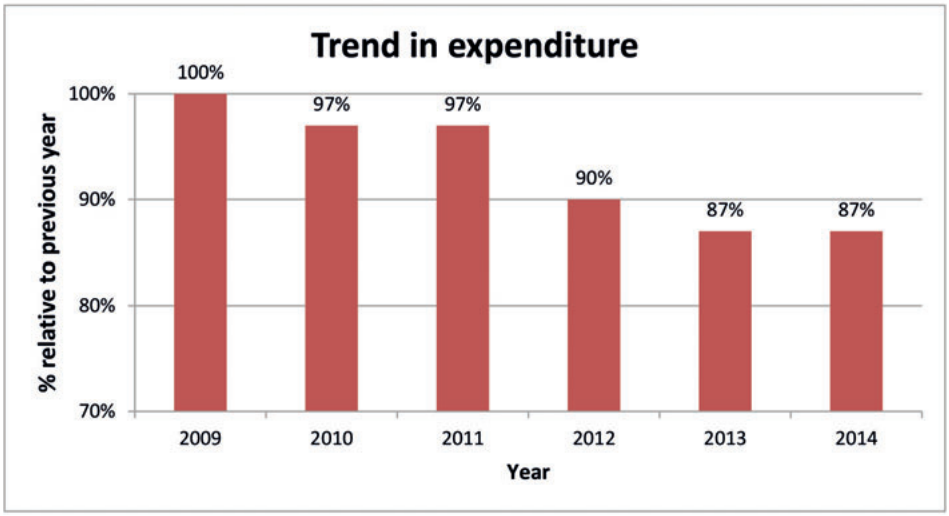

Figure 1 – Trend in expenditure for all diagnostics in the internal medicine department

In our opinion this is one of the first trials performed with a follow up period of six years demonstrating a sustainable effect. One of the elements we believe led to our success was our focus on reducing the amount and costs of inexpensive, high-volume tests rather than expensive, low-volume tests. We believe our success was attributable largely to incorporation of our interventions in daily practice. A culture change was established in which senior physicians acted as role models for junior physicians. The subjects of diagnostic reasoning and (over)utilization were kept under the attention of the caregivers by several senior physicians acting as ambassadors. We learned that it is essential to have sufficient support from senior physicians as well as residents within the department to successfully carry out such a project and that increasing awareness about unnecessary diagnostics created intrinsic motivation with the staff which led to this sustained effect.

The interventions carried out in this project were successfully extended to other departments within the VUmc. In addition, we also recently initiated the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) - project, in which our interventions are introduced in four large teaching hospitals in the Netherlands.

In this project we focus on reducing the volume of laboratory tests within the internal medicine department. We appointed a team consisting of internal medicine supervisor(s), internal medicine resident(s), a clinical chemist and a business intelligence specialist at each participating hospital to coordinate the implementation of the interventions and to optimize support from all physicians within the department. With this team, order patterns are analyzed monthly and (targets for) interventions are developed. An important difference with the project we carried out at the VUmc is the prominent role for residents to act as role models for their peers. The RODEO project is part of the broader Dutch program *"To do or not to do? Reducing low-value care"* aiming to reduce the use of low-value care for the patient, a program initiated by the Dutch Federation of University Medical Centers.[4]

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6

Evidence-based guidelines to eliminate repetitive laboratory testing?

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Evidence-based guidelines to eliminate repetitive laboratory testing

In December 2017, Eaton et al. have published an article in JAMA Internal Medicine's "*Less is More"* series in which they offer an evidence-based blueprint for reducing inappropriate laboratory testing among hospitalized patients. This article encourages action by presenting examples of successful projects.[1]

The article first describes evidence that suggests that routine laboratory testing is associated with preventable patient harms, such as hospital acquired anemia and unnecessary follow-up testing that can occur after diagnostic tests are performed without reasonable pre-test probability for disease. This is followed by describing cost reduction due to reducing unnecessary laboratory testing, through several examples of studies attempting to quantify costs, taking into account that accurate cost assessment is difficult given to the downstream consequences of laboratory testing. Subsequently, interventions from three categories are discussed: education, audit and feedback on ordering practice, and electronic medical record (EMR)-enabled restrictive ordering. In this section, Eaton et al. claim that a multimodal approach combining interventions from all three categories is most effective. Finally, an implementation blueprint is proposed. This blueprint recommends implementing strategies from all three categories and provides several items to take into consideration within each strategy. Furthermore, the article describes the importance of an overall readiness to change within institutions for success of reduction efforts.

In the following paragraphs, we question the conclusion that the multimodal strategy proposed by Eaton et al. is most effective, efficient, and evidence-based, and discuss pros and cons of possible measures to study the reduction of unnecessary testing.

Evidence-based?

We have several difficulties and comments to the claim that the recommendations presented are evidence-based. First of all, no information is provided on the representativeness or methodological quality of the studies discussed, although we know that studies often have methodological limitations, such as the absence of a control group (**Chapter 2**), and quality of studies to reduce unnecessary testing is overall poor.[2,3]

Secondly, the studies described in the article, as well as in other literature, mostly focused on "total reductions" instead of on "unnecessary testing", which would have been more informative when attempting to reduce merely unnecessary tests. For example, depending upon the proportion of unnecessary testing at baseline, an absolute reduction of 15% could correspond to a 100% reduction in unnecessary testing in one study but only a 50% reduction in another. Unnecessary tests can be defined as tests for which the result does not contribute

to diagnostic and clinical management of an individual patient.[4] For some common tests, such as lipase and amylase for which there is sufficient evidence to recommend lipase testing over amylase testing for diagnosing acute pancreatitis, recognizing a test as unnecessary is clear.[5] In other contexts assessing necessity and recognizing test orders as unnecessary can be more difficult, for example in the case of repeated testing for which, in general, evidence-based frequency recommendations are lacking.[6,7] When specifically considering appropriateness of laboratory testing, a systematic method to identify unnecessary tests in individual cases is not readily available.[8]

Thirdly, if total reduction were considered appropriate, we do not see how the study results support the conclusion that a multimodal approach is most effective. For example, May et al.[12] saw a similar reduction with an EMR only approach as opposed to Vidyarthi et al.[13] who used a multimodal approach (12 vs 8%). Moreover, as explained in **Chapter 2**, we find it difficult to compare effectiveness of interventions and to draw conclusions as to which intervention(s) is/are most successful, because of heterogeneity in both interventions studied and outcomes reported.[2] Even if the multimodal strategies were associated with larger absolute reductions, this could be because multimodal strategies may be more often selected when there are high levels of perceived inappropriate testing.

Study of clinically relevant outcome measures

Our final criticism on the paper by Eaton et al. is the lack of critique on outcomes studied in test utilization studies, as these focus mostly on volume and costs. The reasons for this may be because this data is readily accessible, and because studying patient-related outcome measures might be difficult due to a limited sample size and short duration of follow-up. From our review in **Chapter 2** of this thesis, we learned that many papers do not report on possible effects of reduction of laboratory test utilization on patient-related outcomes.[2] In our opinion, investigating these outcomes should receive more attention. Although mortality rate, duration of hospital stay and rate of readmissions are frequently studied outcome measures, these measures are crude and their relevance is questionable, as it is unclear to what extent they are linked to a reduction in laboratory testing. Therefore, we suggest looking broader at outcomes such as imaging rate, antibiotic usage, time to diagnosis and patient satisfaction. Surmounting evidence that reduction of laboratory tests in certain situations is safe and cost-effective will encourage others to follow suit.

Tailored strategy

While the proposed three-pronged blueprint may work in many situations, not all components may be essential and additional interventions may be required. Important principles in

developing interventions is that they should be supported by evidence, have a strong (clinical) basis or rationale, and fit department's needs, preferences and capacities.[14]

Although the focus of reducing unnecessary testing should be on improving quality of care, cost-effectiveness is a key point as well. Although educational interventions and audit and feedback based interventions provide the opportunity for a personal approach, they are relatively costly in the form of human resources, especially in the long run. On the contrary, EMR-based interventions take relatively little effort and after their initial instatement, no further action is needed. Since staffing of laboratories and purchase of diagnostic equipment are based on long running average test volumes, reducing test utilization can only significantly reduce costs if interventions are sustained over the long term. Only then laboratories can consider redeploying laboratory resources without compromising quality of care.[15,16]

We advocate a tailored strategy in which an assessment of the current situation facilitates the selection of interventions to efficiently and sustainably influence change.[17] For example, if there is awareness of the problem and a willingness to change but doctors simply forget to check when the last test was ordered, changes to the EMR alone may be sufficient and, if sustained, cost-effective, as has been shown to be the case in several studies.[18] In the RODEO project, tailoring strategies proved effective, created clinical leaders' ownership, and ensured that the actions fit the local context.[10]

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7

Reducing unnecessary laboratory testing: A step-by-step action plan

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Submitted

Introduction

De-implementation or de-adoption of low-value care is being advocated worldwide through several initiatives, the largest one being the "*Choosing Wisely*" campaign that was initiated in 2012.[1] Many countries, including the Netherlands, have adopted the Choosing Wisely principles and have initiated several other initiatives regarding low (or high)-value care and unnecessary use of care services.[2-4]

The unnecessary use of laboratory tests is often targeted in de-implementation efforts. In this context, the term 'unnecessary' refers to tests in which the results do not contribute to diagnostic and clinical management.[5] Although many studies on this topic have been published over the past decades, there is a lack of literature describing their approach in detail. Similar to other types of intervention studies, reports often focus mainly on describing results, and fail to sufficiently describe the interventions used. This leads to waste of health care research.[6,7]

In 2008 our study group performed a multifaceted intervention aiming to reduce unnecessary diagnostic testing at the internal medicine department of the Amsterdam UMC, location VU University Medical Center (VUmc), a large academic medical center in the Netherlands, through changing the mindset of caregivers.[8,9] After the success of this pilot project, we implemented the same intervention in the internal medicine departments of four large teaching hospitals in the Netherlands in the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) – project.[10] In this project, we successfully reduced the number of laboratory tests and although we mainly focused on laboratory testing within the domain of clinical chemistry, utilization of other diagnostics (e.g. microbiology, radiology and nuclear medicine) also declined, leading us to believe that a change in caregivers' mindset was achieved.[11]

The individual components and their interplay needed for successful de-implementation are conceptualized in several frameworks and models, which are applicable to a wide range of services.[12] To the best of our knowledge, a de-implementation framework specifically targeting unnecessary laboratory testing is lacking. Using our experiences and feedback from physicians participating in the RODEO project, complemented by current literature, we propose a step-by-step action plan that is appropriate for direct use to specifically decrease unnecessary laboratory testing in hospital settings, and follows the general stages of de-implementation of low-value clinical care as described by Niven et al.[13]

Methods

De-implementation framework

The steps for the action plan we propose in this paper for decreasing unnecessary laboratory test utilization broadly follow the stages of de-implementation of low-value clinical care as described by Niven et al.[13], which we further specified to the laboratory setting through experiences in the RODEO study described below. The stages of de-implementation are presented in **Figure 1** and can be used as a reference point for de-implementation efforts.

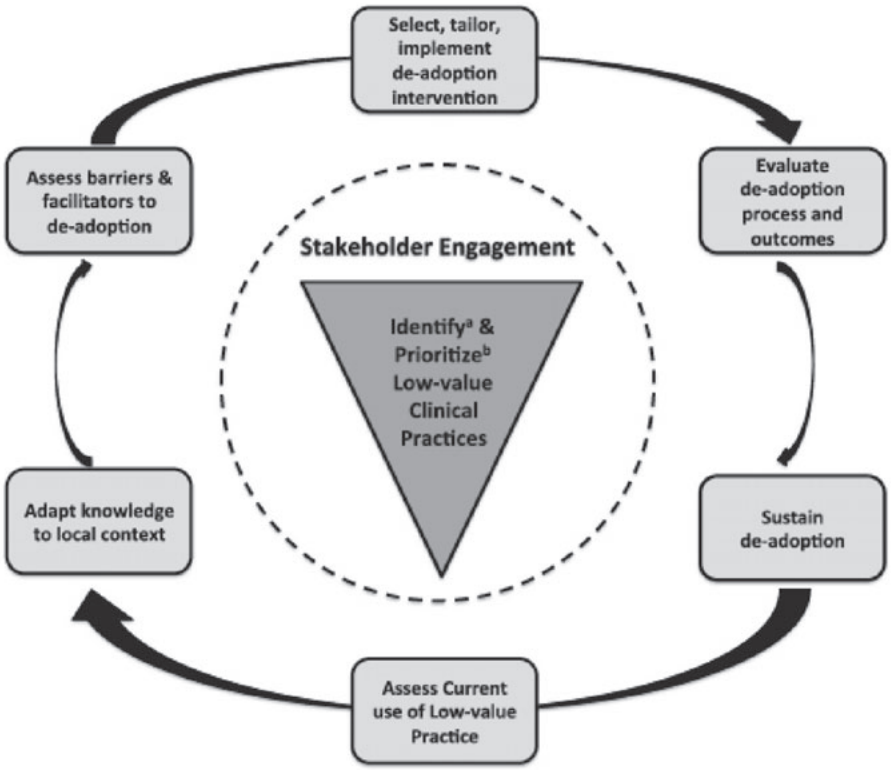

Figure 1 – De-implementation model by Niven et al.(13)

The core of this framework is the identification and prioritization of low-value practices. This involves determining which clinical practice qualifies for de-implementation, and in cases where multiple low-value practices are identified, determining which clinical practice should be addressed first by considering, for example, safety of the low-value practice and potential impact of de-implementation in terms of costs and health outcomes. Involving different stakeholders in de-implementation efforts can serve several purposes, for example acquiring

widespread support. Assessing the use of low-value practices and adapting knowledge to the local context ensures that the process is tailored to the local situation. Selection of strategies and interventions to be performed requires an assessment of factors that might facilitate or hinder de-implementation. Considering these factors, targeted actions can be developed, suitable for the local context. Subsequently, de-implementation efforts should be evaluated, for example by assessing the effect on utilization of the low-value practice, health outcomes, or costs. Finally, a plan for sustainability should be introduced.[13]

RODEO study

The methods of the RODEO study have been previously published, therefore we only describe a brief overview in this section.[10]

The RODEO study was a multicenter before-after study, carried out at the internal medicine departments of four large teaching hospitals in the Netherlands. The study was performed by a coordinating project team (RB, MvB, PN and MtB), together with a local project team at each hospital.

The primary endpoint of the study was to determine the effect of a multifaceted intervention on laboratory test volume. Secondary endpoints were to determine the effects on laboratory test costs, volumes and costs for other diagnostics, and process- and clinical patient-related outcomes. The tertiary endpoint was to assess barriers and facilitators to de-implementation of unnecessary testing. These were identified through questionnaires with the project teams at the beginning of the project[10], during joint conferences, and through a project evaluation questionnaire conducted among all physicians working at participating departments at the end of the project.

The study consisted of three time periods: three to four months pre-intervention, six months intervention, and eight months post-intervention in which sustainability was analyzed. The de-implementation strategy used in this study is previously described.[10]

Development of a step-by-step action plan

To develop our action plan aimed at reducing laboratory testing in hospital settings, we used input from several sources. Firstly, we simplified the many different actions we performed when carrying out the RODEO project to formulate a set of broad, general steps. Secondly, we used existing literature on unnecessary laboratory testing to specify the steps. Thirdly, we used input from the providers involved in, or targeted by, the interventions. This information was acquired through questionnaires with the project teams at the beginning of the project, during multiple joint conferences with members of the local project teams, and through an evaluation

questionnaire conducted among all physicians working at participating departments at the end of the project. Finally, we used our own experiences gained during both the RODEO project and the pilot project at the Amsterdam UMC, location VUmc.[8,9] The acquired knowledge on barriers and facilitators to reduce unnecessary laboratory testing was used to complement the proposed steps, and to point out issues that need explicit attention while carrying out a similar de-implementation initiative. Our steps were compared to the de-implementation framework proposed by Niven et al.[13], to ensure that we did not miss important actions in our step-by-step action plan.

Results

In this section, we propose the step-by-step action plan appropriate for direct use to reduce unnecessary laboratory testing in hospital settings. **Table 1** presents the several steps proposed in our action plan, linked to the stages of de-implementation as described by Niven et al.[13]

Step 1. Introduce the initiative and the importance of reducing unnecessary diagnostic testing in health care. Create a supportive environment, acquire commitment and form a project team.

This first step of our action plan involves *sending a clear message to care providers focusing on the importance of reducing unnecessary laboratory testing in health care*. This can be done by using scientific evidence on the amount of overuse, for example, a review addressing the appropriateness of laboratory testing has reported a mean rate of overutilization of approximately 21% from 1997 to 2012, and by discussing international initiatives, such as the Choosing Wisely campaign.[1,14]

Table 1 – Proposed step-by-step action plan, by stages of de-implementation

Stages of de-implementation	Proposed step in action plan
Stakeholder engagement	**Step 1. Introduce the initiative and the importance of reducing unnecessary diagnostic testing in health care. Create a supportive environment, acquire commitment and form a project team.** - Send a clear message to physicians focusing on importance of reducing unnecessary laboratory testing in health care. - Acquire commitment from department staff, laboratory department, and Board of Directors. - Form a project team to lead the initiative. Include representatives from the staff and resident group to act as role models/clinical champions, and the laboratory and business control/intelligence departments. Make sure different subspecialties and locations are represented.
Identify and prioritize low-value clinical practices Assess current use of low-value clinical practices Assess barriers and facilitators to de-adoption	**Step 2. Analyze the current situation with the project team.** - Provide insight in volume and costs of diagnostics over the previous (at least) three years with the aim of looking at trends in ordering behavior. - Use benchmark data to compare ordering behavior with other hospitals and, if possible, among physicians. **Step 3. Discuss opportunities and possibilities for reduction with the department.** - Assess barriers and facilitators with the department.
This step does not correspond to any of the stages of de-implementation	**Step 4. Set targets for reduction with the local project team.**
Adapt knowledge to local context Select, tailor, implement de-adoption intervention	**Step 5. Develop interventions to reduce unnecessary laboratory testing, taking identified barriers and facilitators into account.** - Place focus on different elements and categories of interventions to increase clinical leaders' ownership and ensure fit in local context. - Assign a prominent role to multiple residents in carrying out the interventions. - Frequently reserve time to explicitly address overuse, in addition to making use of existing meetings.

