The Use of Laboratory Analyses in Sweden

Quality and Cost-Effectiveness in Test Utilization

MIRJA MINDEMARK
Dissertation presented at Uppsala University to be publicly examined in Enghoffsalen, Ing 50, bv, Akademiska sjukhuset, Uppsala, Friday, May 7, 2010 at 09:15 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

Laboratory analyses, essential in screening, diagnosis, treatment, and monitoring of disease, are indispensable in health care, but appropriate utilization is intricate. The overall aim of this thesis was to study the use of laboratory tests in Sweden with the objective to evaluate and optimize test utilization.

Considerable inter-county variations in test utilization in primary health care in Sweden were found; variations likely influenced by local traditions and habits of test ordering leading to over- as well as underutilization. Optimized test utilization was demonstrated to convey improved quality and substantial cost savings.

It was further established that continuing medical education is a suitable means of optimizing test utilization, and consequently enhancing quality and cost-efficiency, as such education was demonstrated to achieve long-lasting improvements in the test ordering habits of primary health care physicians.

Laboratory tests are closely associated with other, greater, health care costs, but their indirect effects on other areas of medicine are rarely evaluated or measured in monetary terms. In an illustrative example of the effects that optimal test utilization may have on associated health care costs it was demonstrated that F-calprotectin, a fecal marker of intestinal inflammation, has the potential to substantially reduce the number of invasive investigations necessary in, and the costs associated with, the diagnosis of Inflammatory Bowel Disease.

Information on trends in test utilization is essential to optimal financial management of laboratories. A longitudinal evaluation revealed that test utilization had increased by 70% in 6 years, and even though the selection of tests more than doubled, a very small number of tests represented a stable, and disproportionately large, share of the total number of tests ordered. The study defines trends and thus has potential predictive values.

In summary, appropriate utilization of laboratory analyses has both clinical and economical benefits on all levels of health care.

Keywords: continuing medical education, cost control, cost savings, physician practice patterns, diagnostic tests, clinical chemistry, primary health care, health care costs, laboratory management, test utilization, trends, cost-effectiveness, inflammatory bowel disease, irritable bowel syndrome, calprotectin, cost avoidance

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“How very imperfect our knowledge must be, both of the healthy and diseased condition of the body, if we do not call in the aid of chemistry to elucidate its phenomena”

–Alfred B. Garrod
List of Papers

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<tr>
<td>ALP</td>
<td>Alkaline Phosphatase</td>
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<td>ALT</td>
<td>Alanine Aminotransferase</td>
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<td>ANOVA</td>
<td>Analysis of Variance</td>
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<td>AST</td>
<td>Aspartate Aminotransaminase</td>
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<td>CD</td>
<td>Crohn’s Disease</td>
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<td>CMA</td>
<td>Cost-Minimization Analysis</td>
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<td>CME</td>
<td>Continuing Medical Education</td>
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<td>CPG</td>
<td>Clinical Practice Guidelines</td>
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<td>CPI</td>
<td>Consumer Price Index</td>
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<td>CRP</td>
<td>C-reactive Protein</td>
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<td>F-calprotectin</td>
<td>Fecal calprotectin</td>
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<td>f-T4</td>
<td>Free Thyroxine</td>
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<tr>
<td>GDP</td>
<td>Gross Domestic Product</td>
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<tr>
<td>HbA1c</td>
<td>Hemoglobin A1c</td>
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<td>HDL</td>
<td>High-Density Lipoprotein</td>
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<td>HSL</td>
<td>Hälsö- och sjukvårdslagen</td>
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<td>IBD</td>
<td>Inflammatory Bowel Disease</td>
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<td>IBS</td>
<td>Irritable Bowel Syndrome</td>
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<tr>
<td>LIS</td>
<td>Laboratory Information System</td>
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<tr>
<td>NPV</td>
<td>Negative Predictive Value</td>
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<tr>
<td>OECD</td>
<td>Organization for Economic Co-operation and Development</td>
</tr>
<tr>
<td>POCT</td>
<td>Point-of-Care Testing</td>
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<tr>
<td>PPV</td>
<td>Positive Predictive Value</td>
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<tr>
<td>rs</td>
<td>Spearman Rank Correlation</td>
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<tr>
<td>SMA</td>
<td>Sequential Multiple Analyzer</td>
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<tr>
<td>SMAC</td>
<td>Sequential Multiple Analyzer plus Computer</td>
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<tr>
<td>T3</td>
<td>Triiodothyronine</td>
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<td>T4</td>
<td>Thyroxine</td>
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<td>TAT</td>
<td>Turn-Around-Time</td>
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<td>TSH</td>
<td>Thyroid-Stimulating Hormone</td>
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<td>U-albumine</td>
<td>Urine albumine</td>
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<td>UC</td>
<td>Ulcerative Colitis</td>
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Introduction

The overall aim and purpose of clinical chemistry, and of laboratory medicine in general, is to aid clinicians in diagnosis, management, and treatment of disease. Being the main source of objective medical data, laboratory tests are an essential part of modern, high-quality health care. The main focus of this thesis is the quality and cost-effectiveness of clinical chemistry laboratory test utilization in Sweden.

The Swedish health care system

Regulation

The Swedish health care system is regulated by The Health and Medical Services Act (HSL, 1982:763) [1]. This framework law was adopted on June 30th 1982, and came into force on January 1st 1983. It has since been revised on several occasions, most recently in 2008. The Health and Medical Services Act states the overall aim of the Swedish health care as “a good health and health care on equal terms for the entire population” [1].

Divisions and responsibilities

According to the Health and Medical Services Act [1] the responsibility for providing good quality health care, and also to act to promote good health in the country as a whole, lies with the counties and regions. Sweden is divided into 18 counties, two regions [2] which have been formed by the merge of a number of counties, and one municipality – the island of Gotland in the Baltic Sea – which carries the same health care responsibilities as the counties [3], see Figure 1. The Health and Medical Services Act also declares that the basis of the counties’ health care planning should be the inhabitants’ need of such health care. In a need-based model such as this, fair and just resource allocation has three dimensions: equity in access, utilization, and quality of care relative to needs [4].

The county of Uppsala is the 6th largest of the 21 counties and regions in the country according to population [5]. The county council directly employs approximately 100 primary health care physicians that work at 31 primary health care centers run by the county council. Each centre is responsible for
its own budget, but the costs of centralized laboratory tests are paid directly by the Primary Health Care Management. There are also a number of independent primary health care physicians with National Insurance Office contracts.