Stages of de-implementation	Proposed step in action plan
Evaluate de-adoption process and outcomes	**Step 6. Evaluate the effects with the project team. Attempt to find an explanation for results. Adjust previously set targets on specific tests. Modify or add interventions if deemed necessary.** - Hold regular evaluation meetings with the project team to follow-up on feasibility, efficacy and effectiveness, and to ensure fit of interventions in the local context. **Step 7. Provide feedback on progress to physicians and laboratory professionals working at the departments.** - If possible, provide feedback on an individual level. - Present examples of successful changes, in addition to items that still have much potential for change and need explicit attention
Sustain de-adoption	**Step 8. Sustain the reduction on both short- and long-term.** - Make sure that new working agreements are sufficiently embedded into daily practice. - Continuously monitor utilization data. - Make agreements on ownership.

In addition, as merely focusing on cost reduction often triggers emotional resistance among physicians and, more importantly, is not the sole purpose of reducing unnecessary laboratory testing, addressing the potential for patient harm and emphasizing the purpose of increasing quality and safety of care can encourage physicians to change their ordering behavior.[15,16] This includes paying attention to a shift from inappropriate to appropriate testing, taking into account whether tests are ordered for the right reasons, and whether the results contribute to diagnostic and clinical management.[5] In the RODEO project, the majority of providers was convinced that fewer laboratory tests would lead to more patient-friendly care (**Table 2**).

The involvement of different stakeholders in reduction efforts serves several purposes. One purpose is to acquire widespread support that is needed for a process that is integrated into clinical practice.[13] Creating a supportive environment within the department is important, as engaged providers committed to change can take ownership of and lead the culture change needed to de-implement practices they are accustomed to.[17] *Part of creating a supportive environment, is acquiring commitment from the staff of the clinical department, the staff of the laboratory department, and the Board of Directors of the hospital.* In addition, involving different stakeholders ensures that there is sufficient expertise to guide de-implementation, and that opinions and beliefs of several disciplines, such as fear of negative effects on income of the laboratory department and fear of an increase in the number of afterwards requested tests, are taken into consideration. The involvement of interdisciplinary experts can provide valuable information about feasibility, efficacy and effectiveness of the initiative.[18]

For specifically reducing unnecessary laboratory testing, *we recommend including motivated representatives from the staff and resident group, at least one clinical chemist, and at least one specialist from the business control/intelligence department, in a project team that will lead the initiative.* Representatives from the staff and resident group can function as clinical champions/clinical leaders and act as role models for their peers. Laboratory professionals are (at least partially) responsible for optimal use of laboratory diagnostics and, as such, should also take a leading role.[19] Their input furthermore increases knowledge base. Business control/intelligence specialists can provide the required utilization data. In the RODEO project we found that the enthusiasm of the project teams was motivating.[11] We noticed that a high turnover of residents, including the residents involved in the project team changing rotation, formed a threat to continuity and support of the project. Therefore, *we recommend including multiple residents and representatives, if possible, from different subspecialties and locations (inpatient- and outpatient clinic, emergency department) in the project team* in future efforts.

Besides clarity on the importance of reducing unnecessary testing for health care and a supportive environment, de-implementation efforts require the establishment of a blame-

free culture in which physicians feel safe, feel free to ask questions, and are committed to improving safety and effectiveness of the care they provide.[17] To this end, the involvement of clinical champions and role models is essential.

Table 2 – Questionnaire RODEO project evaluation' (*n*=75), conducted at the end of the project

Question	*n* (%) Agree	*n* (%) Neutral	*n* (%) Disagree	*n* (%) NA
1. The importance of reducing unnecessary diagnostics was clear.	73 (97.3)	1 (1.3)	0 (0.0)	1 (1.3)
2. The aim of the project was clear.	70 (93.3)	3 (4.0)	0 (0.0)	2 (2.7)
3. Enough attention was paid to the importance for patients of reducing unnecessary diagnostics.	54 (72.0)	15 (20.0)	3 (4.0)	3 (4.0)
4. The environment at the department was such that I felt free to ask questions regarding the usefulness of test requests.	69 (92.0)	1 (1.3)	0 (0)	5 (6.7)
5. The number of questions colleagues have asked me regarding the usefulness of test requests was adequate.	33 (44.0)	29 (38.7)	6 (8.0)	7 (9.3)
6. Internists have asked me, as a resident, an adequate number of questions regarding the usefulness of test requests.	22 (52.4)	14 (33.3)	5 (11.9)	1 (2.4)
7. As internist, I have asked residents an adequate number of questions regarding the usefulness of test requests.	24 (72.7)	6 (18.2)	0 (0.0)	3 (9.1)
8. I have been adequately informed about the progress of the project.	41 (54.7)	22 (29.3)	10 (13.3)	2 (2.7)
9. (Changes in) ordering patterns at department level have been made adequately transparent.	45 (60.0)	18 (24.0)	9 (12.0)	3 (4.0)
10. Reducing unnecessary testing has been adequately supported by scientific evidence.	54 (72.0)	17 (22.7)	3 (4.0)	1 (1.3)
11. There was enough space and opportunity to bring in ideas for the project.	54 (72.0)	14 (18.7)	0 (0.0)	7 (9.3)
12. I have gained new knowledge on diagnostics.	50 (66.7)	11 (14.7)	9 (12.0)	5 (6.7)
13. Novel working agreements have been adequately embedded into daily practice.	53 (70.7)	19 (25.3)	1 (1.3)	2 (2.7)

Table 2 – Continued

Question	*n* (%) Agree	*n* (%) Neutral	*n* (%) Disagree	*n* (%) NA
14. Reducing unnecessary diagnostics leads to higher quality care.	44 (58.7)	22 (29.3)	5 (6.7)	4 (5.3)
15. Reducing unnecessary diagnostics leads to more patient-friendly care.	58 (77.3)	12 (16.0)	2 (2.7)	3 (4.0)
16. I fear to miss clinically relevant information by performing less diagnostic tests.	7 (9.3)	15 (20.0)	50 (66.7)	3 (4.0)
17. During the past month, I have received negative feedback for performing less diagnostic tests.	4 (5.3)	6 (8.0)	58 (77.3)	7 (9.3)
	Never	**< 1x / wk**	**≥ 1x / wk**	**NA**
18. Before the project, how often did you see examples of unnecessary use of diagnostics?	2 (2.7)	19 (25.3)	53 (70.7)	1 (1.3)
19. After the project, how often do you see examples of unnecessary use of diagnostics?	1 (1.3)	26 (34.7)	45 (60.0)	3 (4.0)
20. How often was unnecessary use of diagnostics addressed during morning or afternoon reports?	2 (2.7)	33 (44.0)	40 (53.3)	0 (0.0)
21. How often was unnecessary use of diagnostics addressed during grand rounds?	2 (2.7)	28 (37.3)	42 (56.0)	3 (4.0)
22. How often was unnecessary use of diagnostics addressed during other clinical discussions?	14 (18.7)	39 (52.0)	20 (26.7)	2 (2.7)
23. How often has time been reserved explicitly for discussion of unnecessary use of diagnostics?	17 (22.7)	45 (60.0)	11 (14.7)	2 (2.7)

Abbreviations: NA, not answered; wk, week.

Step 2. Analyze the current situation with the project team.

The next steps in our action plan involve the stages of identifying, prioritizing and assessing current use of low-value clinical practices.

In the RODEO project, we analyzed the current situation by investigating total laboratory test volume and costs, and volumes and costs for individual tests, assessing which individual tests comprised the largest volumes and generated the most expenses in the previous three years. To provide physicians insight into the share of diagnostics spent on laboratory services, we also assessed costs for other diagnostic services, such as radiology and microbiology, which helped increase awareness. *We recommend to provide insight in (some of these) data over the previous, at least three years, to be able to look at trends in ordering behavior per location.*

Identifying tests that might qualify for reduction efforts, which is also done in steps 3 and 4, can be performed through different approaches. In our project, we focused on (1) tests that are known to be frequently overused (for example, tests that are oftentimes ordered in combination with other tests and provide similar information, and tests mentioned in for example the Choosing Wisely campaign or the "*Wise Choices*" list by the Netherlands Society for Clinical Chemistry and Laboratory Medicine (NVKC)[1,20] to be of low-value), (2) tests that are ordered in high frequency or generate high costs to the department (are they being ordered for the right indication?) and (3) tests that are often performed in the patient groups that are treated most. Another approach that might be helpful in recognizing overuse is measuring practice variation in the context of high interphysician or interhospital variability of test orders.[21] In a recent study among internal medicine residents, some residents ordered seven to eight times more tests compared to their peers, suggesting at least some degree of overuse.[22] Therefore, if available, *we recommend using benchmark data to compare, for example the Top-10, Diagnosis-Related Groups (DRGs)/Diagnosis Treatment Combinations (DOTs) generating the highest laboratory expenses with other hospitals and, if possible, between physicians.*

In the RODEO project, timely collection of initial and follow-up data was challenging and was the most important barrier to our de-implementation efforts.[11] However, knowledge on the use of low-value services was essential for conversation and action.[17]

Step 3. Discuss opportunities and possibilities for reduction with the department.

Once the current situation is mapped properly and presented to department staff and resident group, *opportunities, possibilities, ideas and initiatives can be explored*, for example during a brainstorm session with staff, residents and laboratory professionals. Target tests for reduction can be discussed, using the assessment of the current situation as input. Ideas

for possible interventions are listed in **Table 3** and are described in more detail in our recent review on reducing unnecessary laboratory testing.[7]

Clarity on residents' and department staff's perceptions regarding unnecessary laboratory testing, and preferences and capacities with regard to solutions is valuable, as this input can be used to tailor interventions and may provide information about which parts of interventions should be adopted, to ensure fit in the local context.[23] To develop and adjust strategies later on, an assessment of factors potentially hindering or facilitating de-implementation of unnecessary testing is also useful. In the RODEO project, these factors were identified with the project teams through questionnaires at the initiation of the project[10] and during joint conferences, and among all physicians working at participating departments through an evaluation questionnaire conducted at the end of the project. The most important barriers we found were difficulties in data retrieval, difficulties with incorporation of new working agreements in daily practice, and high resident turnover. The most important facilitators were education, continuous attention for overuse of diagnostic testing, feedback, residents' involvement and involvement of local champions (experienced clinical role models).[11]

Although the barriers and facilitators we have incorporated into this step-by-step action plan were collected from and largely common among different settings, other clinics may encounter additional factors. For example, fear of missing diagnoses through decreased testing is often mentioned in literature as driver of overtesting.[24,25] However, upon evaluation of the RODEO project, only 9% of respondents indicated fear of missing clinically relevant information through performing less diagnostic tests (**Table 2**). Literature also mentions requesting driven by perceived expectations from attending physicians as reason for overtesting, although we found upon evaluation that only a small minority of respondents (5.3%) had received negative feedback for ordering less tests (**Table 2**).[25,26] *We therefore do recommend to assess barriers and facilitators and, if necessary, use them to introduce and adjust strategies later on.* Although we used questionnaires and joint conferences throughout the project for our assessment, the brainstorm session with staff and residents could also be a good place to start. Because changing physician ordering practice is an iterative process, identifying barriers and facilitators throughout the various stages of de-implementation can be valuable.[27]

Step 4. Set targets for reduction with the project team.

In the fourth step, concrete targets for percentage reduction are determined with the project team. Setting targets and following up on these provides information indicating whether the actions developed later on are suitable, or whether a different approach should be considered.[28]

Targets for reduction were determined using the knowledge gained and approaches described in steps 2 and 3. According to our experience from the RODEO project, placing focus on too many tests at once was less manageable than focusing on a limited number of tests over a period of time, shifting focus to other tests for the next time period, and so on, and using these specific tests as a way to change physicians' mindset in general.

Step 5. Develop interventions to reduce unnecessary laboratory testing, taking identified barriers and facilitators into account.

After discussing possibilities and ideas and determining concrete targets for reduction in steps 3 and 4, interventions should be developed. Important principles in developing interventions is that they should be supported by evidence, have a strong (clinical) basis or rationale, and fit department's needs, preferences and capacities. In addition, interventions should be developed in such a manner that they can easily be incorporated into daily practice.[23]

In current literature, several types of interventions are being described that have proven to be effective in reducing laboratory testing, including for example, education, audit and feedback on test ordering behavior, and changes in order entry systems.[7,29] Although it is difficult to compare effectiveness of different strategies and draw conclusions as to which intervention(s) is/are most successful, combined approaches are advocated in other literature and have also proven effectiveness in both the VUmc and the RODEO project.[7-9,11]

Achieving and sustaining behavior change often targets the concepts of knowledge and attitude.[30] Increase of knowledge is targeted through education, for example by providing educational sessions, sending newsletters and scientific articles through e-mail, and developing pocket-cards with charges for tests. These efforts can also affect attitude towards unnecessary testing. In addition, attitude can be influenced through clinical champions functioning as role models, and through audit and feedback methods. Knowing that one is being monitored may change one's attitude towards testing, while feedback can also be a learning experience. Moreover, knowledge of performance through audit and feedback can influence social pressure that can contribute to the intention to change behavior.[31] Changes in order entry systems, such as instating time limits that obstruct repeated ordering of tests within a certain time interval, and modifying or eliminating order panels, may have a direct influence on behavior. Furthermore, they can contain educational elements, and they can be helpful in breaking through routine behavior, which is often mentioned as a driving factor for overtesting.[7,25] Establishing and frequently communicating new working agreements on (routinely) performed tests among staff and residents may also directly affect behavior and ensure embedding of the new way of working in daily practice. In the context of establishing new working agreements, revision (and modification) of frequently used clinical guidelines can also be helpful.

In the RODEO project, all of these, and additional interventions were combined, resulting in a multifaceted approach. The local teams were encouraged to develop interventions tailor-made for their department structure, on top of the standard intervention. Thus, while every clinic performed interventions from the same categories, content, timing and intensity of different interventions were determined locally by the project teams. This was done to ensure fit of the interventions in the local context. *As we observed that providing clinics the liberty to place focus on different elements of the standard intervention proved effective and created clinical leaders' ownership, we recommend that in future projects, this same approach should be used, ensuring that the actions fit the local context*. In addition to these locally tailored interventions, other main interventions used in the RODEO project were intensifying residents' supervision regarding test ordering by experienced staff, and involving clinical chemists in clinical meetings.

In our project, we noticed that it was mainly the involvement of residents that facilitated de-implementation.[11] Therefore, *we recommend assigning a prominent role to multiple residents in carrying out the interventions*, for example through residents providing educational sessions, and revising frequently used guidelines and order sets. Upon evaluation of our project, we furthermore learned that changing ordering patterns requires explicit and continuous attention and repetition, as this was mentioned as second most important intervention in the evaluation questionnaire (13/75 respondents). This is not always easy considering physicians' workload, time constraints and other priorities.[11] For this reason, *we also recommend frequently reserving time to explicitly address overuse of laboratory testing and interventions, while also making use of the existing meetings, such as morning reports, daily supervision meetings, and grand rounds.* In these efforts, a prominent role is designated to clinical champions.

The several types of interventions as described above, their pros and cons as experienced in the RODEO project, and our suggestions regarding their implementation are shown in **Table 3.**

Step 6. Evaluate the effects with the project team. Attempt to find an explanation for results. Adjust previously set targets on specific tests. Modify or add interventions if deemed necessary.

Evaluation of the de-implementation process and outcomes can be performed through both quantitative and qualitative methods.

In reducing unnecessary testing, quantitative methods can include for example audits of ordering behavior and analysis of utilization data, and can be used to assess the effects of interventions on volume and costs, process- or patient-related clinical outcomes, or any other measure for which evaluation is desirable. Keep in mind that it might take several months before reduction efforts are translated into consistent changes in ordering patterns. In the RODEO

project, we noticed seasonal patterns in utilization data with relatively high test volumes in winter (data not shown). Therefore, we found it helpful to not only compare utilization data with the previous month, but also with the same month during the previous years.

Qualitative methods include for example discussions with members of the project team in which ideas and experiences can be shared, and the team can reflect on instated interventions.[27]

In the RODEO project, we assessed volumes and costs of total laboratory testing and of several specific tests monthly, and discussed these within the project team. These data were used to follow-up on, and if necessary, adjust previously set targets, and discuss additional targets for reduction. Reflecting on instated interventions and discussing why they deemed successful or not, provided the input needed to adjust used interventions, or introduce new interventions. To this end, attempting to find an explanation for possible unforeseen changes in ordering behavior can also be valuable. *To follow-up on feasibility, efficacy and effectiveness, and to ensure the fit of reduction efforts in local context, we recommend regular evaluation meetings with the project team*. Of note, in the RODEO project, educational interventions were perceived by far the most important interventions by 29 out of 75 respondents to the evaluation questionnaire, followed by continuous attention for overuse (13/75) and order system changes (12/75). To ensure that the interventions do not negatively affect quality of care, we also assessed and followed up on several process- and patient-related clinical outcomes: average duration of hospital stay, and rates of repeated outpatient visits, 30-day readmissions and unexpected prolonged duration of hospital stay for patients admitted for pneumonia. Unfortunately, it was not possible to assess the average number of phlebotomies in a given time period (or per patient) in the RODEO project. In future efforts, this outcome might also be an interesting measure to analyze.

Table 3 - Interventions, pros and cons, and suggestions for implementation

Intervention	Pros	Cons	Suggestions
Education	- Increase in knowledge - Opportunity to actively involve physicians	- Need for repetition due to high resident turnover - Labor-intensive - Exposure to intervention is unclear	Involve multiple physicians in developing and carrying out educational interventions, such as presentations and newsletters. Regularly repeat the same topics.
Feedback on ordering behavior	- Informs physicians on (suboptimal) behavior - Might influence attitude and intention to change	- Labor-intensive depending on type of feedback - Might be difficult on provider level	Provide regular feedback to physicians, if possible, provide individual feedback.
Order system changes	- Ensures sustainability - Ensures exposure to intervention	- Determining which modifications to instate can be labor-intensive - Implementation might be difficult and requires consensus among physicians (and possibly departments) - Rejection of request might be frustrating	Instate time limits, modify or eliminate standard order panels, and, if possible, eliminate tests from request forms.
Continuous attention for (overuse of) diagnostic testing	- Continuous exposure to intervention - Overcomes problem of high resident turnover	- Lack of time	Use existing meetings, such as grand rounds and morning reports, to continuously address overuse. Ideally, address usefulness of tests as a 'check-list item' for each patient discussed.
Involvement of clinical chemist in patient meetings	- Increase in expertise on usefulness of tests	- Lack of time of clinical chemist to attend meetings - Lack of time to provide input during meetings	Involve clinical chemists in existing clinical meetings on a regular basis and reserve time to discuss their input during meetings.
Instatement of new working agreements	- Provides concrete guidance on test ordering	- Lack of consensus between physicians - Embedding might be difficult, partly due to high resident turnover	Establish and frequently communicate new agreements on (routinely) performed tests among staff and residents. Ensure embedding by, for example, displaying agreements on posters, and incorporating them in guidelines and in the introduction program for new employees.

Acquiring timely utilization data needed for evaluation can be challenging and in the RODEO project, this was our most important barrier. One should start by determining which exact data to collect. Naturally, volumes and costs for testing can be affected by patient load. In existing literature on reducing laboratory testing, many different outcome measures are used to adjust utilization data for patient load, for example "number of tests per day", "number of tests per unique patient", and "number of tests per patient day".[7] Although there's something to be said for all of these different measures, we found adjusting for the "number of patient contacts", defined as the sum of the number of visits, day admissions and patient days, most suitable. This was done because we included data from the inpatient and outpatient clinics, as well as from the emergency department, and it was not possible to distinguish between orders placed from each of these locations.[11]

In addition, utilization patterns can be affected by case mix. Intuitively, the sicker patients are, the more diagnostic tests they receive. A change in case mix towards treating sicker patients might explain possible unforeseen changes in ordering patterns. Adjusting for case mix, however, is not an easy task. Theoretically, case mix might be taken into account by classifying patients according to disease severity scores, for example the Charlson co-morbidity score, Pneumonia Severity Index (PSI) score for pneumonia patients, or the acute physiology and chronic health evaluation (APACHE) score in use at the Intensive Care Unit. However, we see practical limitations to this approach, as they only apply to a subgroup of patients, and might not be reported consistently. Another approach one might consider is assessing case mix in terms of most frequently occurring DRGs over a period of time. Although this is certainly not an ideal approach, it might provide an overall idea of whether changes in utilization patterns can be linked to changes in case mix, or at least, occur simultaneously.

In conclusion, no ideal strategy exists to adjust utilization data. Future efforts should be pursued to develop an optimal measure that includes numbers of inpatient admissions, inpatient days, outpatient visits, emergency department visits, day admissions, and case mix. Until then, selection of a suitable outcome measure should be tailored to available data and context.

Step 7. Provide feedback on progress to physicians and laboratory professionals working at the departments.

The seventh step in our action plan is *providing feedback on progress of the initiative and results to staff and residents working at the department*. Feedback methods are used widely in health care, including in quality improvement efforts.[32] Behavior change theories suggest that feedback may work in several ways, including through changes in awareness and beliefs, changes in perceived social norms, and through overcoming health care providers' limited ability of self-

assessment. Physicians are often unaware of their suboptimal way of working, and might be motivated to modify their ways if given feedback that their practice is indeed suboptimal compared to guidelines or peers.[32]

The effectiveness of feedback as an intervention varies considerably and can be affected by multiple factors, including how and when feedback is provided. Feedback on ordering behavior can be provided on a group level or on an individual level, with or without comparison to peers, and, in some cases, anonymously. This level of feedback might influence the extent of commitment and effectiveness.[33-35] Other factors that might enhance the effect of feedback include low baseline performance, a supervisor or colleague as source of feedback, a frequency of delivery at least once a month, delivery in both verbal and written formats, and inclusion of targets and an action plan for improvement.[32]

In our project, feedback entailed changes in (laboratory) test volume and costs on a group level. Feedback was provided by members of the local project team through e-mail, posters, or presentations. Upon evaluation, a minority of physicians indicated that they had preferred individual feedback. Unfortunately, this was not possible in the departments participating in the RODEO project, since residents often place orders under the name of the supervisor instead of under their own name. In providing feedback, we found it useful and stimulating to *present examples of successful changes, in addition to items that still had much potential for change and needed explicit attention.*

Step 8. Sustain the reduction on both short- and long-term.

The final step to successful de-implementation is sustaining the effects. Even though laboratory test reduction has been subject of research for decades, study of sustainability remains an evident shortcoming in this field. Only a minority of studies report follow-up data assessing sustainability, which is striking as this can be considered an outcome of successful de-implementation.[7,12,29,36]

In general, one might say that successful initiation of a change effort often does not lead to sustained change.[37-39] Several models have been proposed outlining factors that contribute to sustainability, one of these being the Sustainability Model developed by the NHS. This is a practical framework that identifies ten components within the domains of 'process', 'staff', and 'organization' that play a role in sustaining change.[40] Many of the components described in this model have been addressed in previous steps of our action plan. With knowledge of these components, complemented with the experience gained through the pilot project and the RODEO project, we recommend several concrete, additional actions.[8,9,11]

On the short-term, make sure that new working agreements are sufficiently embedded into daily practice. One way to do this is by continuously paying attention to overuse of diagnostics and frequently reserving time to explicitly discuss overuse. Upon evaluation of the RODEO project, the majority of physicians indicated that unnecessary testing was addressed more than once a week during morning or afternoon reports (53.3%) and grand rounds (56.0%) (**Table 2**). However, only a small percentage of respondents (14.7%) reported that time was reserved explicitly for discussion of unnecessary testing on a weekly basis (**Table 2**), which should be improved in future projects. Putting up a poster in meeting areas displaying general agreements and principles regarding laboratory testing is another way to ensure that the initiative stays under the attention of physicians. To overcome the problem of high resident turnover, it might be useful to also incorporate agreements and principles in the introductory program for new employees. Another way to embed interventions in daily practice is by introducing modifications in ordering systems, which require no further action once they are instated.

To ensure sustainability on the long-term, *we recommend continued monitoring of utilization data* through evaluating and discussing these with department staff and a clinical chemist. In addition, *we recommend making agreements on ownership* by assigning a member of the staff as responsible for maintaining the results and picking the project back up if there is a relapse.

Discussion

In this paper, we propose a step-by-step action plan appropriate for direct use to specifically reduce unnecessary laboratory testing. This plan is based both on knowledge on de-implementation from previous literature and on our experiences with two large projects in which we successfully and sustainably reduced diagnostic (laboratory) testing.[8-10] Strategies to address the encountered barriers and facilitators are embedded in this action plan.

As highlighted in the different steps of our proposed action plan, several facets should be addressed for successful de-implementation of unnecessary testing. First, de-implementation requires a supportive environment in which physicians feel involved and are aware of the importance of reducing unnecessary testing for health care.[17] This involves explicitly emphasizing the potential for patient harm and addressing the purpose of increasing quality of care and resident training, rather than merely focusing on cost reduction, as this often triggers resistance among physicians.[15,16] Several motivated stakeholders (clinical champions) should be involved that can take leadership and act as role models for their peers, both within the clinical and laboratory departments, and within the business control/intelligence department and the Board of Directors. This contributes to creating a safe, blame-free environment needed for de-

implementation.[17] Involvement of the resident group and department staff is also important, as their input, together with knowledge on barriers and facilitators to de-implementation, can be used to tailor interventions and contributes to ensuring fit in the local context.[23] Furthermore, we learned in the RODEO project that changing ordering behavior requires explicit and frequent attention and repetition. Finally, behavior change can be reinforced by feedback on ordering behavior, as physicians are often unaware of their (suboptimal or subconscious) routine practices leading to unnecessary tests, and might be motivated to modify their ways if given feedback on their routine actions.[32,41]

This papers explains, in detail, a suitable approach to successfully reduce unnecessary laboratory testing. Although we focused on laboratory testing, this approach can also be extended to other diagnostics. This action plan is inspired by projects carried out at internal medicine departments. However, observing positive and sustained effects in different settings, makes us believe that this approach will also be effective in other settings and departments. With this action plan, we thus provide a ready-to-use framework for broader implementation of these interventions to reduce overtesting.

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8

Exploring the value of routinely measured hematology parameters for identification of elderly patients at high risk of death at the Emergency Department

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Abstract

Of the warning scores in use for recognition of high-risk patients at the Emergency Department (ED), few incorporate laboratory results. Although hematological characteristics have shown prognostic value in small studies, large studies in elderly ED populations are lacking. We studied the association between blood cell and platelet counts and characteristics as well as C-reactive protein (CRP) at ED presentation with mortality in non-multi-trauma patients ≥ 65 years. Comparison between survivors and non-survivors showed small, significant differences with AUROCs ranging between 56.6% and 65.2% for 30-day mortality. Combining parameters yielded an evident improvement (AUROC of 70.4%). Efforts should be pursued to study the added value of hematological parameters on top of clinical data when assessing patient risk.

Introduction

Early recognition and prioritization of acutely ill patients at the Emergency Department (ED) can be challenging, especially in elderly, in whom illness often presents in an atypical fashion.[1,2] At least 36 warning scores have been developed to support quick recognition of patients that are most likely to deteriorate, with variable rates of implementation in hospitals worldwide.[3] These scores include variables such as heart rate, respiratory rate and temperature. Of the many scoring systems in use in emergency medicine, laboratory results are incorporated in only a few, even though they are routinely obtained and almost immediately available.[3,4]

The predictive value of inflammatory biomarkers at the ED for poor outcomes has been studied extensively. Studies report on the positive association between C-reactive protein (CRP) taken at or early after hospital presentation and (short-term) mortality.[5-9] In addition, previous work has demonstrated associations between leukocyte counts early after hospital presentation, and mortality.[4,10-12] Other parameters associated with mortality include high neutrophil and low lymphocyte counts[13-14], a high corresponding neutrophil-lymphocyte ratio[15-17] and a high platelet-lymphocyte ratio.[18] Although these parameters are directly associated with short-term mortality, their predictive value is limited. Therefore the search for better markers for mortality prediction continues.

In addition to blood cell and platelet counts and their ratios, it is possible that morphologic characteristics measured by modern hematology analyzers are also predictive of mortality. These devices provide information such as cell size, intrinsic properties and cell viability.[19,20] Until now, morphologic parameters have mainly been studied for diagnostic purposes, such as for diagnosing bacterial infections[21], defining asthma phenotypes,[22] and discriminating between lymphocyte pathologies.[23] Yet several smaller studies suggest that some of these parameters, such as neutrophil volume[24,25], coefficient of variation (CV) for lymphocyte cell size[19], platelet volume and distribution width[26] and red cell distribution width (RDW)[27], might also be of prognostic value in selected patient populations.

Large-scale studies on the association between early blood cell and platelet counts and characteristics with mortality in elderly populations are lacking. The aim of this study was to explore the associations of these parameters with 7- and 30-day mortality in an elderly population presenting to the ED, aiming to see if they are more useful in predicting mortality than the well-known markers, CRP and leukocyte count. Additionally, the predictive performance of the combination of these parameters will be assessed, to assess whether prediction models that include these parameters show promise. We specifically chose to study a largely unselected population to explore whether we could identify parameters useful in

patients for whom only little clinical information is known so that they might potentially serve as a triage tool for prioritization of elderly ED patients.

Methods

Study design

In this retrospective observational study using routinely collected health care data, we assessed the association of (morphological) red blood cell (RBC), leukocyte and platelet characteristics and CRP at ED presentation with mortality, aiming to identify parameters more useful in predicting mortality than CRP or leukocyte count.

Setting and study population

For this study, data from the Utrecht Patient Oriented Database (UPOD) were used. UPOD is an infrastructure of relational databases comprising data on patient characteristics, hospital discharge diagnoses, medical procedures, medication orders and laboratory tests for all patients treated at the University Medical Center Utrecht (UMC Utrecht) since 2004. UPOD data acquisition and management is in accordance with current regulations concerning privacy and ethics. The structure and content of UPOD have been described in more detail elsewhere.[28]

The UMC Utrecht is a 1,042-bed academic teaching hospital in the center of the Netherlands, with around 28,000 clinical and 15,000 day-care hospitalizations, and 334,000 outpatient visits annually. The hospital has a large ED, providing emergency care to approximately 21,300 patients annually for all medical specialties.

We retrospectively evaluated patients aged 65 years or older presenting to the ED of the UMC Utrecht from June 1st, 2011, to December 31st, 2017, for whom mortality outcomes and hematology parameters were available. Patients for whom a multi-trauma was registered at the ED were excluded from analyses. For patients who had more than one ED visit during the study period, all visits were included.

Data

The following clinical data were obtained per ED visit: sex, age, treating specialty, the first result for CRP and hematological tests at hospital presentation and data on 7-day and 30-day mortality.

Hematological parameters

The hematological parameters used in this study were obtained through complete blood count analysis, using the Cell-Dyn Sapphire hematology analyzer (Abbott Diagnostics, Santa Clara,

USA). The analyzer provides information on RBC count, leukocyte count and blood platelet count and their characteristics, using spectrophotometry, electrical impedance, laser light scattering and three-color fluorescent technologies.

RBC parameters are measured through impedance measurement and optically using intermediate angle scatter (IAS, 7° scatter) for cell complexity/granularity and FL-3 fluorescence for cell viability. Leukocyte characteristics are measured using the following five optical scatter signals: axial light loss (ALL, 0° scatter) for cell size, intermediate angle scatter (IAS, 7° scatter) for cell complexity/granularity, polarized side scatter (PSS, 90° scatter) for nuclear lobularity, depolarized side scatter (DSS, 90° scatter) for depolarization and red fluorescence (FL-3) for viability. Platelet parameters are measured through IAS scatter (7° scatter) for platelet complexity/granularity and PSS (90° scatter) for platelet lobularity.

Outcomes

Our primary outcome was mortality within 30 days of ED visit, our secondary outcome was mortality within 7 days of ED visit. Information on mortality was extracted from the hospital database and was not available for all patients. A patient was confirmed 'deceased' if death occurred within 7 or 30 days (1) at the ED or during hospitalization or (2) if the date of death was communicated and registered in the hospital system. Patients were confirmed alive after 7 or 30 days if there was contact with the patient any time after 30 days until data extraction was performed in April 2018. For the remainder of patients, mortality status was unknown.

Statistical analysis

For comparison of laboratory values between groups (mortality vs no mortality), Student's T-test or Mann-Whitney-U test was used as appropriate. We corrected for multiple testing using a Bonferroni correction and considered *P* value < .0008 (*P* value 0.05/62 laboratory tests) significant. The predictive power of parameters was expressed as area under the receiver operating curve (AUROC). We adjusted for age and nonlinearity of the data. The shape of the relation with outcome was studied for each parameter using the Hosmer-Lemeshow test, in which we assumed linearity for *P* values > .05. Parameters displaying a nonlinear relation with mortality were transformed by adding splines until the optimal AIC value was reached at which the AUROC was calculated. We also studied the risk of mortality within deciles of laboratory values.

We then explored the predictive power of combinations of hematological parameters for 30-day mortality. Note that CRP was not included as the goal was only to study hematological parameters. The hematological parameters, together with age and gender, were entered into a random forest classification model. No variable selection was performed. We built 100

decision trees and considered five variables at each split in the individual trees to acquire the smallest out-of-bag error. Predictive power was expressed as AUROC.

All analyses were performed using R version 3.4.3. The random forest model was built using the 'randomForest' package.

Missing data

If mortality outcomes or any of the hematological parameters were missing for a visit, this visit was excluded from all analyses. If CRP was missing for a visit, this visit was still included for analyses regarding hematological parameters, yet excluded for analyses regarding CRP.

Results

Between June 1st, 2011, and December 31st, 2017, there were 34,672 visits to the ED by 17,462 unique patients aged 65 years or older for non-multi-trauma causes. Of these, 17,319 visits were excluded due to either missing mortality data or hematological parameters. We included 17,353 visits for analysis of hematological parameters, of which 16,705 were included for analyses regarding CRP. Characteristics of the study population are presented in **Table 1**.

Table 1 – Characteristics of study population

	Mortality data and hematology available	**Mortality data, CRP and hematology available**
Number of ED visits, *n*	17,353	16,705
Male sex, *n* (%)	9,804 (56.5)	9,420 (56.4)
Age in years, median (IQR)	74 (69-80)	74 (69-80)
Top 5 ED specialties, *n (%)*	3,590 (20.7)	3,531 (21.1)
1. Cardiology	2,646 (15.2)	2,600 (15.6)
2. Neurology	2,562 (14.8)	2,488 (14.9)
3. Internal medicine	1,581 (9.1)	1,565 (9.4)
4. Pulmonary medicine	1,245 (7.2)	1,145 (6.9)
5. Surgery		
Destination after ED presentation, *n (%)*	14,165 (81.6)	13,714 (82.1)
Continued care within UMCU	219 (1.3)	215 (1.3)
Transfer to other institution	64 (0.4)	58 (0.3)
Died at ED	2,726 (15.7)	2,561 (15.3)
Discharge	179 (1.0)	157 (0.9)
Other		
Outcome, *n (%)*	1,842 (10.6)	1,784 (10.7)
30-day mortality	870 (5.0)	845 (5.1)
7-day mortality		

Abbreviations: ED, emergency department; IQR, interquartile range; UMCU, University Medical Center Utrecht.