Akademiska sjukhuset in Uppsala is one of the largest tertiary care medical centers in Sweden, and, having been founded over 300 years ago, also the country’s oldest university hospital. In 2008 the hospital had approximately 1 100 beds, 58 000 admissions per year, and more than 750 000 outpatient visits annually. Akademiska sjukhuset serves a population of approximately 327 000 people in the county of Uppsala, as well as the population in the surrounding counties.

Figure 1. Map of counties and regions in Sweden with their respective letter labeling. aMunicipality, bregion.
Three levels of health care

Nationally there are three different levels of health care; primary health care, county or secondary health care, and regional or tertiary health care, each of which has distinct responsibilities. In the 21 counties and regions, including the municipality of Gotland, there are more than 1 000 [6] primary health care centers, approximately 70 county or district hospitals [6], and eight [7] regional or university hospitals, as displayed in Figure 2.

![Figure 2](image)

*Figure 2.* The three levels of health care in Sweden, the foundation of which are the primary health care centers.

The health care centers in Sweden, approximately 25% of which are privately run [3], constitute the foundation of the Swedish primary health care system. According to the Health and Medical Services Act the primary health care sector is responsible for providing the population with such medical attention, nurturance, preventive measures and rehabilitation that does not require the medical or technical resources, or other special abilities, of the hospitals [1]. Primary health care is the second largest of the health care budget entries, and it constituted approximately 17% of the country’s total net health care costs in 2006 [8]. On an average day, more than 50 000 primary physician consultations are performed, along with 92 100 additional primary health care visits [2]. Most of the larger primary health care centers have some kind of point-of-care testing devices on site, but instrumentation varies between counties, and also between health care centers in the same
county, depending on for example the distance between the health care center and the closest central laboratory. Common analyses performed point-of-care at the primary health care centers are for example HbA1c, glucose, U-albumin, CRP, and hematology tests.

The district hospitals are less specialized than the county hospitals, but provide care in a limited number of specialties. The county hospitals, on the other hand, also offer emergency room services, have advanced medical equipment and provide care in most specialties.

All rare and/or complicated diseases and injuries are treated at the regional or university hospitals [6], which work in close co-operation with the medical universities with respect to education and research. The counties and regions that do not have their own university or regional hospitals have an agreement with another county or region, to which they can refer patients in need of highly specialized care. Furthermore, six health care regions have been set up for more advanced care, and the country as a whole serves as one region or service area for the most advanced specialized care in order to ensure maintained competency and skills.

Management and financing

The heavily decentralized responsibility for providing health care in Sweden is, as previously stated, appointed to the counties, and, in a few cases, to the municipalities. The counties have local self-government, which enables them to organize their activities based on local conditions as they see fit. The Swedish health care system is funded through local taxation, government grants, patient fees and other sources of income [3]. The counties are allowed to levy taxes as a percentage of the inhabitants’ income, and in 2007 tax revenues made up approximately 74% of the counties’ total income [9], see Figure 3. Only about 3% of the income is represented by patient fees.

To guarantee equity in resource allocation between the counties, despite large differences in mean income of the inhabitants, as well as in costs of providing care, the tax revenues are subjected to a state-managed tax equalization process [10]. The revenues are equalized and then reallocated based on the counties’ tax bases and levels of expenditure.
Figure 3. The average health care income distribution of the Swedish health care system in 2007.

History of laboratory medicine

The use of more or less sophisticated methods to elucidate the phenomena of the healthy and diseased condition of the body is ancient. Early examples of pioneers in laboratory medicine are Hippocrates (460–370 B.C.), that had a keen interest in microscopy and thought the importance of it, Ayus Veda (500 A.D.), who noted that insects were selectively attracted to the sweet urine of diabetic patients, and Paracelsus (16th century), who urged the alchemists of his time to turn their efforts to the application of chemistry to medicine [11].

The French chemist Antoine François comte de Fourcroy once stated “I feel it strongly and I am convinced that the efforts of chemistry will change the face of medicine” [12]. In line with this conviction, three fundamental beliefs outlined the development of clinical chemistry [13]:

- the idea that a substantial part of the processes in living organisms is of a chemical nature
- the belief that chemical processes can be the cause of diseases
- the idea that chemical phenomena are observable as medical signs in patients and can be used to diagnose and prognosticate disease

In the late 18th century practical implementation was destined to fail because of a lack of adequate chemical methods [14], which resulted in a limited clinical usefulness of laboratory tests at the time. However, as the knowledge
of chemistry expanded, and the analytical methods grew more user-friendly, the applicability and usefulness of laboratory tests increased [15].

The development of clinical laboratories began over 200 years ago, and the first person to use the term ‘clinical chemical laboratory’ is said to be Johann Joseph Scherer [14]. In 1791, A. F. Fourcroy proposed that a chemical laboratory, in which excretions, urines, and various discharges of the sick should be subjected to chemical analysis, should be set up in hospitals in close proximity to the wards [15]. It was around that same time that, among others, George Owen Rees observed the concentrations of blood substances in the urine to commonly be the greatest in the early stages of disease, even before the onset of clinical symptoms, thus revealing chemistry as a valuable asset to improve medicine [16]. Before that, chemistry had not to any greater extent been able to assist the physicians’ diagnosis of disease, a fundamental condition for the creation of laboratories in clinics and hospitals.

Pivotal role in modern health care

The role of laboratories and of laboratory tests has evolved greatly over time. In the beginning, the analytical techniques, mainly of a qualitative nature, were too cumbersome and time-consuming to be adapted for routine use in a clinical laboratory, and hence of questionable use to the practice of medicine. This scenario is far from the sensitive tests with rapid turn-around times of significant benefit for the clinicians’ diagnosis of disease seen today. Laboratory analyses are nowadays routinely used in health care, and it is estimated that laboratory test results leverage 60–70% of all critical decisions such as admittance, discharge and medication [17], positioning laboratory tests as an essential part of an efficient health care system. However, naturally, the relative importance of laboratory tests compared to history-taking and patient examination is dependent on the medical problem at hand and the investigations chosen to elucidate that particular phenomenon [18]. Tests are ordered for several different reasons, some of the most common ones being diagnosis, assessment of disease severity and prognosis, monitoring the course of a disease or the response to therapy, detection of complications, and screening [19]. It is, however, important to keep in mind, that, ultimately, the goal of testing is not the acquisition of information per se, but to improve the outcomes for the patient.