Characteristics of excluded visits are presented in **Appendix 1**. Of visits that were excluded due to missing mortality data, the vast majority resulted in ED discharge (90.0%). For visits with missing hematology parameters, slightly more than half (50.8%) were followed by ED discharge.

Comparison of laboratory values between groups

Table 2 presents the results of the studied laboratory parameters (*n*=62), stratified by the occurrence of death within 30 days. From the acquired hematology parameters, the following ratios were also calculated: neutrophils-to-lymphocytes, platelets-to-lymphocytes and monocytes-to-lymphocytes. After correction for multiple testing, 50 parameters showed statistically significant differences between the two groups, yet, the differences in absolute values were small for the majority of tests.

For 7-day mortality, 36 parameters differed significantly between the two groups (**Appendix 2**). Here too, absolute differences were small for the majority of tests. Absolute values for most tests did not differ much from those in survivors and non-survivors after 30 days.

Table 2 – All laboratory values, stratified by occurrence of death within 30 days

Laboratory value, unit	Alive after 30 days, *n* (visits)=22,143	Deceased within 30 days, *n* (visits)=2,634	*P* value	AUROC (95% CI)
CRP, mg/L	15.00 (3.50-64.00)	40.00 (8.00-121.00)	< .0008	63.8 (62.4-65.2)
Leukocyte count, 10^9/L	9.37 (7.07-12.49)	11.31 (8.21-15.97)	< .0008	65.1 (63.8-66.4)
Neutrophils				
Count, 10^9/L	6.75 (4.60-9.84)	8.84 (5.83-13.02)	< .0008	65.2 (63.9-66.5)
% of total leukocyte count	74.12 (63.95-82.79)	80.26 (70.41-87.14)	< .0008	64.4 (63.1-65.7)
Mean cell size, AU	150.10 (144.80-156.0)	151.90 (145.80-159.90)	< .0008	60.8 (59.4-62.2)
Mean complexity/granularity, AU	136.33 (131.99-140.71)	135.70 (131.40-140.30)	.0009	58.0 (56.6-59.4)
Mean lobularity, AU	123.40 (115.19-131.39)	120.31 (110.50-128.87)	< .0008	60.1 (58.7-61.5)
Mean depolarization, AU	27.59±4.18	27.04±4.81	< .0008	58.6 (57.2-60.0)
Mean viability/red fluorescence, AU	70.99 (69.34-72.67)	71.63 (69.80-73.34)	< .0008	59.6 (58.3-61.0)
CV of cell size, %	2.78 (2.45-3.17)	2.83 (2.50-3.23)	< .0008	57.2 (55.8-58.6)
CV of complexity/granularity, %	3.66±0.65	3.77±0.78	< .0008	59.6 (58.2-61.0)
CV of lobularity, %	8.82 (7.18-9.96)	9.28 (7.88-10.40)	< .0008	60.0 (58.6-61.4)
CV of depolarization, %	15.49±2.43	15.78±3.06	< .0008	58.7 (57.3-60.1)
CV of viability/red fluorescence, %	8.03 (7.12-8.76)	8.05 (7.17-8.74)	.38	57.0 (55.6-58.4)
Segments				
Count, 10^9/L	6.67 (4.57-9.59)	8.53 (5.62-12.17)	< .0008	64.9 (63.6-66.2)
% of total leukocyte count	72.56 (62.99-80.37)	76.63 (65.30-83.14)	< .0008	61.8 (60.5-63.2)
Lymphocytes				
Count, 10^9/L	1.36 (0.88-1.97)	1.15 (0.72-1.84)	< .0008	60.4 (59.0-61.8)
% of total leukocyte count	15.24 (8.95-23.56)	10.82 (6.15-18.33)	< .0008	64.1 (62.8-65.4)
Mean cell size, AU	100.75±5.60	99.25±6.83	< .0008	60.7 (59.3-62.1)
Mean complexity/granularity, AU	76.91±3.45	76.78±3.98	.17	58.3 (56.9-59.7)
CV of cell size, %	4.26 (3.11-5.24)	3.97 (2.67-5.03)	< .0008	58.3 (56.9-59.7)
CV of complexity/granularity, %	4.37±1.17	4.16±1.28	< .0008	59.3 (57.9-60.7)

Table 2 – Continued

Laboratory value, unit	Alive after 30 days, *n* (visits)=22,143	Deceased within 30 days, *n* (visits)=2,634	*P* value	AUROC (95% CI)
Monocytes				
Count, 10^9/L	0.70 (0.51-0.95)	0.75 (0.49-1.07)	< .0008	60.6 (59.3-62.0)
% of total leukocyte count	7.68 (5.74-9.77)	6.65 (4.59-8.95)	< .0008	62.0 (60.6-63.3)
Eosinophils				
Count, 10^9/L	0.09 (0.04-0.18)	0.13 (0.02-0.14)	< .0008	60.5 (59.1-61.9)
% of total leukocyte count	0.98 (0.38-2.14)	0.55 (0.21-1.39)	< .0008	62.9 (61.5-64.2)
Basophils				
Count, 10^9/L	0.03 (0.01-0.05)	0.02 (0.01-0.05)	< .0008	58.9 (57.5-60.3)
% of total leukocyte count	0.32 (0.14-0.58)	0.21 (0.08-0.42)	< .0008	61.7 (60.4-63.0)
Red blood cells				
Count, 10^9/L	4.17±0.73	3.99±0.80	< .0008	60.4 (59.0-61.7)
MCV, fL	90.64±6.77	91.47±7.75	< .0008	58.4 (57.0-59.8)
% red blood cells with MCV>120 fL	1.96 (1.11-3.67)	2.60 (1.45-5.34)	< .0008	61.3 (59.9-62.7)
% red blood cells with MCV<60 fL	0.94 (0.61-1.73)	1.16 (0.72-2.19)	< .0008	60.2 (58.8-61.5)
RDW, %	12.93 (12.09-14.38)	13.70 (12.52-15.57)	< .0008	63.4 (62.1-64.7)
Hb, mmol/L	7.91±1.43	7.55±1.48	< .0008	60.7 (59.3-62.0)
MCH, fmol	1.91 (1.82-2.00)	1.90 (1.80-2.00)	.44	56.6 (55.2-58.0)
MCHC, mmol/L	0.21 (0.21-0.22)	0.21 (0.20-0.21)	< .0008	60.6 (59.3-62.0)
% red blood cells with Hb<28 g/dL	3.64 (1.47-8.97)	5.80 (2.32-13.71)	< .0008	61.8 (60.5-63.2)
% red blood cells with Hb>41 g/dL	0.01 (0.00-0.10)	0.00 (0.00-0.07)	< .0008	58.2 (56.8-59.6)
CV of Hb concentration, %	7.42 (6.74-8.22)	7.52 (6.84-8.33)	< .0008	57.2 (55.8-58.6)
Ht, L/L	38.28 (33.77-42.10)	36.68 (31.75-41.29)	< .0008	60.2 (58.8-61.6)
Mean complexity/granularity, AU	181.80 (180.10-183.40)	182.20 (180.60-183.80)	< .0008	58.4 (57.0-59.8)
Mean viability/red fluorescence, AU	82.90±9.21	82.92±9.85	.93	56.6 (55.2-58.0)
CV of complexity/granularity, %	1.64 (1.52-1.80)	1.65 (1.52-1.80)	.79	56.8 (55.4-58.2)
CV of viability/red fluorescence, %	12.17 (10.86-13.73)	12.33 (11.02-14.05)	< .0008	57.3 (55.9-58.7)

Table 2 – Continued

Laboratory value, unit	Alive after 30 days, *n* (visits)=22,143	Deceased within 30 days, *n* (visits)=2,634	*P* value	AUROC (95% CI)
Reticulocytes				
Count, 10^9/L	66.78 (50.48-87.42)	69.90 (50.44-94.50)	< .0008	58.9 (57.5-60.3)
% of RBC	1.57 (1.19-2.12)	1.69 (1.27-2.42)	< .0008	59.7 (58.3-61.0)
Immature reticulocyte fraction	0.30 (0.28-0.37)	0.33 (0.26-0.41)	< .0008	61.8 (60.4-63.2)
MCV, fL	98.29±13.10	99.24±14.56	.008	59.5 (58.1-60.9)
MCH, fmol	29.61 (27.32-31.32)	29.31 (26.68-31.37)	.009	58.3 (56.9-59.7)
MCHC, mmol/L	29.14 (28.02-30.18)	28.54 (27.42-29.66)	< .0008	61.4 (60.1-62.8)
Platelets				
Count, 10^9/L	239.00 (184.80-309.90)	238.20 (169.60-325.30)	.07	60.8 (59.4-62.2)
MPV, fL	7.57 (6.89-8.37)	7.74 (7.01-8.64)	< .0008	58.6 (57.2-60.0)
PDW, 10 (GSD)	16.16 (15.74-16.62)	16.15 (15.74-16.64)	.47	57.5 (56.1-59.0)
PCT, mL/L	0.18 (0.15-0.23)	0.18 (0.14-0.24)	.69	61.1 (59.7-62.5)
Reticulated platelets, %	2.66 (1.89-3.84)	3.47 (2.35-5.13)	< .0008	64.9 (63.5-66.2)
Mean complexity/granularity, AU	144.40±6.76	144.20±7.88	.33	56.7 (55.3-58.1)
Mean lobularity, AU	124.20 (121.30-127.30)	123.20 (120.10-126.60)	< .0008	59.2 (57.8-60.6)
CV of complexity/granularity, %	17.27 (16.64-17.93)	17.54 (16.80-18.36)	< .0008	61.0 (59.7-62.4)
CV of lobularity, %	13.36 (12.76-14.15)	13.70 (12.93-14.65)	< .0008	60.8 (59.4-62.1)
Ratios				
Neutrophil-to-lymphocyte ratio	5.00 (3.00-9.00)	7.32 (3.84-14.01)	< .0008	63.2 (61.9-64.5)
Platelet-to-lymphocyte ratio	178.00 (115.00-284.00)	206.00 (113.00-338.00)	< .0008	56.7 (55.3-58.1)
Monocyte-to-lymphocyte ratio	0.50 (0.33-0.80)	0.61 (0.36-1.03)	< .0008	61.8 (60.4-63.2)

Values are expressed in "median (interquartile range)" for non-normally distributed data and in "mean±SD" for normally distributed data. After Bonferroni correction, *P* values < .0008 were considered significant. AUROCs after adjustment for age and nonlinearity are presented. Abbreviations: AUROC, area under the receiver operating curve; CRP, C-reactive protein; AU, arbitrary unit; CV, coefficient of variation; MCV, mean corpuscular volume; RDW, red blood cell distribution width; Hb, hemoglobin; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Ht, hematocrit; MPV, mean platelet volume; PDW, platelet distribution width; GSD, geometric standard deviation; PCT, plateletcrit.

Predictive ability of individual laboratory parameters for 30-day mortality

To study the predictive ability of laboratory parameters for 30-day mortality, we assessed the AUROC for individual parameters. AUROCs ranged between 50.2% and 62.5% (data not shown). When adjusted for age and nonlinearity, AUROCs ranged between 56.6% and 65.2% (**Table 2**).

We found an AUROC of 65.1% for leukocyte count and 63.8% for CRP. Neutrophil count (65.2%) performed similarly to leukocyte count and marginally better than CRP. Segment count and percentages of reticulated platelets (both 64.9%), neutrophils (64.4%) and lymphocytes (64.1%) performed better than CRP.

Risk of mortality

To study the association between absolute values and mortality, we studied the risk of mortality within deciles of values. In our study population, 30-day mortality rate was approximately 11% and 7-day mortality rate was approximately 5%. Mortality rates within deciles of CRP and leukocytes are displayed in **Figure 1**. For other parameters, mortality rates within deciles are plotted in **Appendices 3** (for 30-day mortality) and **4** (for 7-day mortality).

CRP

Mortality rates increase in a linear fashion with increasing CRP values. 30-day mortality rates were higher than the overall rate for patients within 6th (12.0%) to 10th (19.5%) decile. For 7-days, mortality rate was higher than the overall rate for patients within the 10th decile (9.2%).

Leukocytes

Leukocyte counts display a U-shaped relation with mortality. Both 30- and 7-day mortality rates were higher than the overall rates for patients within the 9th (15.3% and 7.6%) and 10th decile (21.6% and 11.9%). For patients in the first decile, both 30- and 7-day mortality rates were almost equal to the overall rates.

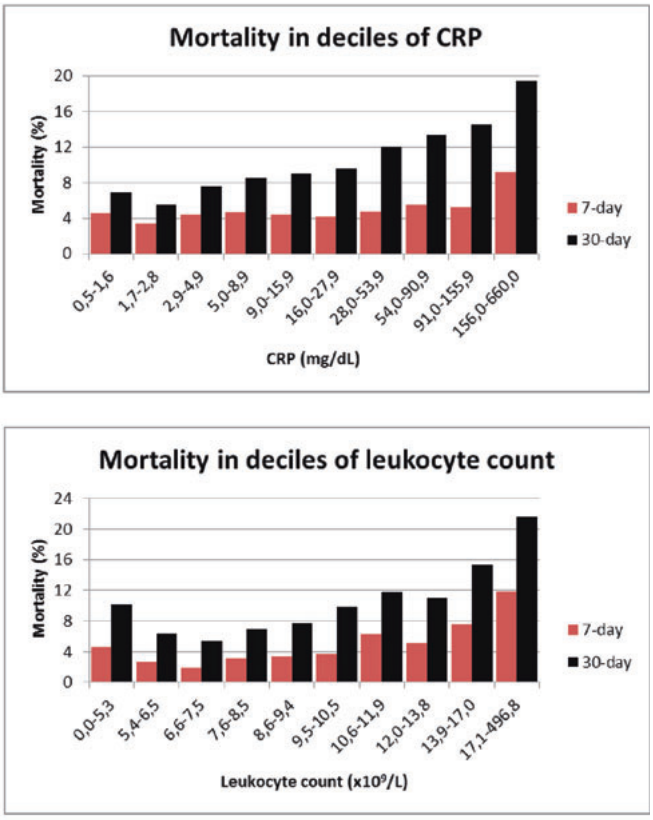

Figure 1 – Mortality rates within deciles of CRP and leukocyte count

Predictive ability of combinations of hematological parameters for 30-day mortality

Joint modeling of all hematology parameters through a random forest model yielded an evident improvement in predictive ability compared with the individual parameters, with an AUROC of 70.4%. Importance of parameters in the random forest model is plotted in **Figure 2**. Importance is expressed as "mean decrease in accuracy", which represents how much the model accuracy would decrease if we were to drop that variable.

According to variable importance, leukocyte count is the most predictive for mortality. Counts and percentages of neutrophils, monocytes, lymphocytes and segments were also important parameters, as were platelet counts and the platelet-to-lymphocyte ratio. In addition, reticulocyte and RBC MCV appeared important, as did RDW and parameters related to hemoglobin concentration.

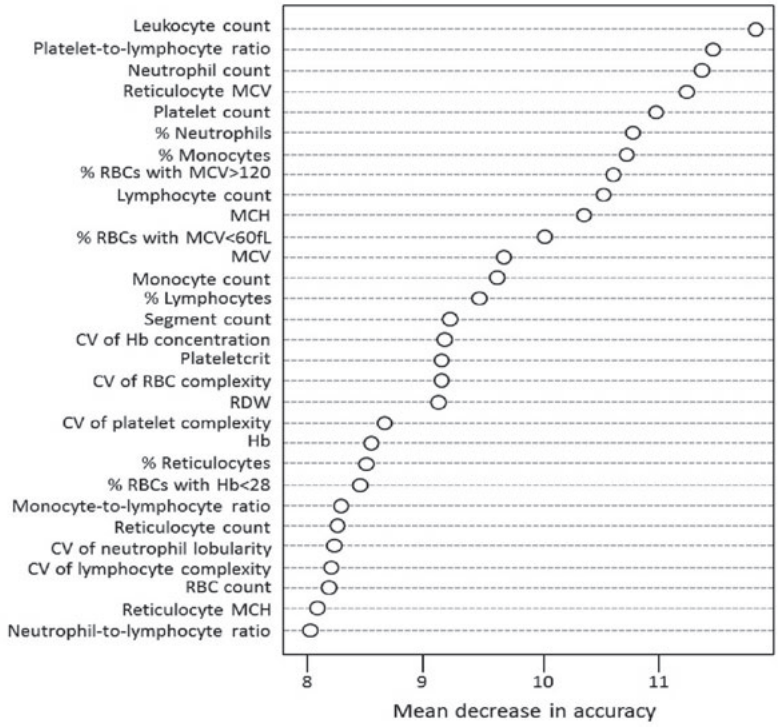

Figure 2 – Variable importance in random forest classification model
Abbreviations: MCV, mean corpuscular volume; RBC, red blood cell; MCH, mean corpuscular hemoglobin; CV, coefficient of variation; Hb, hemoglobin; RDW, red blood cell distribution width.

Discussion

In this paper, we explored the associations of blood cell and platelet counts and characteristics and CRP, at presentation, with short-term mortality in an elderly ED population from a Dutch academic hospital. We found that the differences in absolute values for the studied parameters were statistically significant, yet small, and AUROCs ranged between 56.6% and 65.2% for 30-day mortality. When combining parameters, an evident improvement in predictive ability was found over individual parameters, with an AUROC of 70.4%. Leukocyte count, counts and percentages of most subsets, platelet count, platelet-to-lymphocyte ratio, and measures of reticulocyte and RBC cell size were among the most important variables.

Leukocyte and differential

Upon exploration of our random forest model, leukocyte count seemed to be the most important predictor. Previous studies established a clear positive association between leukocyte count and short-term mortality in acutely admitted patients.[4,10] Although we found,

in line with these studies, that leukocyte count was associated with mortality and that counts were significantly higher in non-survivors, the absolute difference between groups was small.

The higher leukocyte count in deceased patients seemed mainly attributable to an increase in neutrophil and segment counts, parameters that also appeared to be important predictors in our random forest model. It is known that the production of these cells increases in response to stress and inflammation and that they can contribute to tissue injury.[29,30] This association of neutrophils with short- as well as long-term mortality was also established in other studies.[8,31]

Monocyte percentage and count were also important variables in our model. Compared to survivors, non-survivors had significantly higher counts of monocytes, which matches previous research. Although a high monocyte count is often mentioned in the context of cardiovascular disease, it was also identified as a prognostic marker for 30-day mortality in patients with a wide range of pathologies presenting to the ED.[19,32]

Furthermore, lymphocyte count and percentage appeared to be important predictors and, in line with previous studies, we found lower lymphocyte counts in non-survivors.[14,33,34] One of the explanations proposed for this finding is that a low lymphocyte count is a marker of the stress response commonly encountered in acutely ill patients.[30,33]

Red blood cells

From our random forest model, it becomes clear that both the proportions of RBCs with a high MCV as RBCs with a low MCV are important mortality predictors. The red blood cell distribution width (RDW) is a measure of this variability in RBC size. Although the pathways through which higher RDW levels are associated with mortality have not been fully elucidated, it is believed that inflammation and oxidative stress can reduce RBC survival and disrupt erythropoiesis, leading to more heterogeneity in cell sizes.[35] The increased risk of mortality as RDW increases was confirmed by our findings, although its AUROC was not as high as described by some other authors.[27,36,37] For parameters such as hemoglobin and RBC count, their association with mortality is widely known.[38,39]

Platelets

Among platelet parameters, the platelet-to-lymphocyte ratio was a highly important parameter in our random forest model. Its prognostic value has been demonstrated in patients with sepsis[26], acute coronary syndrome[40], acute pulmonary embolism[41], and several malignancies.[42-44] Platelet count also appeared an important predictor of mortality. High counts are believed to reflect underlying inflammation as their proliferation is stimulated by inflammatory mediators, while on the other hand, a low lymphocyte count is believed to be a result of the stress response encountered upon acute illness.[30,33]

Strengths and limitations

To our knowledge, this is the first paper reporting the exploration of (morphological) blood cell and platelet characteristics and counts in an elderly ED population. The size of this study population allows us to explore the combination of multiple hematological parameters in a model.

This study suffers from several limitations. First, mortality outcomes were missing for a large group of patients. Although these patients were similar to the patients we studied in terms of age and presenting specialty, the vast majority of their visits resulted in discharge, which leads us to believe that their risk of mortality was deemed lower than in patients for whom mortality outcomes were known. Secondly, hematological parameters were missing for a large amount of visits. Thirdly, we did not study subgroups of patients. Although this might have led to increased performance, our aim was to identify parameters useful in an unselected population. A final limitation is the lack of validation in a different patient population, such as in patients visiting the ED at a non-academic hospital.

Conclusions and implications

We performed an explorative study on the value of hematological characteristics in predicting short-term mortality in a large, elderly population presenting to the ED and found that a combination of hematological parameters showed good predictive ability. Especially seeing as how these parameters are inexpensive and rapidly available, future research should assess the place of such prediction models in clinical practice, whether that be to add such markers to existing models or to provide these predictions along with laboratory results. Also, the prognostic value of serial measurements of hematological parameters might be an interesting sequel to our study. Applications such as clinical decision support systems provide the opportunity to integrate different types of patient data into information that might aid clinicians' decision making, ideally through yielding a risk prediction for each individual patient.

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Appendices

Appendix 1 – Characteristics of excluded visits

	Missing data on mortality		Missing hematology parameters	
Number of ED visits, *n*	9,895		12,697	
Male sex, *n* (%)	5,231 (52.9)		7,163 (56.4)	
Age in years, median (IQR)	73 (68-78)		73 (69-79)	
Top 5 ED specialties, *n* (%)	Cardiology	2,304 (23.3)	Cardiology	2,399 (18.9)
1	Surgery	1,137 (11.5)	Neurology	1,469 (11.6)
2	Neurology	1,092 (11.0)	Surgery	1,195 (9.4)
3	Int med	987 (10.0)	Int med	1,019 (8.0)
4	Urology	669 (6.8)	Pulmonology	899 (7.1)
5				
Destination after ED presentation, *n (%)*	220 (2.2)		5,541 (43.6)	
Continued care within UMCU	424 (4.3)		232 (1.8)	
Transfer to other institution	-		70 (0.6)	
Died at ED	8,902 (90.0)		6,444 (50.8)	
Discharge	349 (3.5)		410 (3.2)	
Other				
Outcome, *n (%)*	-		792 (6.2)	
30-day mortality	-		356 (2.8)	
7-day mortality	9,895 (100.0)		5,273 (41.5)	
Unknown				

The *'Number of ED visits, n'* for the columns (9,895 + 12,697) do not add up to the actual number of visits that were excluded (*n*=17,319), as overlap exists between both exclusion criteria. For a part of the visits, both mortality data and hematology parameters were missing. Abbreviations: ED, emergency department; IQR, interquartile range; Int med, Internal medicine; UMCU, University Medical Center Utrecht.

Appendix 2 – All laboratory values, stratified by occurrence of death within 7 days

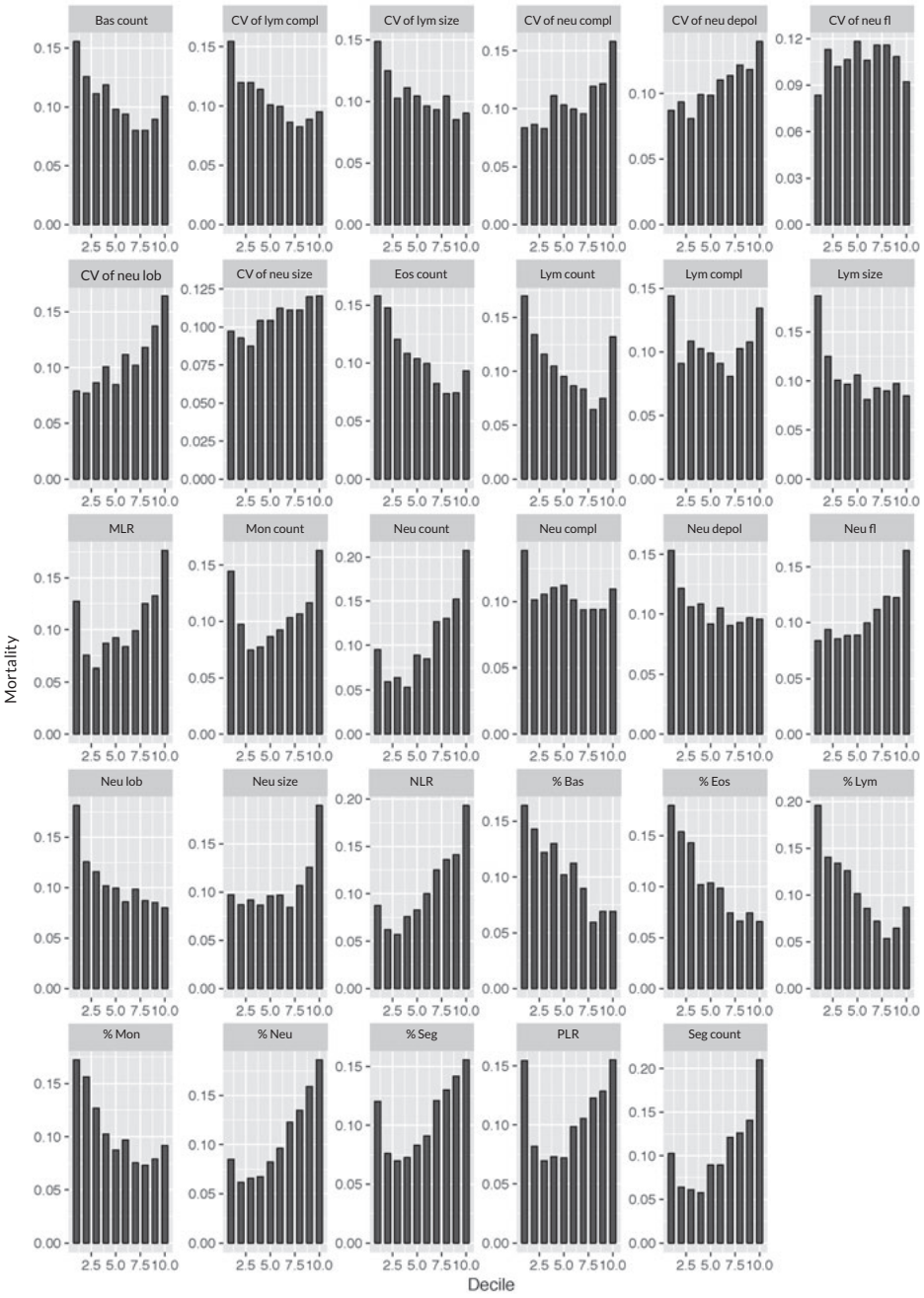
Laboratory value, unit	Alive after 7 days, *n* (visits)=22,143	Deceased within 7 days, *n* (visits)=2,634	*P* value
CRP, mg/L	16.00 (3.80-68.00)	27.00 (5.43-113.00)	< .0008
Leukocyte count, 10^9/L	9.44 (7.10-12.64)	11.89 (8.58-16.55)	< .0008
Neutrophils			
Count, 10^9/L	6.85 (4.63-9.97)	9.45 (6.15-13.58)	< .0008
% of total leukocyte count	74.50 (64.31-83.11)	80.87 (69.48-87.79)	< .0008
Mean cell size, AU	150.10 (144.80-156.20)	152.50 (145.80-160.60)	< .0008
Mean complexity/granularity, AU	136.30 (131.95-140.69)	135.70 (131.50-140.60)	.049
Mean lobularity, AU	123.20 (114.85-131.17)	121.40 (111.55-130.69)	< .0008
Mean depolarization, AU	27.53±4.22	27.39±4.90	.40
Mean viability/red fluorescence, AU	71.03 (69.37-72.71)	71.58 (69.73-73.21)	< .0008
CV of cell size, %	2.78 (2.45-3.17)	2.85 (2.52-3.23)	.0009
CV of complexity/granularity, %	3.66±0.65	3.79±0.81	< .0008
CV of lobularity, %	8.84 (7.22-9.99)	9.31 (7.93-10.41)	< .0008
CV of depolarization, %	15.51±2.45	15.66±3.37	.21
CV of viability/red fluorescence, %	8.03 (7.12-8.76)	8.03 (7.25-8.71)	.64
Segments			
Count, 10^9/L	6.75 (4.59-9.73)	9.03 (5.95-12-65)	< .0008
% of total leukocyte count	72.78 (63.12-80.55)	75.92 (63.20-83.49)	< .0008
Lymphocytes			
Count, 10^9/L	1.35 (0.87-1.95)	1.26 (0.71-2.18)	.06
% of total leukocyte count	14.92 (8.74-23.26)	10.72 (5.92-19.98)	< .0008
Mean cell size, AU	100.67±5.68	98.98±6.89	< .0008
Mean complexity/granularity, AU	76.89±3.49	77.03±3.93	.30
CV of cell size, %	4.24 (3.09-5.23)	4.04 (2.77-5.01)	< .0008
CV of complexity/granularity, %	4.36±1.18	4.26±1.40	.04
Monocytes			
Count, 10^9/L	0.70 (0.51-0.96)	0.74 (0.48-1.05)	.05
% of total leukocyte count	7.65 (5.69-9.76)	6.20 (4.25-8.33)	< .0008
Eosinophils			
Count, 10^9/L	0.09 (0.04-0.18)	0.06 (0.02-0.14)	< .0008
% of total leukocyte count	0.95 (0.37-2.10)	0.47 (0.18-1.26)	< .0008
Basophils			
Count, 10^9/L	0.03 (0.01-0.05)	0.02 (0.01-0.05)	< .0008
% of total leukocyte count	0.31 (0.13-0.57)	0.21 (0.08-0.42)	< .0008
Red blood cells			
Count, 10^9/L	4.16±0.74	4.06±0.82	< .0008
MCV, fL	90.72±6.84	91.82±7.64	< .0008
% red blood cells with MCV > 120 fL	0.96 (0.62-1.77)	1.05 (0.64-1.94)	< .0008
% red blood cells with MCV < 60 fL	1.99 (1.12-3.76)	2.59 (1.49-5.26)	.01
RDW, %	12.99 (12.11-14.48)	13.34 (12.33-15.24)	< .0008
Hb, mmol/L	7.88±1.44	7.71±1.48	.001

Appendix 2 – Continued

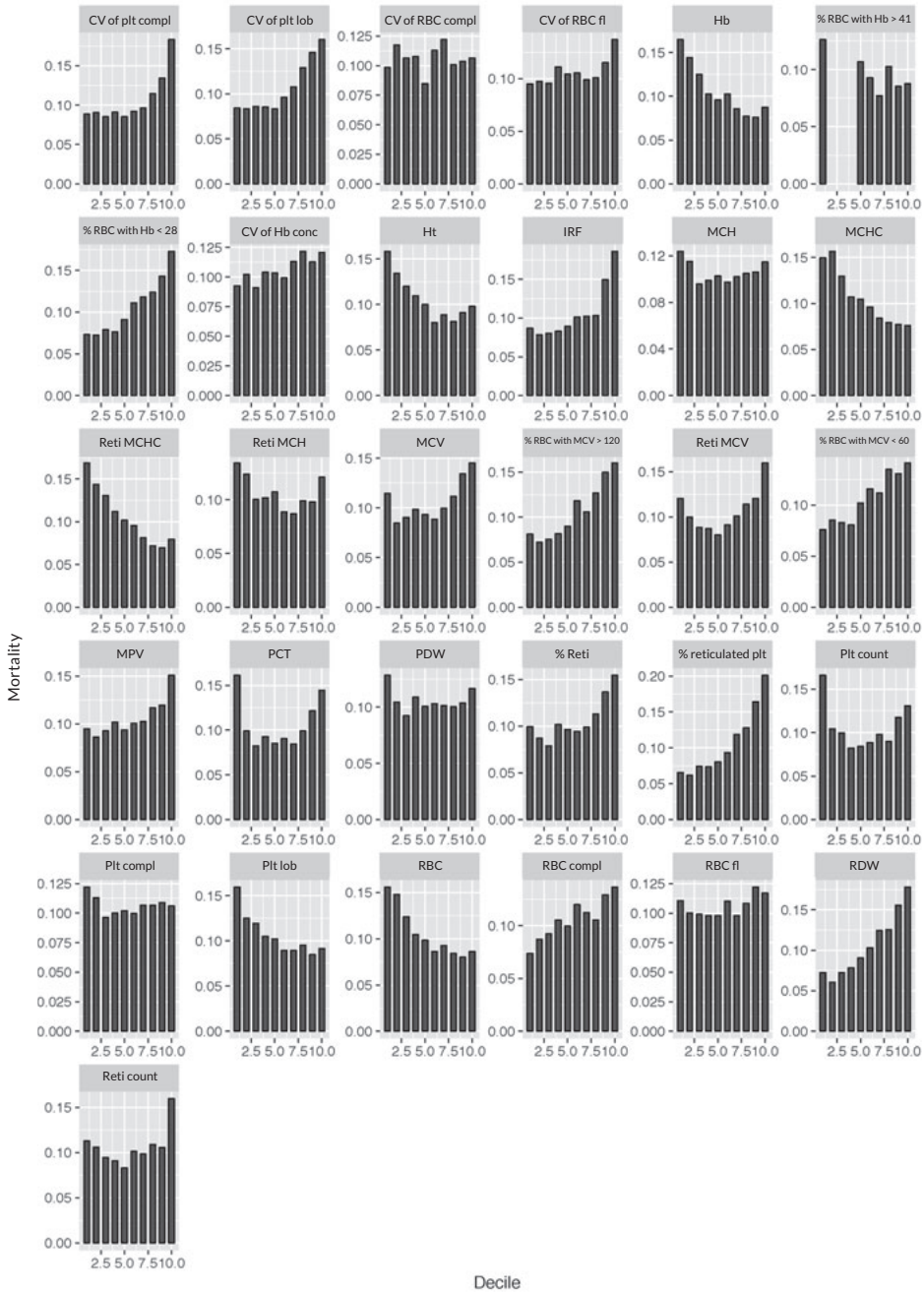
Laboratory value, unit	Alive after 7 days, *n* (visits)=22,143	Deceased within 7 days, *n* (visits)=2,634	*P* value
MCH, fmol	1.91 (1.81-2.00)	1.92 (1.81-2.02)	.11
MCHC, mmol/L	0.21 (0.20-0.22)	0.21 (0.20-0.21)	< .0008
% red blood cells with Hb < 28 g/dL	3.77 (1.51-9.22)	5.44 (2.05-13.88)	< .0008
% red blood cells with Hb > 41 g/dL	0.01 (0.00-0.10)	0.00 (0.00-0.08)	< .0008
CV of Hb concentration, %	7.44 (6.76-8.24)	7.44 (6.75-8.22)	.93
Ht, L/L	38.15 (33.58-42.02)	37.64 (32.79-41.99)	.08
Mean complexity/granularity, AU	181.80 (180.10-183.40)	182.30 (180.60-183.90)	< .0008
Mean viability/red fluorescence, AU	82.89±9.27	83.06±9.44	.62
CV of complexity/granularity, %	1.65 (1.52-1.80)	1.65 (1.51-1.79)	.79
CV of viability/red fluorescence, %	12.19 (10.87-13.75)	12.17 (10.92-13.88)	.36
Reticulocytes			
Count, 10^9/L	66.97 (50.48-87.98)	69.34 (50.25-93.99)	.02
% of RBC	1.58 (1.19-2.14)	1.65 (1.24-2.36)	< .0008
Immature reticulocyte fraction	0.30 (0.24-0.37)	0.32 (0.25-0.41)	< .0008
MCV, fL	98.34±13.18	99.46±14.72	.03
MCH, fmol	29.59 (27.27-31.32)	29.47 (27.04-31.32)	.57
MCHC, mmol/L	29.14 (27.94-30.18)	28.63 (27.42-29.79)	< .0008
Platelets			
Count, 10^9/L	239.10 (184.20-311.30)	234.00 (167.40-311.30)	.001
MPV, fL	7.58 (6.89-8.38)	7.81 (7.13-8.76)	< .0008
PDW, 10 (GSD)	16.15 (15.74-16.62)	16.20 (15.78-16.71)	.07
PCT, mL/L	0.18 (0.15-0.23)	0.18 (0.14-0.24)	.13
Reticulated platelets, %	2.70 (1.91-3.90)	3.37 (2.21-4.99)	< .0008
Mean complexity/granularity, AU	144.40±6.83	144.50±7.85	.67
Mean lobularity, AU	124.20 (121.20-127.30)	123.40 (120.20-126.80)	< .0008
CV of complexity/granularity, %	17.29 (16.65-17.96)	17.52 (16.83-18.40)	< .0008
CV of lobularity, %	13.37 (12.76-14.17)	13.77 (12.95-14.84)	< .0008
Ratios			
Neutrophil-to-lymphocyte ratio	5.00 (3.00-9.00)	7.35 (3.49-14.60)	< .008
Platelet-to-lymphocyte ratio	179.00 (115.00-289.00)	189.00 (94.00-329.00)	.57
Monocyte-to-lymphocyte ratio	0.51 (0.33-0.82)	0.55 (0.30-1.01)	.03

Values are expressed in "median (interquartile range)" for non-normally distributed data and in "mean±SD" for normally distributed data. After Bonferroni correction, *P* values < .0008 were considered significant. Abbreviations: CRP, C-reactive protein; AU, arbitrary unit; CV, coefficient of variation; MCV, mean corpuscular volume; RDW, red blood cell distribution width; Hb, hemoglobin; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Ht, hematocrit; MPV, mean platelet volume; PDW, platelet distribution width; GSD, geometric standard deviation; PCT, plateletcrit.