Over-, under-, and misutilization

The utilization of laboratory tests, and thus the costs associated with testing, increases steadily [20-26], and overrequisition of tests has been put forward as a factor potentially contributing to the escalating health care costs. How-
ever, despite ever-increasing test utilization, no positive correlation has been established between the frequency of laboratory usage and the quality of care [22, 27, 28]. Thus, a large portion of tests ordered are deemed unnecessary, inappropriate or superfluous [29-33]. Excess test ordering has been reported to represent as much as 25–40% of all tests [29], and 20–95% of selected tests [30]. It has also been indicated that a significantly larger share of the most commonly ordered laboratory tests are overutilized as compared to less frequently ordered tests [34].

Apart from the increased costs of excess testing, other drawbacks of overutilization include increased unnecessary patient discomfort [35] and an increased risk of generating false positive test results [36]. The risk of generating false positive test results correlates with the number tests that a person is subjected to. In the plausible scenario of a patient undergoing 20 laboratory investigations, chance alone will decrease the likelihood of the patient being classified as normal for all results to 36%, even if he or she is perfectly healthy [37]. This is simply a statistical phenomenon as the normal ranges used when evaluating a test result are designed to include 95% of the healthy population because the reference intervals are defined as the mean of the population ± two standard deviations, see Figure 4.

Figure 4. The principle of the normal reference ranges. \( \sigma \) denotes the standard deviation.

False positive test results contribute to the increasing costs of testing, not only directly through the costs of the individual tests, but also indirectly by increasing costs associated with testing. Abnormal test results may lead to subsequent unnecessary investigations and require follow-up consultations with a physician, costs that are much larger than the cost of the test itself. False positive test results may also cause unnecessary worry, further investigations, and be harmful to patients [38].

To make matters worse, additional tests are often ordered as a consequence of abnormal test results. As many as 10% of requested tests are or-
dered because of previous test results outside the normal reference ranges [39]. Furthermore, the vast numbers of laboratory results produced as a result of overutilization may lead to important abnormal test results being overlooked due to sheer information overload, which, in turn, can lead to delayed treatment [40].

Even though focus has mostly been on excessive testing, misutilization does not only comprise overutilization of tests. Underutilization is likely an as inappropriate occurring issue as overutilization, although not as emphasized [41]. To not perform a test on a patient who could benefit from it is equally inappropriate as overutilization of non-beneficial tests.

**Underlying causes of overutilization**

Many factors are known to influence physicians’ overutilization of laboratory services. These include years of practice and working hours per week [42], uncertainty of likely diagnosis, desire for diagnostic completeness, lack of understanding of the basis, sensitivity and specificity of tests [29], personal routines, tolerance of diagnostic uncertainty, time pressure and tactical motives for test ordering [43], as well as a vast number of various other reasons [39]. Concern about insurance compensation and malpractice suits are yet other factors believed to contribute to overutilization through defensive ordering of tests [44].

The problem of overutilization probably also stems in part from the use of automated ‘continuous flow’ chemistry analyzers, such as the AutoAnalyzer invented by Leonard T. Skeggs in 1957 [45]. Reagents were continuously fed through this kind of analyzer irrespective of the number of ordered tests. Thus, the cost for providing multiple test results was identical to that of providing one for instruments like the Technicon ‘SMA 12/60’ and the ‘SMAC’ [46]. This is problematic, as once a habit of test ordering has been established, it may prove more difficult to change than it would have been if clear guidelines had been provided at the time of test introduction [47].

**Variations in test utilization**

Not only are laboratory tests overutilized, there are also large variations in the test ordering behavior of physicians [28, 48-50]. Variations in clinical practice has been revealed as an important determinant of expenditure for laboratory tests [51], and could therefore further increase the financial burden on the already strained budgets of the health care sector.
Factors previously described as explanatory of variations in test utilization

Several non-evidence-based medicine factors are held as explanatory of variations in test ordering [52]. However, the results are somewhat contradictory, possibly in part due to heterogeneous study structure and differences in the setting and selection of tests studied. A few examples of variation-inducing factors are briefly described below.

The age distribution of the patient population could potentially contribute to variations in test ordering, although findings are not completely unanimous. Studies have reported the highest number of laboratory tests to be ordered for patients 25–64 years of age [49], 65–74 years of age [49], 65–84 years of age [53], as well as that tests are requested more often with increasing age of the patient [54].

Furthermore, a large percentage of the population living in rural areas implies that more primary health care centers are likely to be situated further away from a hospital or laboratory, which in turn has been demonstrated to contribute to variations in test ordering [49, 55]. It might also be more difficult to recruit physicians to such areas, resulting in the proportion of substitute physicians being likely to be greater and the turnover of physicians hence higher, which has been demonstrated to be positively associated with test ordering quantities [54]. Moreover, substitutes as well as regular physicians with heavy workloads are likely to be more difficult to reach with educational efforts on optimal test utilization. Physician density has also sometimes been highlighted as a factor contributing to variations in test utilization [49, 56, 57].

Methods of influencing test utilization

As the resources of the health care sector are scarce, demands are raised to lower the costs while maintaining the quality of care. Appropriate utilization of laboratory analyses has both clinical and economical benefits on all levels of health care [58]. Optimization and standardization of test utilization is therefore essential from an economic perspective, but also from a health care quality point of view. Many attempts have thus been made to alter the test ordering patterns of physicians.

In the quest for optimized and standardized test utilization, several different techniques have been employed, to various degrees of success [59-61]. Even for a specific type of intervention the effects may vary considerably [62]. The apprehension that complex or multifaceted interventions, i.e. a combination of various kinds of interventions targeting more than one behavioral factor, generally is more successful than their simple counterparts in achieving changes in practice [30, 63-65] is lately being questioned [66-68].
In either case, physician behavior is an acquired characteristic, and there are indications that it is much more difficult to change physicians’ test ordering of well established tests than of newly introduced ones [47].

There are several different ways to categorize interventions aimed at changing physicians’ practices. For example, six general methods of reducing the number of unnecessary tests have been suggested; education, feedback, participation by physicians in the effort to change, administrative rules, financial incentives, and financial penalties [69]. However, the interventions may also be categorized as being of a predisposing, enabling, or reinforcing nature [70]. Regardless of categorization, the separate intervention types can be difficult to distinguish as they are often intertwined or used in combination. An uncategorized selection of commonly used methods aimed at improving test utilization is briefly described below.

**Continuing medical education**

Continuing medical education (CME) is a widely used method to promote rational test utilization, generally classified as being of a predisposing nature. The effects of CME have been rather varying [71, 72], but CME has generally produced small or moderate changes in professional practice [68]. However, CME interventions are quite divergent, which makes outcomes difficult to generalize, even though CME interventions using practice-enabling or reinforcing strategies have been demonstrated to consistently improve physician performance [73].

CME has often been reported to have an initial positive effect on the test ordering behavior of physicians, but this effect has in some cases been demonstrated to diminish shortly after the interventions were stopped [31, 74]. However, as most studies have been short – only 45% of a rather large number of studies examined by Solomon et al. analyzed test ordering after the intervention ended [64] – sufficient data on the long-term effects are lacking.

**Feedback and reminders**

Feedback can be described as a method aimed at changing physicians’ future test ordering behavior by providing them with information on their past performance and the consequences of their previous activities. In itself a reinforcing interventional method, feedback is often used in combination with some kind of predisposing educational or audit intervention. The term ‘feedback’ is generally used when the information is provided after or during the performance concerned, whereas feedback given before the performance is fully executed is commonly termed reminders [75]. In line with other methods of influencing physicians’ test requesting, feedback and reminders constructed to change test ordering can be aimed at either, or both, the quantitative or the qualitative aspects of test ordering, i.e. the number of tests re-
quested or the appropriateness or rationality of the ordered tests. The effects of feedback and reminders have been extensively studied, yet it has not been found to be consistently effective [76, 77], its effectiveness ranging from none to moderate [63], nor has an added effect of reminders to that of feedback alone been established [67, 77]. Another influential factor, vital to the effect of feedback, seems to be the intensity with which the feedback is provided [78, 79] and whether it is provided at the correct decision level [79, 80]. Other proposed enhancers of the effects of feedback are achievable benchmarks [81, 82] and the addition of peer interaction and social influence [83]. Whether feedback is economically worthwhile is not yet fully established [84], although occasional studies indicate that it might be [85, 86].

Design of the test request form
A sometimes foreseen way for the laboratory to communicate with and to provide the clinicians with proactive and widespread guidance to appropriate test ordering is the design of the test request form itself, whether it be digital or on paper. Redesigning of the requisition form has been confirmed to be able to significantly decrease the utilization of laboratory tests [87], possibly as a result of increased awareness of the clinical value of the tests, along with a shift in ordering practices from panels to single analyses [88]. Depending on their design, test request forms may allow a more discriminating test utilization [89]. Van Walraven et al. [90] and Zaat et al. [20] both demonstrated that removal of test options from the requisition form resulted in a significant decrease in laboratory utilization. This is not surprising, because, as Lundberg [91] so illustratively put it, “As diners rarely order meals not listed on a restaurant’s menu, physicians are less likely to order tests that are not listed on the requisition form”.

Increased cost awareness
Studies on the effects of interventions aimed at increasing physicians’ awareness of laboratory test charges report contradictory results [30]. For example, Tierney et al. [92], on the one hand, concluded that information on the charges of diagnostic tests at the time of order placement significantly reduced the number and costs of tests ordered, even though the effects did not persist after discontinuation of displaying of charges. Further, Hampers et al. found that even though price information significantly reduced the costs of testing, it was associated with a slightly higher rate of unscheduled follow-up [93]. On the other hand, Bates et al. [94] could not establish any effects of computerized display of test charges on the number of laboratory tests ordered.

Clinical chemistry tests are a typical example of low-cost medical procedures with high aggregate costs [95]. Even if information on the charges of
laboratory tests are displayed at the time an order is placed, it is possible that the prohibitive effect fails to appear as “the deceptively small economic stakes may lull physicians into overlooking overuse of low-cost practices” [96]. This is a dilemma, as it has been demonstrated that low-cost high-frequency tests account for the major share of total laboratory costs [97]. This, in combination with the fact that little technologies may account for far more of the overutilization than big expensive technologies [98], builds up to a catch-22 situation.

Clinical practice guidelines

CPGs originated in the US in the early 1980s, initially as a cost containment exercise [99], and they rapidly grew in popularity. The standard definition of CPGs is “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances” [100]. The goal of CPGs is to standardize selected aspects of medical care to ensure high quality, consistency, and cost-effectiveness [101].

Put to use, CPGs are recommendations designed to reduce practice variations, improve health care quality and consistency, and decrease the costs of care through a reduction in laboratory test utilization [102]. Although guidelines can improve clinical practice, the extent of the improvement may vary considerably [103]. Most interventions have accomplished only modest to moderate improvements in care, and the evidence base to support which method would be the most efficient in disseminating and implementing guidelines is inadequate [66].

There does not appear to be a single effective way to ensure that guidelines are used in practice [99]. For example, guidelines implemented in combination with changed order template design and educational efforts only demonstrated a modest reduction in routine testing, and, despite the intervention, the absolute number of laboratory tests ordered remained higher than would be predicted on the basis of the guidelines [104]. Other studies have demonstrated a decrease in the utilization of tests targeted in the guidelines, but with a simultaneous increase in the use of other tests [105].

Effects of altered test utilization

The laboratories are often among the first disciplines to be targeted for budget reductions, most likely because of a combination of easily discernable costs and of the assumption that reduced utilization of laboratory services would bring about an immediate and comparable reduction in costs. It has, however, been demonstrated that a reduction in test utilization produces disproportionately small true cost reductions; a 50% reduction in overall laboratory testing would only achieve a 20% cost reduction [106]. Further-
more, it does not necessarily follow that a reduction in test utilization will lead to a decrease in the overall health care costs. One further concern that has been raised in connection with implementation of methods designed to alter the test ordering habits of physicians is that reduced laboratory test utilization would result in more hospital referrals. However, in a study by Winkens et al., where the use of diagnostic tests was reduced through feedback, those suspicions were refuted [107].

**Proper test utilization**

Appropriate test utilization involves choosing the right investigation in the right patient population, at the right time interval. In achieving proper test utilization, focus should, however, not merely be put on the act of test ordering alone. The aspect of appropriate test utilization should instead be widened to comprise also the question of whether the information generated in the form of test results is appropriately used by clinicians.

In the interface of laboratory and physician, two phases have been described, the first one being the phase in which tests are requested, and the second one when test results are delivered to and responded to by the physician. These phases are labeled utilization and response phases, respectively [108]. The utilization phase could be considered to contain four fundamental questions:

1. What tests should be ordered?
2. Which tests should not be ordered?
3. In what sequence should the tests be ordered?
4. How frequently should the tests be ordered?