Appendix 3 - 30-day mortality in deciles of laboratory values

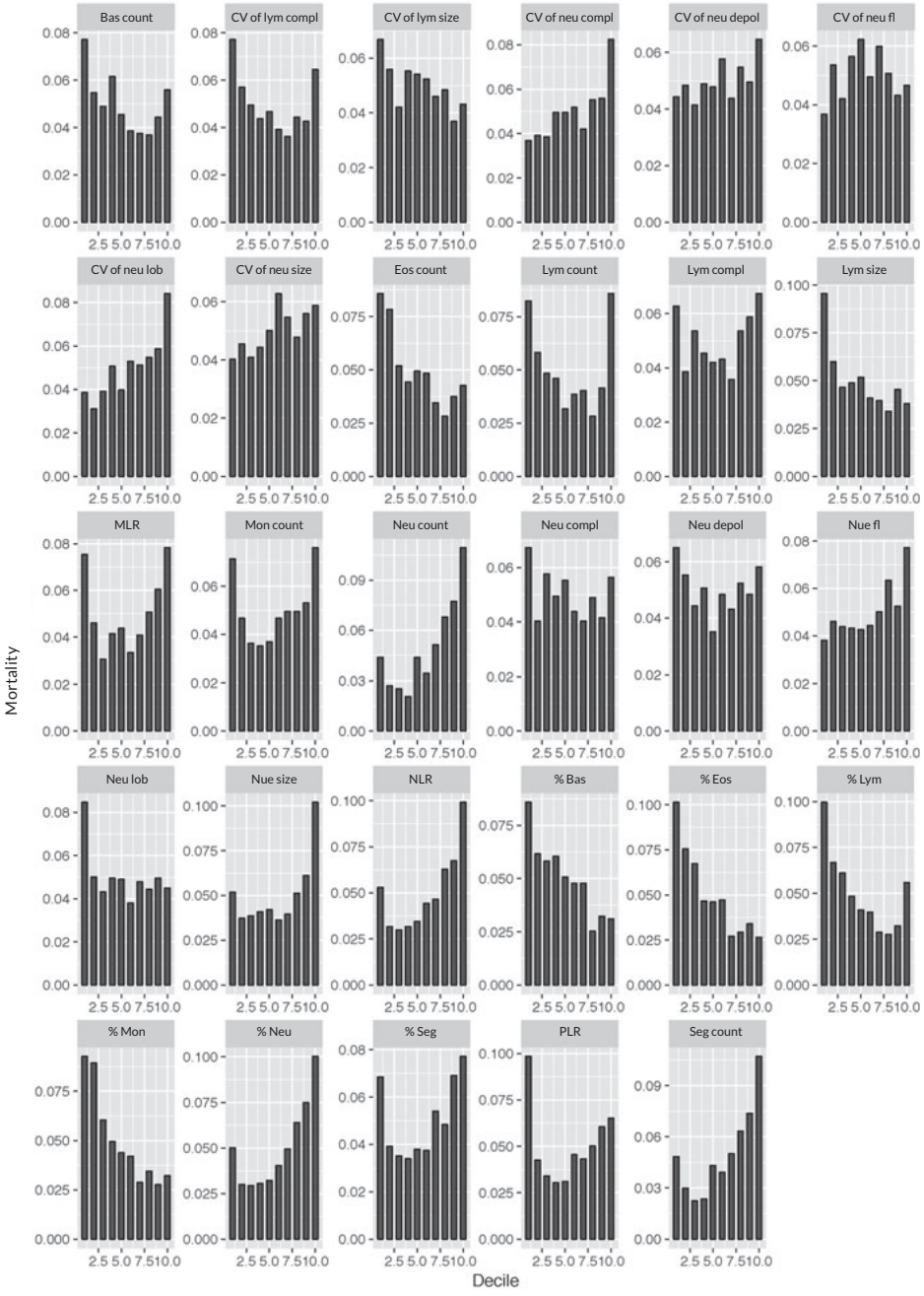


Abbreviations: Bas, basophil; CV, coefficient of variation; lym, lymphocyte; compl, complexity/granularity; neu, neutrophil; depol, depolarization; fl, viability/red fluorescence; lob, lobularity; eos, eosinophil; MLR, monocyte-to-lymphocyte ratio; mon, monocyte; NLR, neutrophil-to-lymphocyte ratio; seg, segment; PLR, platelet-to-lymphocyte ratio;

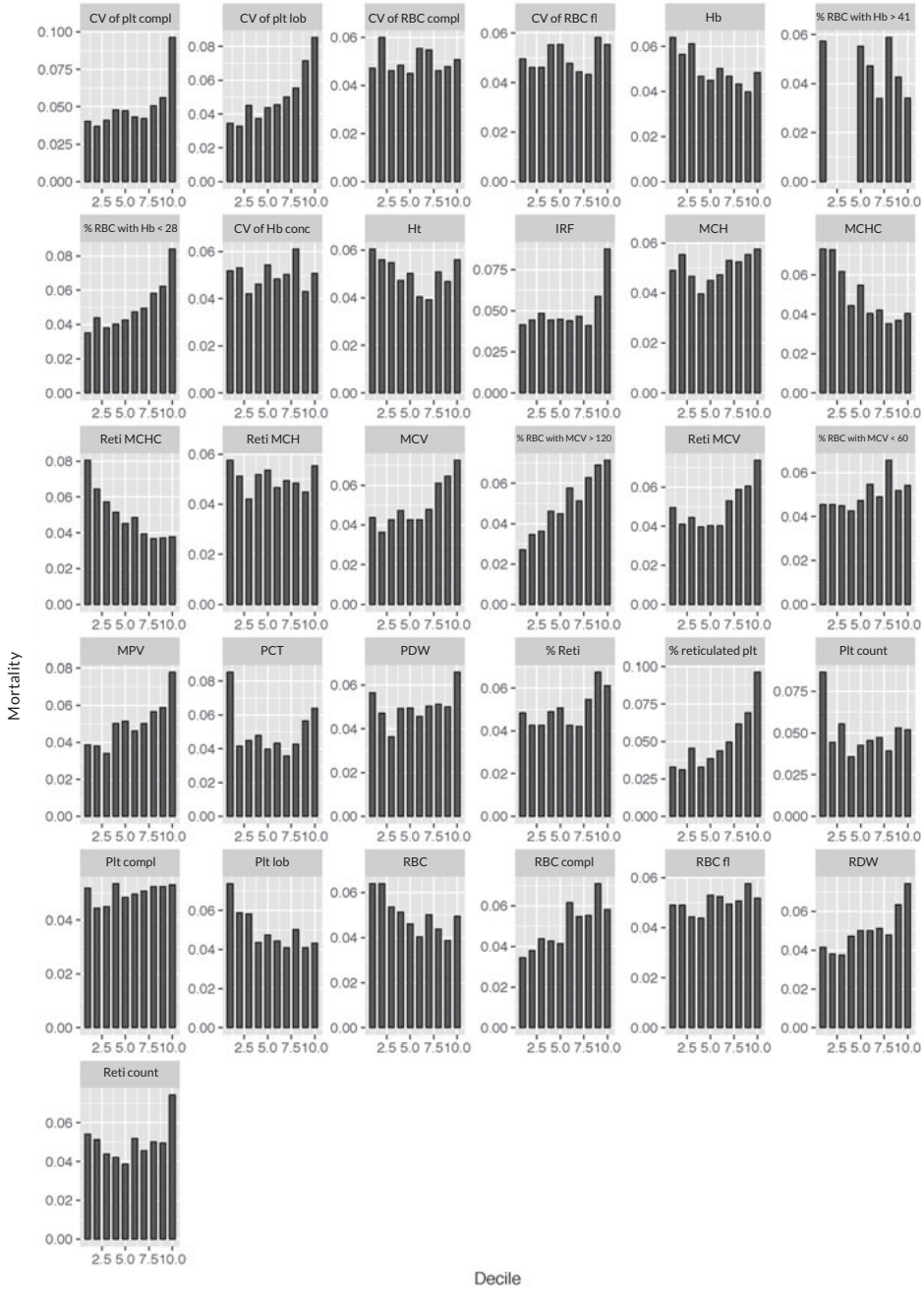


plt, platelet; RBC, red blood cell; Hb, hemoglobin; Ht, hematocrit; IRF, immature reticulocyte fraction; MCH, mean corpuscular hemoglobin; mean corpuscular hemoglobin concentration; reti, reticulocyte; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit; PDW, platelet distribution width; RDW, red blood cell distribution width.

Appendix 4- 7-day mortality in deciles of laboratory values



Abbreviations: Bas, basophil; CV, coefficient of variation; lym, lymphocyte; compl, complexity/granularity; neu, neutrophil; depol, depolarization; fl, viability/red fluorescence; lob, lobularity; eos, eosinophil; MLR, monocyte-to-lymphocyte ratio; mon, monocyte; NLR, neutrophil-to-lymphocyte ratio; seg, segment; PLR, platelet-to-lymphocyte ratio;



plt, platelet; RBC, red blood cell; Hb, hemoglobin; Ht, hematocrit; IRF, immature reticulocyte fraction; MCH, mean corpuscular hemoglobin; mean corpuscular hemoglobin concentration; reti, reticulocyte; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit; PDW, platelet distribution width; RDW, red blood cell distribution width.

9

Summary and general discussion

Value in health care is often defined as 'quality' divided by 'costs'. Determining value in diagnostic testing requires an assessment of whether a test provides benefits that weigh up to its costs or harms, whether a test is more or less (cost-) effective than alternative care, and whether a test fits patient preferences.[1-3] Although targeted through several campaigns and initiatives internationally, de-implementing low-value care and stimulating or preserving high quality care, remains a challenge. Many small scale studies have focused on de-implementing diagnostic testing that is of low value, and on stimulating appropriate use.[4-6] In laboratory medicine, appropriate use entails performing the *Right test, using the Right method, at the Right time, for the Right patient, at the Right cost, for the Right outcome.*[7] Thus, inappropriate use includes overuse, as well as misuse and underuse.

In this thesis, value was mainly addressed by studying overuse of laboratory services in the clinical setting. The purpose of this thesis was to investigate and implement strategies that can be used to reduce unnecessary testing. In the following sections, the most important findings and implications of our studies are discussed. Furthermore, shortcomings in the current body of literature and knowledge gaps are addressed.

The first section of this chapter focuses on overuse of laboratory testing. First, we will describe how to choose strategies to successfully de-implement unnecessary testing. Thereafter, we will address several areas that are in need of improvement. The second section of this chapter describes our vision on the road towards efficient use of tests. Finally, we will discuss implications for future research.

Overuse of laboratory testing

Although the clinical laboratory is considered essential to patient care, the influence of laboratory tests on medical decisions has been difficult to estimate. A study of more than 70,000 patient encounters representing a comprehensive range of conditions and services at an academic medical center determined that, overall, 35% of encounters had one or more laboratory tests ordered. In addition, laboratory test utilization varied with treatment area: 98% of inpatients, 56% of emergency department patients, and 29% of outpatients had at least one test ordered.[8] Internationally, estimates of approximately 20% and 44.8% have been reported for overuse and underuse, respectively, of laboratory testing.[9] Thus, it is conceivable to think that a significant portion of laboratory tests does not add to diagnosis or management of clinical care and does not influence medical decision making. The extent of inappropriate use of tests likely varies depending on the type of tests requested. A study among 200 cases of patients under evaluation for bleeding or thrombotic disorders, in which each case was individually reviewed for appropriateness, revealed over- or underutilization in 77.5% of cases.[10]

For laboratory testing specifically, several organizations such as the American Society for Clinical Pathology (ASCP) and the Netherlands Society for Clinical Chemistry and Laboratory Medicine (NVKC) have developed recommendations on appropriate utilization.[11,12] Although many of these recommendations are supported by some evidence, evidence-based guidelines on laboratory testing guiding indications and recommended frequencies for commonly used tests are lacking. Thus, determining over- or underuse is not always easy. In line with this, optimizing laboratory testing can be difficult.[13,14]

Unfortunately, data on the volume of overuse of tests in the Netherlands are lacking. The same accounts for exact numbers on the volume of low-value care in general that is delivered in the Netherlands, however, several studies targeting different care services indicate that this number varies between 9% and 32%.[15]

Besides wasting resources, poorly chosen diagnostics with overtesting can actually harm patients by carrying a risk of producing false-positive or false-negative results, which can lead to subjecting patients to more, potentially invasive or harmful tests and procedures, or to false reassurance and a derangement of clinical decision making.[16]

The literature review we performed (**Chapter 2** of this thesis) included 84 papers in which several strategies were described that have proven effectiveness in reducing unnecessary laboratory testing. The knowledge gained from this review, and experience from a pilot project at a large academic medical center in Amsterdam, the Netherlands, were used in the "***R***eduction ***o***f Unnecessary ***D***iagnostics through Attitud***e*** Change ***o***f the Caregivers" (RODEO) – project, which was carried out as part of the nationwide "*Doen of laten?*" program aiming to reduce low-value care and was introduced in **Chapter 3** of this thesis.[17-20] As described in **Chapter 4**, we demonstrated that it is possible to reduce volume and costs of diagnostic testing, focusing on laboratory testing, by implementing a multifaceted intervention aimed at changing caregivers' mindset.[21]

How to choose strategies to successfully de-implement unnecessary laboratory testing

Strategies to successfully de-implement unnecessary testing should be supported by evidence and be tailored to the local context.[22,23] Their development furthermore requires an assessment of facilitators and barriers.[24] In this subsection, we will address possible strategies, principles to take into account when determining suitable strategies, and several facilitators and barriers.

From our review in **Chapter 2**, we concluded that strategies effective in reducing unnecessary testing can be categorized into educational, order system-based, audit and feedback, and

other interventions. Nearly all published studies reported positive outcomes. However, heterogeneity in reporting of outcomes between studies made it difficult to compare the effectiveness of different strategies and draw conclusions about which intervention(s) is/are most successful. Still, combined approaches are advocated in other literature and have also proven effectiveness in both our pilot- and the RODEO project.[4-6,17,21]

Important principles in developing interventions and strategies to be used in de-implementation efforts, are that they should be supported by evidence and have a strong clinical basis or rationale.[22,23] In addition, they should fit department's needs, preferences and capacities, and should be developed in such a manner that they can easily be incorporated into daily practice. To ensure a fit in the local context, involving residents and department staff during development of strategies can be valuable as they can provide input that can be used to tailor interventions, and might provide information about which parts are likely to be adopted.[22] The latter was also observed in the RODEO project, in which their involvement was considered a strong facilitating factor.[21]

Developing a de-implementation strategy furthermore requires an assessment of factors enabling ('facilitators') or obstructing ('barriers') that might be of influence.[24] In the RODEO project, we assessed facilitators and barriers throughout the project, in order to tailor strategies and determine the most suitable approach. Using a subdivision made by Grol and Wensing, these factors were divided into individual caregiver or patient factors, social factors, organizational factors, and environmental factors.[25]

Facilitators to de-implementation

Important facilitators identified in the RODEO project included factors from several categories. On an individual physician level, educational interventions supported by scientific evidence, continuous attention for (overuse of) diagnostic testing and enthusiasm of caregivers and clinical leaders acting as role models (clinical champions), were perceived facilitators. With respect to social factors, receiving feedback on ordering behavior and involving different stakeholders, including clinical chemists and especially residents, also facilitated de-implementation. Another enabling social factor involved widespread support from department staff and residents, which is crucial in any de-implementation effort as engaged providers committed to change can take ownership and lead the culture change needed to de-implement practices they are accustomed to.[26] A final social factor facilitating de-implementation was incorporation of newly instated working agreements in day-to-day practice. Finally, on an organizational level, order system changes, for example through modifying standard order panels, instating a pop-up upon ordering a test that is potentially redundant, or installing time limits impeding a repeated order within a pre-specified time interval, were perceived enabling. Our findings regarding factors facilitating

de-implementation of unnecessary testing are consistent with previous literature.[27-29] An additional facilitator identified in previous literature that was not explicitly found in the RODEO project involves de-implementation of unnecessary care leading to lower health care costs.[27]

Barriers to de-implementation

Considering physicians' motivation from previous literature for requesting tests that they themselves perceive unnecessary, barriers to de-implementation involve factors regarding both individual physicians and patients. On the physician side, overutilization can arise by ordering tests out of routine behavior, residents feeling the need for thorough evaluation, perceived expectations from attending physicians for ordering certain tests, and fear of missing clinically relevant information.[30-32] On an environmental level, fear of malpractice lawsuits has been mentioned to be a driver of overtesting in previous literature. In addition, patients often feel that receiving more care, means receiving better care, and their request for testing can contribute to overutilization.[30,33]

Throughout the RODEO project, we identified additional barriers to reducing unnecessary laboratory testing. With regard to social and organizational factors, although the teams aimed to establish clear working agreements, incorporation in daily practice was hampered by the high rate of turnover of residents, which required regular repetition. The most important barrier was on an organizational level, namely obtaining reliable data on ordering behavior. While modifying order systems was an important facilitator, rigidness of modification was sometimes considered a barrier, as providers were not always immediately informed when a test request was rejected, and the time limits for repeated requests were sometimes considered too strict.