The thereupon following response or decision making phase, on the other hand, is deemed as having two principal considerations:

1. What do the laboratory results mean?
2. What action should take place based upon the results?

The concern as to whether test results are optimally utilized by physicians has been demonstrated not to be fully without foundation. Available laboratory data may in as many as 30% of cases fail to elicit an appropriate clinical response [109, 110], and laboratory findings may even pass unnoticed [111].

In their different ways physicians, the laboratory, the hospital, the public, and third-party payers, at all levels of health care, all stand to benefit economically as well as clinically from appropriate test utilization [58].
Health care costs & laboratory expenditures

The cost of health care in Sweden, as well as in many other countries, increases every year [21, 22, 112], and more rapidly so than the GDP [113]. In 2001, the net costs of health care in Sweden were €14 106 million (inflation-adjusted according to the consumer price index in 2008 euros). By 2008, the total expenditure had reached €20 640 million [114]; an increase by over 46% in only seven years [115]. The GDP, on the other hand, had during the same period only increased by approximately 20% [116]. The costs of health care in Sweden, expressed as a percentage of GDP, were in 2005 9.2% [117], which is slightly above the 8.9% average of the OECD-countries [118]. That puts Sweden in 11th place (see Table 1), spending a significantly lower percentage of GDP on health care compared to the top-ranked United States, which spent 15.2% of GDP on health care in 2005 [118].

Table 1. Total expenditure on health care expressed as a percentage of GDP.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Country</th>
<th>% of GDP spent on health care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>United States</td>
<td>15.2%</td>
</tr>
<tr>
<td>2</td>
<td>Switzerland</td>
<td>11.4%</td>
</tr>
<tr>
<td>3</td>
<td>France</td>
<td>11.1%</td>
</tr>
<tr>
<td>4</td>
<td>Germany</td>
<td>10.7%</td>
</tr>
<tr>
<td>5</td>
<td>Belgium</td>
<td>10.6%</td>
</tr>
<tr>
<td>6</td>
<td>Austria</td>
<td>10.3%</td>
</tr>
<tr>
<td>7</td>
<td>Portugal</td>
<td>10.2%</td>
</tr>
<tr>
<td>8</td>
<td>Canada</td>
<td>9.9%</td>
</tr>
<tr>
<td>9</td>
<td>Denmark</td>
<td>9.5%</td>
</tr>
<tr>
<td>10</td>
<td>Iceland</td>
<td>9.4%</td>
</tr>
<tr>
<td>11</td>
<td>Sweden</td>
<td>9.2%</td>
</tr>
<tr>
<td>12</td>
<td>Norway</td>
<td>9.1%</td>
</tr>
<tr>
<td>13</td>
<td>Greece</td>
<td>9.0%</td>
</tr>
<tr>
<td>14</td>
<td>Italy</td>
<td>8.9%</td>
</tr>
<tr>
<td>15</td>
<td>Australia</td>
<td>8.8%</td>
</tr>
</tbody>
</table>

Of the total health care costs, laboratory expenditures only account for approximately 4% in Sweden [119]. The corresponding figures are 20% in the United States, 4% in the United Kingdom, 5.2% in Australia, and 7–10% in Canada [120]. In 2000, the total annual cost of laboratory testing in Sweden was estimated at approximately €0.7 billion, half of which was constituted by the costs of clinical chemistry tests [50], the largest of the laboratory medicine subspecialties.

Although they only account for a very small part of the total health care costs, the laboratories are often among the first disciplines to be targeted for budget reductions as their costs are easily discernable. However, the impact of laboratory test utilization on health care as a whole is widespread and the monetary value of the effects are difficult to measure.
IBD and IBS

An illustrative example of the effects that laboratory test utilization may have on associated health care costs is in the differential diagnosis between Inflammatory Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS) through the use of the laboratory test F-calprotectin.

IBD, which includes Crohn’s disease (CD) and ulcerative colitis (UC), and IBS are both chronic gastrointestinal disorders that share the characteristic symptoms of, among others, abdominal pain, bloating, and altered bowel habits [121]. Although they have many key symptoms in common, IBD and IBS are fundamentally different as the former is organic and the latter functional in character. The functional gastrointestinal disorders, of which IBS is the most common, account for up to 40% of referrals to gastroenterologists, and are characterized by gastrointestinal symptoms that cannot be explained by structural or biochemical abnormalities [122]. Up to 22% of the population in North America is reported as having symptoms of IBS, and the prevalence is similar in Japan and China [123]. In comparison, the prevalence rates of CD and UC in Europe range from 8.3 to 214 and from 21.4 to 243 per 100 000 people, respectively. In North America the prevalence rates of CD range from 26.0 to 198.5 and for UC from 37.5 to 246 per 100 000 people [124]. IBD was previously most common in the Western world, but is now increasing in incidence in other parts of the world where it used to be rare [125].

As IBD and IBS share key symptoms and are both commonly occurring, although IBS is by far the more frequent, gastroenterologists are often faced with the diagnostic challenge of differentiating patients with IBD from those with IBS. Due to the symptom overlap it can be difficult to distinguish between the two based on anamnesis and clinical assessment alone [126]. Differential diagnosis, although broad [127], is essential and of great importance to the direction of further diagnostic interventions, medication, and prognosis. Prompt diagnosis is vital in facilitating early initiation of treatment, especially in children and adolescents, to prevent adverse effects such as delayed onset of puberty, impaired growth, and unnecessary suffering [128].

Treatmentwise, and for prognostic reasons, it is thus essential to successfully distinguish the organic from the functional gastrointestinal diseases. The gold standard for diagnosing IBD is endoscopy, primarily colonoscopy, with histological assessment of biopsy specimens [129]. As there is no single pathognomonic symptom for either IBD or IBS, many IBS patients are also, unnecessarily, investigated extensively with invasive imaging techniques such as endoscopy to reach a diagnosis of exclusion. Endoscopy is not only invasive, but also resource intensive, requires patient preparations [130], and is associated with the inherent risks of such invasive procedures [131], as well as a hesitancy of patients to undergo them [132]. Endoscopies are thus
not suitable for frequent use, especially not in children, where general anesthesia is often required. There is consequently a need for a non-invasive, simple, and cheap test that could provide objective evidence of whether the underlying disease is organic or functional. A test that will effectively rule out IBD, which requires further investigations, could aid clinicians in deciding which invasive investigations to request or possibly to avoid in cases in which the diagnosis indicated is IBS. The most striking difference between IBD and IBS is that the former is inflammatory in nature. Thus, one possibility to differentiate between the two would be to measure surrogate markers of intestinal inflammation.

Calprotectin

Calprotectin was first described by Fagerhol et al. in 1980 [133]. This protein, earlier referred to as L1 [134], MRP-8/14 or S100A8/S100A9 [135, 136], calgranulin [137], and cystic fibrosis antigen [138], has a molecular mass of 36.5 kDa and consists of two heavy and one light chain [139]. It is a calcium- [136] and zinc-binding [140] phagocyte-specific S100 protein [141], which comprises about 60% of the cytosolic protein contents of neutrophil granulocytes [142]. Each granulocyte contains 2–5 pg calprotectin per cell [139], comparative to the amount of hemoglobin in one erythrocyte [143].

Calprotectin is released from the neutrophils when they are activated and the protein concentration in feces can rise to over 100 times the normal level in connection with for example IBD [144]. Estimation of calprotectin is advocated for early assessment in patients who present with symptoms suggestive of IBD. Patients with active IBD will have markedly elevated levels of fecal calprotectin, whereas patients with IBS will have normal levels [145, 146]. The cut-offs most commonly used clinically when distinguishing IBD from other gastrointestinal diagnoses is 50 μg/g feces and 100 μg/g feces, respectively. Initially a higher diagnostic precision in distinguishing IBD from non-IBD diagnoses was demonstrated for a cut-off of 100 μg/g [147], but recently the use of a cut-off of 50 μg/g has been suggested [148, 149].

Lately, calprotectin has been recognized as a promising marker of neutrophilic intestinal inflammation, which, when measured in feces, has a good overall diagnostic precision in discriminating IBD from non-IBD diagnoses, e.g. IBS, and is equally good in children and adults [150-154]. F-calprotectin also has potential in treatment follow-up, monitoring of disease activity, and as a prognostic marker for relapse in patients with known IBD who are in remission: situations in which evaluation of F-calprotectin levels has demonstrated promising results as an investigative method alternative to endoscopy [155-164].
Aims

The utilization of laboratory tests increases steadily, and consequently also the costs associated with such testing. Many of the tests ordered are, however, deemed unnecessary, and, as the demands to lower the costs of care rise, the need for information about test usage increases.

The overall aim of this thesis was to study the use of laboratory tests in Sweden with the objective to evaluate and optimize laboratory test utilization. Considering the importance of laboratory analyses in modern health care, it is of utmost importance to increase the understanding of the usage of such tests. Efficient test utilization is a major part of cost-efficient, high-quality health care. In more detail, the aims of the individual papers were as follows:

Paper I
To study the long-term effects of continuing medical education on the utilization of a number of clinical chemistry laboratory analyses to determine the permanence of educational effects on test ordering behavior.

Paper II
To determine the extent of regional variations in test utilization and the influence of factors earlier described as explanatory, as well as to calculate the achievable cost savings associated with optimized test ordering.

Paper III
To assess the cost-effectiveness of using F-calprotectin as a first-line screening test to minimize unnecessary invasive procedures and set direction for the overall diagnostic approach for IBD.
Paper IV

To describe and evaluate longitudinal trends in costs, charges, and test utilization at the Clinical Chemistry and Pharmacology Laboratory at Akademi- ska sjukhuset, a large tertiary care university hospital in Uppsala, Sweden.
Materials

The data used in the studies included in this thesis were retrieved from the following sources:

The Laboratory Information System of the Clinical Chemistry and Pharmacology Laboratory at Akademiska sjukhuset (Papers I–IV)

In Paper I, the test orders of the included primary health care physicians were monitored by production statistics obtained from the Laboratory Information System (LIS). The test orders of 2004 for 23 general practitioners at 16 primary health care centers that participated in the initial continuing education as well as the ones placed by the same physicians in 1997 were retrieved.

In Paper II, data on all tests ordered by the primary health care centers in the county of Uppsala in 2004 were retrieved.

In Paper III, data on the initial F-calprotectin test results of 3 639 patients at Akademiska sjukhuset performed during 2008 were extracted from the LIS of the Clinical Chemistry and Pharmacology Laboratory.

In Paper IV, data on all test results generated at the Clinical Chemistry and Pharmacology Laboratory from January 1 2002 through December 31 2008 were retrospectively extracted.

The Laboratory Information Systems in the studied counties, excluding Uppsala (Paper II)

Variations in the use of 16 clinical chemistry tests were evaluated for 223 primary health care centers in eight counties in Sweden using test request data. Representatives in the respective counties were contacted and asked to provide data on all the test orders made by physicians at all primary health care centers in their county.
Annual reports (Paper IV)

Demographic data as well as data on institutional characterization of Akademiska sjukhuset and of the Clinical Chemistry and Pharmacology Laboratory, respectively, were extracted from the annual reports of 2002 and 2008 of Akademiska sjukhuset as well as of the Academic Laboratory, of which the Clinical Chemistry and Pharmacology Laboratory is one of the six sub-units.

Sjukvårdsdata i fokus (Papers II and IV)

Information and statistics on the number of consultations with a primary health care physician per year, as well as per inhabitant per year, along with data on physician density, and the total net costs of health care in Sweden, were retrieved from the online database ‘Sjukvårdsdata i fokus’ [Health care data in focus] provided by the Swedish Association of Local Authorities and Regions (Sveriges Kommuner och Landsting).

Statistics Sweden (Papers II–IV)

Data on changes in CPI and GDP, the age distribution of the population in the studied counties, the number of inhabitants in the Swedish counties, as well as the country as a whole, were retrieved from the online ‘Statistics database’ provided by Statistics Sweden (Statistiska centralbyrån).

Swedish National Rural Development Agency (Paper II)

Data on the percentage of the population in each county living in rural areas were retrieved from the statistics database of the Swedish National Rural Development Agency (Glesbygdsverket).

The official fee schedules of Akademiska sjukhuset (Papers II–IV)

The charges for laboratory tests and colonoscopies were retrieved from the respective official fee schedules of Akademiska sjukhuset.
Methods

Statistical analyses were performed using SAS 9.1 software, StatSoft Statistica 8.0 statistical software, or Microsoft Excel 2003. The statistical methods used in this thesis include the following:

Sign Test (Paper I)
Due to sample size and the data not being normally distributed, a non-parametric test was most suitable for the statistical calculations performed in Paper I. Sign Test, a non-parametric alternative to the paired \( t \)-test to compare two sets of results for the same samples, was used for all comparisons of differences in ratios between 1997 and 2004 evaluated in Paper I. The level of significance was set to 5% for each test. Calculations were made using StatSoft Statistica 8.0 statistical software.