Room for improvement in investigating de-implementation of unnecessary testing

Although many studies have focused on de-implementing unnecessary testing, several facets remain understudied, which will be the focus of the following subsection. Firstly, **sustainability** will be addressed, along with the components that play a role in sustaining change. We will use these components to reflect on the RODEO project and identify opportunities and possible pitfalls for sustaining its success. Secondly, this subsection discusses the assessment of effects of reducing laboratory testing on **quality of care**, including measures that might be interesting to investigate in this type of research. Hereafter, the use of **administrative data** in reduction efforts will be discussed, along with limitations to their potential in practice. Finally, **outcome reporting** will be addressed, which we think should be improved in order to perform this type of research better and more efficiently.

Sustainability

Even though laboratory test reduction has been subject of research for decades with literature going back as far as studies originating from the 1960's, an evident shortcoming in de-

implementation research remains the study of sustainability of reduction efforts. Sustainability refers to holding the gains of change, as change has become an integrated way of working instead of something 'added on', even in the face of challenge and variation.[34] In accordance with findings from previous literature, we found in our review in **Chapter 2** that only a minority of studies on interventions for changing the use of laboratory tests reported follow-up data assessing sustainability, which is striking as it can be considered an outcome of successful de-implementation.[4,6,35,36]

In general, one might say that successful initiation of a change effort often does not lead to sustained change.[34,37,38] Sustaining behavior change is believed to be more likely when driven by providers themselves, as this ensures change that improves effectiveness and efficiency and meets patient needs.[37,39] As is the case with initiation of change-, quality improvement-, or de-implementation efforts, identifying factors that might increase or decrease the chances of sustained success is helpful in deciding the most suitable approach, and it is recommended to start planning for sustainability early on. [34,40]

Several models have been proposed outlining factors that contribute to sustainability. [40-43] Of these, the Sustainability Model developed by the NHS is the most comprehensive, and includes components mentioned in other sustainability models. The NHS model is a practical framework that identifies 10 components that play a role in sustaining change. [40] Based on various components related to process, staff and organization, this model yields a score that reflects the likelihood of sustainability of the initiative, and indicates which components need to be addressed further. These components are explained in the following paragraphs, and are used to reflect on the RODEO project.

Process components of sustainability

According to the NHS model, the first component that plays a role in sustaining change is establishing whether the initiative has benefits beyond helping patients: has working become more efficient, is workload or waste reduced? The second component reflects credibility of the benefits: is change supported by evidence, and are the benefits clear and visible? The third concerns adaptability: is the initiative equipped to overcome internal pressure, does the initiative rely on an individual or a group of people, and can the initiative continue when they are not in place? The final process factor entails the effectiveness of the system to monitor progress.

When considering the RODEO project, there were several clear benefits beyond helping patients, including educating physicians, achieving physicians' awareness, and reducing waste. Regarding credibility, the need to reduce unnecessary testing was supported by evidence on potential harms of overtesting and on the financial impact. [44,45] To ensure continuity and

gain widespread support, the local project teams from each participating department were expanded during the project. This way we ensured that when an individual member of the team was not in place, the project continued to receive sufficient support and attention. This proved an effective measure, as residents often change rotation. The data needed to monitor progress were provided by members of the local project teams through existing hospital data sources. Once a blueprint was made by business intelligence/control specialists for extracting these data, collection of data needed to monitor progress could be carried out more efficiently. Physicians working at participating departments were periodically informed on progress.

Staff components of sustainability

The first staff-related component is involvement and training of the staff to sustain the process: is staff involved in the change, and are they trained in the new process? The second component is staff behavior towards sustaining the change, including whether staff is able to share ideas regularly and whether their input is acknowledged. The third and fourth components involve engagement and support from senior physicians and clinical leaders/champions: are leaders respected, trusted and influential, are they involved in the initiative, and do they continuously promote it?

In the RODEO project, staff was informed by local project teams at the beginning of the project, and their input was requested regularly. Staff was instructed to intensify resident supervision regarding test ordering, and they were subjected to all additional interventions, such as educational sessions and order system changes, some of which were continued after the active intervention period had ended. The Boards of Directors of participating hospitals were informed and asked for approval upon initiation of the project. The extent to which they were involved and informed of progress throughout the project differed between clinics. At each participating department, respected physicians/educators were included in the project teams. These were all considered respected clinicians that were highly involved and supportive of the initiative, which was confirmed by physicians working at participating departments upon evaluation of the project. In addition, a key figure from the staff was present in each of the project teams.

Organizational components of sustainability

The first organizational component reflects whether the initiative fits within the organization's strategic aims and culture. The second component has to do with infrastructure to support ongoing change: are physicians trained and competent, are there procedures in place supporting the change, and are facilities and equipment appropriate to sustain change?

The aim of reducing unnecessary testing through the RODEO project was embraced in all participating hospitals. The extent to which this was in line with hospital-wide aims and efforts,

was not fully clear. However, in some clinics, other departments were motivated to carry out a similar project. In a broader perspective, there is increasing attention for reducing low-value care and delivering high quality care through several nationwide projects, including the "*Doen of laten?*" program, which the RODEO project was part of.[20] With regard to infrastructure, providers were continuously confronted with reducing unnecessary testing through, for example, explicit attention, involvement of a clinical chemist in patient discussions, and regular educational sessions, which were continued after the active intervention period had ended. As a high rate of resident turnover might be a threat to continuity, the RODEO principles and new working agreements were repeated regularly through presentations and posters and by inclusion in the introductory program for new employees. In addition, new working agreements were introduced through modification of protocols and electronic ordering systems, which continued to be in place after the active intervention period had ended. All of these efforts contributed to incorporation of the RODEO principles in daily practice. Finally, clinical leaders/champions responsible for ongoing efforts, and tools for monitoring and providing feedback, were appropriate to sustain the effects of the project.

Opportunities and pitfalls

Due to the limited time available for the RODEO project, follow-up was only possible for eight months after the active intervention period ended. However, when considering the components described in the NHS Sustainability Model and reflecting on the extent to which these components were addressed in the RODEO project, it is conceivable to think that the success of the RODEO project will be sustained in the long-term. Naturally, when reflecting on the project, we do see opportunities and pitfalls for sustainability.

Firstly, assessing the full range of benefits of reducing unnecessary testing is not easy. Although carrying out this type of project can improve understanding, awareness and diagnostic reasoning, assessing true cost savings and effects on patient-related clinical outcomes remains difficult. This last facet was previously brought under the attention in **Chapter 6** and will be discussed in more detail below.

Secondly, acquiring data needed for monitoring of effects proved to be difficult and labor-intensive in some clinics, which might be a threat to sustainability. In the RODEO project, this hampered monthly evaluation of ordering behavior in two clinics, and resulted in incomplete data collection and analysis in one. The difficulties encountered upon data acquisition will be discussed further below.

Finally, although staff were instructed to pay specific attention to test ordering practices, we learned upon evaluation of the project that only slightly more than half of residents (53%) felt

like staff members have asked them an adequate number of questions regarding usefulness of test requests. This was striking, since nearly three-quarters of staff members (73%) felt like they had questioned residents adequately. This suggests that there is room for improvement when aiming to sustain the success of the RODEO project, which might be achieved through formal training of staff, or by making the discussion of usefulness of tests part of a checklist of items to address for each patient.

For the pilot project, we were able to assess sustainability for up to six years, which was described in **Chapter 5**. We believe the sustained success of this project was largely attributable to incorporation of interventions in daily practice, establishment of a culture of change in which senior physicians acted as role models for residents, and keeping diagnostic reasoning and (over)utilization under the attention of physicians by several senior physicians acting as clinical leaders/champions. From a practical point of view, diagnostic test ordering patterns and total costs of diagnostics were monitored and presented to the Board of Directors and departmental heads every three months. When unexpected increases in ordering volume or expenses were noted, the topics of overutilization and costs were explicitly brought under the attention of physicians again. Following up on ordering patterns during a prolonged period of time allowed us to take immediate action upon unexpected increases in ordering volume or expenses, thereby contributing to sustainability.

Quality of care

As highlighted several times throughout this thesis, quality of care in terms of patient outcomes is an important feature to consider in efforts to reduce low-value care. From our review in **Chapter 2**, however, we learned that many papers did not report on quality of care in terms of process- or patient-related clinical outcomes, as only 45 of 84 included studies took this into consideration. Of process- and patient-related clinical outcomes, mortality rate (58%), duration of hospital stay (49%), duration of stay at the Intensive Care Unit (ICU) (31%) and rate of readmissions (24%) were the most frequently studied measures.[6] As described in **Chapter 4**, to investigate whether our intervention affected quality of care in the RODEO project, average duration of hospital stay, and rates of repeated outpatient visits, 30-day readmissions and unexpected prolonged duration of hospital stay for patients admitted for pneumonia, were assessed.[21]

Similar to most other studies and in line with the findings from our review, patient-related clinical outcomes were not affected in the RODEO project.[6,21] Although this contributes to the assumption that laboratory testing can be reduced safely, we are aware that the measures currently in use are crude and that their relevance is questionable, as it is unclear to what extent these measures are linked to a reduction in laboratory testing.

Since laboratory testing is often initially performed for diagnostic purposes, investigating consequences of reduced testing in terms of actually missing diagnoses or in time-to-diagnosis would be interesting measures to consider. However, this would require analysis of individual patient files and be relatively labor-intensive. With disease monitoring being another purpose of testing, it can be desirable to monitor measures such as glycated hemoglobin (HbA1c), which might be acquired through the clinical chemistry department. Also, as overtesting can lead to additional downstream tests or procedures, biopsy- and imaging rates might be of interest, although this might also require analysis of individual patient files. In addition, attention should be paid to patient satisfaction, which can be assessed by simply asking patients for their perceptions.

Use of administrative data

As mentioned several times before throughout this thesis, the most important barrier we encountered in the RODEO project was timely collection of reliable utilization data for the Department of Internal Medicine. This was partly because of turnover of the business intelligence/control specialist included in the project team, which is, of course, specific to our project. More common among the departments participating in our project, we noticed that administrative data was often not transparent enough or in the right format to be of direct use, which limited its potential in practice and might have influenced the success of the project, as providing timely feedback on ordering patterns was not always possible. Limitations to the use of administrative data in practice will be illustrated through several examples over the following paragraphs.

Ideally, a test ordered by resident A or staff member B, is registered on the name of either resident A or staff member B, and on behalf of treating specialty C. In some participating hospitals, we noticed that orders by resident A were being registered on the name of staff member B for treating specialty C. This took away the possibility of providing individualized feedback to either resident A or staff member B, which can be desirable since literature shows that a considerable amount of interphysician variation exists in test ordering behavior, indicating at least some degree of overuse.[46,47]

Another situation we encountered that made collection of utilization data for a department difficult, occurred when resident A changed rotation to specialty D. In one clinic, resident A's test orders were still registered for treating specialty C, although the order was placed on behalf of treating specialty D. This occurred because resident A was registered in hospital systems as working at specialty C. Naturally, this was undesirable as it provided large inaccuracies in utilization data for both specialties C and D, that had to be corrected through a complex process to be useful for our project. Although we cannot provide exact numbers, the overestimation of utilization at specialty C was considerable, especially when resident A had changed rotation to a high-utilizing specialty D, such as the ICU.

A third example that limits practical use of utilization data, involves the inability to distinguish between orders placed from different locations. In some clinics it was not possible to trace orders back to those placed in the inpatient, outpatient, or emergency department. This distinction might be helpful in explaining overuse, and in developing and monitoring reduction strategies.

A final example that deserves to be brought under the attention is registration of services after merging of hospitals. In the RODEO project, we included two hospitals that had recently gone through a merger. For one hospital, one location was included and it was possible to exclusively extract data from the included location. For the other hospital, both locations were included and, unfortunately, it was not possible to make a distinction between orders placed at either location. Similar to the previous example, this distinction might be helpful in explaining overuse, and in developing and monitoring (local) strategies.

In conclusion, it seems as though hospital administrative systems are currently not sufficiently equipped for optimal use in efforts to de-implement unnecessary testing, and possibly also to de-implement other types of low-value care. Hospitals should, in our opinion, invest in strategies to more efficiently register and extract relevant data for this purpose. This encompasses registration of orders (or other care services) on the name of the ordering physician, on behalf of the ordering specialty, and by location. Suitable registration methods for this purpose are needed, especially in an era in which de-implementation of low-value care is increasingly important.

In a broader sense, electronic health record (EHR) data can also be used for numerous other purposes, such as those related to improving clinical practice, quality assurance, and provision of information for administrative databases used in research.[48,49] In addition, EHR data can be used for development of clinical decision support tools, which will be further discussed in the subsection "Towards efficient use: the potential of teamwork and clinical decision support" below. Abernathy et al.[49] have described several steps to be of key importance in development of EHR-based datasets that can be of use in quality improvement. These steps include, but are not limited to, an improvement in initial data collection, and transforming content into analyzable data in order to be of practical use. One way to improve data collection is to define which exact data are needed in order to integrate these into a standard workflow. Once data has been collected, content should be transformed into an analyzable format. For structured data, for example laboratory results or clinical patient data such as heart rate or temperature, standardization might be performed computational, given that appropriate rules are instated that ensure accurate mapping. Transforming unstructured data, such as data entered in free-text fields, into analyzable formats can be more complex. For these types of data, the

use of computer algorithms combined with manual review might provide more reliable and accurate mapping. After aggregation and transformation of EHR data into analyzable data, and addressing quality and completeness of data, datasets can be used for quality improvement.[49]

Reporting of outcomes and burden of disease

A final area that needs to be improved in order to perform research on unnecessary testing better and more efficiently, involves the analysis and reporting of the effects of interventions on utilization. As was described in **Chapter 7**, volumes and costs of testing, but also other types of low-value care, are affected by patient load and case mix. In literature on reducing unnecessary laboratory testing, a variety of measures is used to adjust utilization data for patient load. Thus, results of reduction efforts are expressed in many different ways, including, for example, "number of tests per patient", "number of tests per patient day", and "number of tests per admission, visit or discharge".[6] Although there is something to be said for all of the different outcome measures, this heterogeneous way of reporting effects makes comparison between different strategies difficult.

In addition to patient load, utilization data can be affected by case mix. Intuitively, the sicker patients are, the more (diagnostic or monitoring) tests they receive. However, as described in **Chapter 7**, adjusting for case mix is not easy. Theoretically, case mix might be taken into account by classifying patients according to disease severity scores. However, lack of registration of data needed to calculate severity scores, as we encountered upon data collection for the study described in **Chapter 8**, can be a limitation to this approach. Another approach one might consider is assessing case mix in terms of most frequently occurring Diagnosis-Related Groups (DRGs)/Diagnosis Treatment Combinations (DOTs) over a period of time. Although this is not an ideal approach, it might provide an overall idea of whether changes in utilization patterns can be linked to changes in case mix, or at least, occur simultaneously. Finally, case mix might be taken into account by classifying patients according to their DRG/DOT, thus studying only a subgroup of patients for a specific department.

Considering these drawbacks, efforts should be pursued to develop an optimal measure that includes numbers of inpatient admissions, inpatient days, outpatient visits, emergency department visits, day admissions, and case mix, to adjust utilization data. It might be desirable to assign a different weight to each of these components, for example, assigning more weight to an emergency department visit than to a day admission, as one might expect that more diagnostics will be performed during an average emergency department visit. Comparing the average number of tests performed during an emergency department visit with the average number during a day admission, might provide information on the relative weight that should be assigned to each of these components. The same approach might be used for inpatient admissions, inpatient days, and outpatient visits.

Until an ideal strategy is developed, comparing different approaches remains a challenge and fluctuations in utilization might not be fully explained.

Towards efficient use: The potential of teamwork and clinical decision support

Although innovations and medical technologies continuously alter medical practice, physician-patient communication remains at the core of care. By taking the medical history, physicians can gather 60% to 80% of the information that is relevant for making a diagnosis. Of note, patients generally speak of their problems within the first 60 seconds of clinical encounter.[50,51] It is suggested that up to 80% of diagnoses can be made on history-taking alone. Physical examination, laboratory investigations and other medical investigations such as imaging might be necessary or highly important in some clinical scenarios, for example in suspected heart disease, yet seem to remain complementary to thorough history-taking in excluding other diagnostic possibilities and increase physicians' confidence in their diagnoses.[52-54] Thus, making a diagnosis can be viewed as a processing pathway, with a presenting complaint leading to a prior probability of a certain diagnosis, this probability being modified after taking a patient history, again being modified after a clinical examination, and again after complementary investigations or diagnostics, each step increasing or decreasing the probability of disease. By viewing it as such, it becomes clear that additional steps in the diagnostic pathway are not always necessary, for example when disease-probability is already very high based on medical history alone. Conversely, when diagnostic data is not viewed in the context of a diagnostic pathway, it is more likely for investigations to be used inappropriately.[55]

While the diagnostic process is a fundamental step in patient care, this process is not often considered a target for potential improvement.[56] In contrast to the classical vision of an individual physician determining diagnosis, it is suggested that successful diagnosis will increasingly become a team-based activity involving professionals from different disciplines. In this context, formation of an (extended) diagnostic team has been described. The core of this team is formed by the patient and by the primary care team, including treating physicians, nurses, etcetera. If necessary, other professionals may be included in the extended team, including for example clinical chemists, radiologists, pathologists, physical therapists, psychologists and social workers. In these teams, each team member's particular expertise can be put to use. Effective teamwork in the clinical setting requires several conditions to be met that show similarities with the actions performed in the RODEO project. These include direct interdisciplinary interaction, for example by inviting a clinical chemist to clinical patient meetings, requesting feedback on performance, both internally within the team as well as externally through for example patient surveys, and stimulating active participation and seeking input from team members, hereby creating support and enthusiasm.[21,57] In addition

to improving the diagnostic process, we believe this team-based approach can also be valuable for optimizing other care processes and stimulate appropriateness of care.