Kruskal–Wallis test (Paper II)
The Kruskal–Wallis test was used for the between-group comparisons when assessing the extent of differences in practice between the investigated counties regarding the laboratory test utilization, as judged by the median test ratios. Kruskal–Wallis is the non-parametric equivalent of the parametric one-way ANOVA. It is applied to the comparison of the medians of three or more unmatched samples that need not have the same number of measurements. These calculations were performed using SAS 9.1 software.

Bootstrap (Paper II)
The 95% confidence interval for the median of each of the 13 investigated ratios was calculated for each county using a bootstrap procedure with 10,000 replications. The bootstrapping method allows an estimate of the distribution of the statistic to be made through establishment of a number of hypothetical datasets. The random sampling was performed with replacement, meaning that some ratios will be included in the sample multiple
times, whereas other ratios might not appear at all. These statistical analyses were performed using SAS 9.1 software.

Spearman’s Rank Correlation Coefficient (Paper II)
When investigating if variables earlier described in the literature as explanatory of variations in test ordering were correlated to the inter-county variations in test ordering seen in Paper II, the non-parametric Spearman Rank Correlation Coefficients were calculated for the evaluated factors using StatSoft Statistica 8.0 statistical software.

Cost-minimization analysis (Paper III)
In cost-minimization analysis (CMA) input costs are measured and compared, and outcomes are assumed to be equivalent. CMA can be used to determine the least costly option for a specific situation, such as in Paper III, the least costly method in the diagnostic work-up of IBD. The CMA was performed using Microsoft Excel 2003.
Results and Discussion

Paper I. Long-term effects of an education programme on the optimal use of clinical chemistry testing in primary health care

CME, a widely used method to promote rational test utilization, has often been reported to have an initial positive effect, although this effect has occasionally been shown to decline once the intervention is concluded [31, 74]. However, as most studies on the effects of CME have been short, long-term data are lacking [64]. The objective of this study was to determine the long-term effects of a short audit CME intervention that had displayed positive short-term influence on laboratory test utilization [165].

The educational effects were monitored using ratios of laboratory tests. Maintained or improved ratios were interpreted as a sustained educational impact. 92% of the studied ratios had remained at the same level or improved further since the short-term follow-up, suggesting long-term educational effects. Table 2 and Table 3 display the changes in medians between 1997 and 2004 for the ratios investigated.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AST/ALT</td>
<td>0.057</td>
<td>0.031</td>
<td>−0.026</td>
<td>0.302</td>
<td>ns</td>
</tr>
<tr>
<td>Bilirubin/ALP</td>
<td>0.250</td>
<td>0.139</td>
<td>−0.111</td>
<td>0.485</td>
<td>ns</td>
</tr>
<tr>
<td>Cholesterol/HDL-cholesterol</td>
<td>1.000</td>
<td>1.217</td>
<td>0.217</td>
<td>1.129</td>
<td>ns</td>
</tr>
<tr>
<td>Cholesterol/all tests</td>
<td>0.026</td>
<td>0.058</td>
<td>0.032</td>
<td>0.076</td>
<td>ns</td>
</tr>
<tr>
<td>Sodium/potassium</td>
<td>0.032</td>
<td>0.075</td>
<td>0.043</td>
<td>0.144</td>
<td>ns</td>
</tr>
<tr>
<td>T3/TSH</td>
<td>0.029</td>
<td>0.022</td>
<td>−0.009</td>
<td>0.091</td>
<td>ns</td>
</tr>
<tr>
<td>T4+tT4/TSH</td>
<td>0.273</td>
<td>0.237</td>
<td>−0.036</td>
<td>0.174</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns = not significant.

As attitudes toward an intervention highly predict behavioral intention [166, 167], we sought to evaluate the participants’ attitudes towards the educational intervention and the contents of it. Our CME aimed to bring about changes in test ordering by creating an understanding of why optimization...
was necessary and what improvements the altered test ordering behavior would convey. The education was designed to use scientifically supported recommendations regarding test utilization to convince the participants of the benefits of changing their test ordering pattern rather than forcing change by economic means of control. Thus, in addition to the evaluation of changes in the participants’ test ratios over time, a short questionnaire was used to investigate the physicians’ attitudes toward the contents of the course and the perceived importance of similar educational efforts. The absolute majority stated that they regarded the information given in the course as being very useful in performing their daily work, and the general opinion conveyed that continuous implementation of the education should be pursued. The fact that the physicians have such positive attitudes toward the continuing education and the knowledge acquired during the course is very important, as “neither doctors nor other personnel can be expected to respond favorably to change with which they do not agree” [165].

The results suggest that CME can bring about long-lasting changes in test ordering. CME is thus a suitable means of improving quality and cost-efficiency in test utilization.

Table 3. Ratios that were expected to have remained the same or to have increased.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium/all tests</td>
<td>0.000</td>
<td>0.019</td>
<td>0.019</td>
<td>0.017</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Methylmalonate/all tests</td>
<td>0.000</td>
<td>0.001</td>
<td>0.001</td>
<td>0.004</td>
<td>ns</td>
</tr>
<tr>
<td>Ferritin/all tests</td>
<td>0.011</td>
<td>0.006</td>
<td>−0.005</td>
<td>0.010</td>
<td>ns</td>
</tr>
<tr>
<td>TSH/all tests</td>
<td>0.115</td>
<td>0.072</td>
<td>−0.043</td>
<td>0.169</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Triglycerides/cholesterol</td>
<td>0.842</td>
<td>0.813</td>
<td>−0.029</td>
<td>0.533</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns = not significant.

Paper II. Costly regional variations in primary health care test utilization in Sweden

Variations in clinical practice have been demonstrated to be an important determinant of expenditure for laboratory tests in primary physician services [51]. The responsibility for cost control and proper use of laboratory investigations has been argued to be particularly important for primary health care physicians who often are the first to see and assess patients and thus determine the initial number of tests to be ordered [21]. In this study we therefore determined and evaluated the variations in test utilization in primary health care. For all ratios investigated, there were significant inter-county differences (see Figure 5 and Figure 6) yet, separately, none of the demographic variables investigated were able to explain the variations, see Table 4. The inter-county
differences in test utilization are likely influenced by over- as well as under- and misutilization in combination with local traditions and habits.

Table 4. The investigated variables and their respective Spearman Rank Correlation Coefficients.