To this end, computerized decision support systems (CDSS) also show potential, and these types of applications have been mentioned for their potential to reduce errors and increase quality and efficiency of care.[58] By using artificial intelligence methods, such as machine learning techniques, to combine both clinical and patient data and clinical guidelines, CDSS can provide personalized, evidence-based advice on either appropriate diagnostics, management, treatment strategies, or other care processes and decisions, which might aid clinicians' decision making.[59,60]

Taking a first step in this direction, **Chapter 8** described our efforts to explore the clinical usefulness of readily available laboratory markers in order to predict mortality risk. We studied the association between blood cell and platelet counts, percentages and characteristics, and CRP, taken at presentation, with 30-day mortality in an elderly population presenting at the emergency department of the University Medical Center Utrecht (UMC Utrecht), the Netherlands. Although individual parameters were demonstrated to be of limited value in predicting mortality, combining parameters showed good predictive ability. In the face of practical application of these findings, it would be desirable to construct a risk prediction score for individual patients based on these data, complemented with readily available clinical data, such as blood pressure, respiratory rate, heart rate, and temperature. Acquiring a risk prediction score for individual patients might aid in determining the best possible care, and care tailored to patient preferences. With this study, we have explored one area in which CDSS can be added in an attempt to improve or better direct usual care.

When specifically considering appropriateness of laboratory testing, a systematic method to identify unnecessary tests in individual cases is not readily available. However, a recent study among nearly 200,000 inpatients from three academic medical centers describes efforts to systematically identify low-yield laboratory tests by predicting the level of uncertainty and expected information gain through data-driven methods, with the potential to discourage low-value laboratory testing.[61]

Besides in the field of test order appropriateness, the potential of CDSS is being investigated in several other areas of clinical patient care as well, such as safety of drug prescription and guideline adherence.[62,63] Although development of CDSS is complex and has yet to be optimized, their use shows promising improvements in care processes.[64-66] Worldwide, many companies and care providers, including tech giants such as Microsoft, Apple and Google, are investing in developing CDSS and using data-analytics in health care.[67-70] For example, Google and Verily have developed a machine learning algorithm to recognize diabetic eye disease

allowing physicians to improve efficiency and increase screening volume.[71] In collaboration with the ICU of the Amsterdam UMC, location VU University Medical Center, algorithms are being developed to aid physicians in making ICU discharge decisions by using a predictive model that provides each patient with a readmission probability at the moment of possible discharge, based on unexpected readmissions in the past.[68] Other projects, carried out at the UMC Utrecht, include for example development of a prediction model for severity of rheumatoid arthritis aiming to personalize therapy, a model aiming to guide therapy based on personalized predictions for the risk of cardiovascular disease, and a model for early recognition of the risk of cardiovascular complications.[69]

Implications for future research

In an international perspective, the Dutch health care system functions particularly well, and the Netherlands has consistently been among the top three in the ranking of the Euro Health Consumer Index since 2005.[72] Still, the prospect of health care expenses becoming unsustainable if current growth trend continues, calls for improvement.[73] As was the focus of this thesis, one area of improvement entails addressing low-value care. In this context, physicians, policy-makers, health care insurers, and other stakeholders should collectively pursue efforts to stimulate appropriate use. Delivering appropriate, cost-effective and high quality care that fits patient preferences, should be considered a joint responsibility. In the *"Zorgevaluatie en gepast gebruik"* (translated to "Care evaluation and appropriate use'") program, that is being commissioned by the Dutch Ministry of Health, Welfare and Sport, several stakeholders are brought together aiming to evaluate care and stimulate appropriate use. Care evaluation ensures that patients and caregivers can choose the most suitable care, based on scientific evidence, and that available resources are put to appropriate use. The program aims to integrate care evaluation into the regular care process within five years.[74]

An essential step that applies to the Netherlands, and is required to direct further efforts to reduce low-value care in general, is gaining insight into the landscape of low-value care. Knowledge on the volume, the physicians providing, and the patients receiving low-value care, is needed to help identify and prioritize care services that should be addressed, and to determine the most suitable approach. Determining an ideal strategy to gain insight into the extent and specifics of low-value care is challenging and requires analysis of several databases, such as the Dutch Health Authority's (NZa) 'DIS' database that contains information on all diagnoses, activities and care products registered in medical specialist care in the Netherlands[75], and health care insurers databases. When considering low-value laboratory testing, evidence-based guidelines regarding indications and, especially, recommended frequency of commonly used tests are lacking. Future efforts should therefore invest in

development of further diagnostics and treatment guidelines, in collaboration with physicians and laboratory specialists, aiming to more accurately define inappropriate use.

As described in previous sections, more extensive use of electronic systems forms an additional approach to de-implementing low-value care and stimulate appropriate care. In line with this, electronic registration systems offer the possibility to use data-analytics to guide future efforts towards more efficient and appropriate care, thus putting the enormous amounts of data registered in hospitals to additional use, for example through development of CDSS. This furthermore involves the use of benchmark data, i.e., comparing for example performance and utilization data with other institutions. Joint efforts between multiple stakeholders, including physicians, other (medical) professionals, and business intelligence/control specialists are needed to identify areas of improvement to be used as input to formulate improvement goals and strategies, ultimately aiming to increase the quality of care against lower costs.[76]

The rapidly expanding field of (expensive) technological developments and innovations make it possible to diagnose and treat increasing numbers of diseases and patients. Although they provide the opportunity to improve quality and accessibility of care, they are often used on top of existing care rather than as a replacement, thus further driving up costs.[73,77] Therefore, when implementing new diagnostic methods or tests, future efforts should simultaneously focus on de-implementing the old.

A final important concept that requires increased attention is underutilization of tests. Although this thesis focused on overuse of diagnostics, the burden of underuse is also significant and estimated to be approximately 45%.[9] Underuse refers to tests that are indicated but not ordered, possibly leading to delayed diagnosis or misdiagnosis, more downstream diagnostics, and increased costs.[10] Despite these potentially serious consequences, the field of underutilization remains understudied, and should receive more attention in the context of stimulating appropriate use in the future.

In conclusion, further efforts should be pursued to stimulate appropriate use of care services to both increase the quality and safety of health care, and to curb the increase in health care expenditure. To optimally direct future efforts, insight should be gained into volume and specifics of low-value care in the Netherlands. Many strategies have proven to be effective and should be used and tailored to the local context to de-implement low-value care services. More extensive use of electronic systems forms an additional approach by providing the opportunity to integrate patient data into information that might aid clinicians' decision making, and by using data-analytics and machine learning to direct individualized and appropriate care. Lastly, valuable care processes should be considered a joint responsibility and require teamwork.

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Samenvatting
Dankwoord
Curriculum Vitae

Samenvatting

Onnodig gebruik van laboratoriumtesten is een bekend fenomeen in de klinische praktijk. Verschillende soorten interventies zijn bewezen effectief in het reduceren van onnodig laboratoriumonderzoek. Naast het kostenaspect leidt onnodige bloedafname tot minder patiëntvriendelijke zorg en zorgt onnodige diagnostiek voor een toename in het aantal fout-positieve testresultaten. Dit kan leiden tot meer, potentieel schadelijke diagnostische onderzoeken. Hiernaast kunnen overbodige bloedafnames leiden tot iatrogene anemie.

Hoofdstuk 2 van dit proefschrift beschrijft een review van 84 gepubliceerde studies waarin getracht werd om onnodige laboratoriumtesten in de klinische praktijk terug te dringen. Beschikbare interventies werden gecategoriseerd in educatieve interventies, aanpassingen in aanvraagsystemen, audit- en feedback, en overige. In bijna alle studies werd een reductie in volume van testaanvragen gerapporteerd en in 15 studies werd de duurzaamheid van het effect tot twee jaar bestudeerd. Patiënt-gerelateerde klinische uitkomsten werden in 45 studies gerapporteerd, in twee studies werden nadelige effecten gevonden.

Reeds in 2008 is onze studiegroep gestart met het uitvoeren van een project met als doel onnodige diagnostiek terug te dringen door het vergroten van het bewustzijn door middel van een multi-step interventie op de afdeling Interne Geneeskunde van het Amsterdam UMC, locatie VUmc. Hoewel de focus lag op laboratoriumdiagnostiek, nam ook het gebruik van andere diagnostische modaliteiten af. In het kader van het "*Doen of laten?*" programma, uitgevoerd door de Nederlandse Federatie van Universitair Medische Centra, werd dezelfde aanpak geïmplementeerd in vier grote opleidingsziekenhuizen in Nederland in het "***R***eductie van ***O***nnodige ***D***iagnosti***e***k d***o***or Attitudeverandering van Zorgverleners" (RODEO) – project. Het protocol van dit project wordt beschreven in **Hoofdstuk 3** van dit proefschrift, de resultaten worden beschreven in **Hoofdstuk 4**.

De interventie uitgevoerd in het RODEO project bestond onder andere uit het creëren van bewustzijn door middel van onderwijs en feedback, intensivering van supervisie van arts-assistenten rondom laboratoriumaanvragen, en veranderingen in (elektronische) aanvraagsystemen. Interventies werden uitgevoerd door lokale project teams onder begeleiding van een centraal project team gedurende een interventieperiode van zes maanden. Duurzaamheid van het effect werd gedurende een additionele periode van acht maanden bestudeerd. Onze primaire uitkomstmaat was verandering in het aantal laboratoriumtesten. Secundaire uitkomstmaten waren verandering in kosten van laboratoriumtesten, aantallen en kosten van aanvragen voor radiologie, microbiologie en nucleaire geneeskunde, en klinische uitkomsten. Het effect van de interventie werd geanalyseerd met behulp van

een 'autoregressive integrated moving average' (ARIMA) model met correctie voor seizoeneffecten. Data over aantallen aanvragen van negentien vergelijkbare ziekenhuizen werd als controle gebruikt.

De slope voor het aantal laboratoriumaanvragen per patiënt contact is significant veranderd in ziekenhuis 1 (verandering in slope, -1.55; 95% CI, -1.98, -1.11; *P* <.001), 3 (verandering in slope, -0.74; 95% CI, -1.42, -0.07; *P* = .03) en 4 (verandering in slope, -2.18; 95% CI, -3.27, -1.08; *P* <.001). In ziekenhuis 2 werd geen significante verandering gezien (verandering in slope, -0.34; 95% CI, -2.27, 1.58; *P* =.73). Het aantal laboratoriumtesten per patiënt contact nam af met gemiddeld 11.4%, terwijl dit aantal in negentien vergelijkbare ziekenhuizen met 2.4% toe nam. Slopes voor kosten van laboratoriumaanvragen en aantallen en kosten voor aanvragen van andere diagnostiek veranderden ook significant in verschillende klinieken. Er was geen duidelijk negatief effect op klinische uitkomsten waarneembaar. Belangrijke bevorderende factoren waren onderwijs en wetenschappelijke onderbouwing, continue aandacht, feedback over aanvraaggedrag en betrokkenheid van arts-assistenten. Belangrijke belemmerende factoren waren een hoge turnover van arts-assistenten en beperkingen in de beschikbaarheid van data.

Hoewel er reeds veel studies gepubliceerd zijn over interventies met als doel het reduceren van onnodige laboratoriumdiagnostiek, zijn de lange termijn effecten van dergelijke initiatieven vooralsnog onderbelicht. **Hoofdstuk 5** beschrijft de duurzaamheid van het effect van de interventies uitgevoerd in het eerder beschreven project op de afdeling Interne Geneeskunde van het Amsterdam UMC, locatie VUmc. In dit hoofdstuk worden ook de elementen beschreven welke hebben bijgedragen aan een langdurige reductie van laboratoriumdiagnostiek, waaronder onze focus op verminderen van het aantal relatief goedkope, veel aangevraagde testen in plaats van op relatief dure, weinig aangevraagde testen. Hiernaast waren ook incorporatie van interventies in de dagelijkse praktijk en een cultuuromslag waarin supervisoren een rolmodel vormden voor arts-assistenten belangrijke aspecten die hebben bijgedragen aan langdurige reductie.

Naast het gebrek aan follow-up in studies naar reduceren van onnodige diagnostiek, is er sprake van heterogeniteit in rapporteren van uitkomsten en zijn de klinische uitkomstmaten die momenteel gebruikt worden in studies naar onnodige diagnostiek discutabel. Hier wordt in **Hoofdstuk 6** verder op ingegaan. Hiernaast is er in de huidige literatuur tevens een gebrek aan gedetailleerde beschrijving van uitgevoerde interventies, wat replicatie van succesvolle interventies bemoeilijkt. In **Hoofdstuk 7** van dit proefschrift presenteren we een stapsgewijs actieplan geschikt voor direct gebruik om onnodige laboratoriumdiagnostiek te reduceren, gebaseerd op bekende stadia van de-implementatie, aangevuld met inzichten uit de huidige literatuur en onze eigen ervaringen uit het VUmc project en het RODEO project.

In de verschillende hoofdstukken komt als interventie voor het sturen van aanvraaggedrag ook het aanpassen van elektronische (aanvraag)systemen aan bod. Toepassingen zoals klinische beslis-ondersteuningssystemen bieden de gelegenheid om verschillende soorten patiëntdata te integreren tot informatie welke behulpzaam kan zijn voor het nemen van klinische beslissingen, waaronder beslissingen over gepast gebruik van bijvoorbeeld laboratoriumtesten. **Hoofdstuk 8** beschrijft een eerste stap in het ontwikkelen van een dergelijk systeem. De associatie tussen erytrocyt-, leukocyt- en trombocyt aantal en karakteristieken en C-reactive protein (CRP) met 30-dagen mortaliteit werd bestudeerd in 17 353 en 16 705 non multi-trauma gerelateerde Spoedeisende Hulp bezoeken (voor respectievelijk hematologische parameters en CRP) in het UMC Utrecht. Vergelijking van de laboratoriumwaarden tussen 'survivors' en 'non-survivors' toonde kleine, significante verschillen met areas under the receiver operating curve (AUROCs) tussen 56.6% en 65.2% voor 30-dagen mortaliteit. Combineren van parameters leverde een evidente verbetering op met een AUROC van 70.4%. In de context van praktische toepassing van deze bevindingen zou het wenselijk zijn om een risico predictie score voor individuele patiënten te ontwikkelen gebaseerd op deze data, aangevuld met klinische data zoals bloeddruk, ademhalingsfrequentie, hartfrequentie en lichaamstemperatuur. Het verkrijgen van een risicoscore voor individuele patiënten kan behulpzaam zijn bij het vaststellen van de best mogelijke zorg en het aanpassen van de zorg naar de voorkeur van patiënten. Door middel van deze studie hebben we één gebied belicht waarin klinische beslis-ondersteuningssystemen ingezet kunnen worden teneinde de zorg te verbeteren. Hiernaast vormen dergelijke toepassingen ook potentie in bredere zin, bijvoorbeeld in het kader van veiligheid van medicatie voorschriften.

In internationaal perspectief functioneert het Nederlandse zorgstelsel bijzonder goed. Desondanks roept het vooruitzicht op niet-houdbare zorgkosten om verbetering. Om toekomstige initiatieven zo goed mogelijk te sturen zou inzicht verkregen moeten worden in volume en specifieke kenmerken van low-value care in Nederland. Meerdere strategieën zijn bewezen effectief in het reduceren van low-value care en dienen ingezet te worden, aangepast aan de lokale situatie. Gebruik van elektronische systemen heeft veel potentie en zou behulpzaam kunnen zijn bij het sturen van aanvraaggedrag en bij het nemen van andere klinische beslissingen. Toekomstig onderzoek zal de waarde en plaats moeten vaststellen van dergelijke toepassingen in de dagelijkse praktijk. Tenslotte moet het leveren van gepaste zorg en voorkomen van onnodige zorg beschouwd worden als gezamenlijke verantwoordelijkheid van artsen, beleidsmakers, zorgverzekeraars en andere betrokkenen en moet samenwerking tussen verschillende partijen worden gestimuleerd. In het kader van terugdringen van low-value laboratoriumdiagnostiek is hierbij expliciet een rol voor de klinisch chemicus weggelegd in intensieve samenwerking met artsen.

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Curriculum Vitae

Renuka Soraya Chedi-Bindraban was born on the 26th of July 1991 in Amsterdam, the Netherlands, as the second daughter of Rayen Bindraban and Vydia Bindraban-Ramcharan. After graduating high school at the Scholengemeenschap Reigersbos in Amsterdam in 2009, she began her medical study at the University of Amsterdam. She obtained her medical degree in 2015. After graduating, she started working as an internal medicine resident (not in training) at the Spaarne Gasthuis in Haarlem. After this residency, Renuka started working as a PhD candidate at the Laboratory of Clinical Chemistry and Haematology of the University Medical Center Utrecht. Under supervision of Professor Wouter van Solinge and Professor Mark Kramer (affiliated at the Amsterdam University Medical Center, Vrije Universiteit) she studied the value of laboratory diagnostics in the clinical setting. The results of this research are presented in this thesis. In 2019, Renuka started her training in Internal Medicine at the Ziekenhuis Amstelland in Amstelveen. Renuka lives with her husband Wisjaal (2019) in Amsterdam.