<table>
<thead>
<tr>
<th>County</th>
<th>Tests/1 000(^a) inhabitants</th>
<th>% ≥65 years(^b)</th>
<th>% in rural areas(^c)</th>
<th>Consultations per year(^d)</th>
<th>Physician density(^e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalarna</td>
<td>1 788</td>
<td>19.9</td>
<td>3.7</td>
<td>1.25</td>
<td>0.5</td>
</tr>
<tr>
<td>Gävleborg</td>
<td>2 030</td>
<td>20.0</td>
<td>1.4</td>
<td>1.36</td>
<td>0.6</td>
</tr>
<tr>
<td>Halland</td>
<td>1 743</td>
<td>17.9</td>
<td>0.002</td>
<td>1.52</td>
<td>0.6</td>
</tr>
<tr>
<td>Jämtland</td>
<td>4 452</td>
<td>19.9</td>
<td>29.4</td>
<td>1.37</td>
<td>0.6</td>
</tr>
<tr>
<td>Kalmar</td>
<td>3 348</td>
<td>20.6</td>
<td>0.99</td>
<td>1.33</td>
<td>0.6</td>
</tr>
<tr>
<td>Sörmland</td>
<td>2 325</td>
<td>18.7</td>
<td>0.03</td>
<td>1.26</td>
<td>0.5</td>
</tr>
<tr>
<td>Uppsala</td>
<td>1 853</td>
<td>14.6</td>
<td>0.31</td>
<td>1.10</td>
<td>0.6</td>
</tr>
<tr>
<td>Östergötland</td>
<td>2 019</td>
<td>17.8</td>
<td>0.19</td>
<td>1.05</td>
<td>0.5</td>
</tr>
</tbody>
</table>

\(r_s/\) 0.527 0.429 0.167

\(^a\)The number of clinical chemistry tests ordered per 1 000 inhabitants, \(^b\)The percentage of the population aged ≥65 years [167], \(^c\)The percentage of the population living in rural areas [168], \(^d\)The mean number of consultations with a primary health care physician per inhabitant per year [169], \(^e\)The physician density per 1 000 inhabitants [169], \(^f\)The Spearman Rank Correlation Coefficient for correlations between the number of ordered tests per 1 000 inhabitants and the respective variables.

The estimated total savings achievable over a period of one year per 100 000 inhabitants ranged from €13 920 to €184 598, see Table 5. The median savings associated with optimized utilization of the tests in group A outweighed the median costs incurred by optimized usage of the group B tests by about 10%.

Table 5. Achievable cost savings.

<table>
<thead>
<tr>
<th></th>
<th>Highest median ratio(^a)</th>
<th>Second lowest median ratio(^a)</th>
<th>Lowest median ratio(^a)</th>
<th>Cost per numerator test</th>
<th>Range of yearly savings/1 000 inhabitants(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST/ALT</td>
<td>0.998</td>
<td>0.107</td>
<td>0.002</td>
<td>€4.1</td>
<td>€505–58 682</td>
</tr>
<tr>
<td>Bilirubin/ALP</td>
<td>1.000</td>
<td>0.325</td>
<td>0.314</td>
<td>€1.6</td>
<td>€95–15 402</td>
</tr>
<tr>
<td>Cholesterol/HDL-cholesterol</td>
<td>1.454</td>
<td>1.023</td>
<td>1.013</td>
<td>€2.1</td>
<td>€116–5 391</td>
</tr>
<tr>
<td>Cholesterol/all tests</td>
<td>0.047</td>
<td>0.022</td>
<td>0.018</td>
<td>€2.1</td>
<td>€3 740–10 888</td>
</tr>
<tr>
<td>Sodium/potassium</td>
<td>0.994</td>
<td>0.187</td>
<td>0.057</td>
<td>€1.6</td>
<td>€1 788–30 858</td>
</tr>
<tr>
<td>f-T3/TSH</td>
<td>0.267</td>
<td>0.056</td>
<td>0.028</td>
<td>€8.8</td>
<td>€1 869–21 664</td>
</tr>
<tr>
<td>f-T4/TSH</td>
<td>0.995</td>
<td>0.426</td>
<td>0.344</td>
<td>€5.7</td>
<td>€5 818–41 713</td>
</tr>
<tr>
<td>Total savings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>€13 920–184 598</td>
</tr>
</tbody>
</table>

\(^a\)Each of the highest, second lowest and lowest median ratios in group A are displayed irrespective of county origin to indicate achievable ranges of savings. \(^b\)The range of total savings per 100 000 inhabitants that could be achieved through optimized test ordering is indicated in 2008 euros based on the official fee schedule of Akademiska sjukhuset for 2008.
Figure 5. Group A ratios. The numerator analyses should be low in relation to the denominator analyses. The median ratios and their 95% confidence intervals are presented. The county with the lowest median ratio is displayed at the top.
Figure 6. Group B ratios. The numerator analyses should be high in relation to the denominator analyses. The median ratios and their 95% confidence intervals are presented. The county with the highest median ratio is displayed at the top.
The study revealed large regional differences in test utilization in primary health care in Sweden, and it was established that the total yearly expenditures for laboratory tests could be substantially reduced. Even when the costs incurred by extended use of the group B tests were taken into account, the savings from optimized ordering of the group A tests still outbalanced the increased costs. Optimized utilization of laboratory tests will most certainly also have effects beyond the direct laboratory cost savings. As the number of ordered tests decrease, so will the risk of generating false positive test results that demand attention and follow-up. Such indirect effects may be just as important as the direct savings and their economic effects as great as or greater than the direct savings.

The considerable inter-county variations found here along with the estimative calculations of the savings associated with optimized test utilization indicate that large cost savings could be achieved alongside a quality improvement.

**Paper III. Ruling out IBD: the cost-effectiveness of pre-endoscopic screening with F-calprotectin**

Differentiation of patients with IBD from patients with IBS poses a diagnostic challenge, and differential diagnosis based on clinical assessment alone is very difficult [126]. However, colonoscopy, the gold-standard for diagnosing IBD, has several drawbacks rendering it unsuitable for frequent use [130-132]. F-calprotectin, on the other hand, is a non-invasive, cheap test that is very useful in distinguishing IBD from IBS [121, 168]. In this study, the cost-effectiveness of using F-calprotectin tests to minimize unnecessary colonoscopies was estimated. For the outline of the sequential testing strategy evaluated, see *Figure 7*. The characteristics of the data set are presented in Table 6.

![Figure 7. The outline of the sequential testing strategy.](image-url)
### Table 6. Characteristics of the data set.

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>F-calprotectin &lt;50 µg/g,</th>
<th>F-calprotectin &lt;100 µg/g,</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 3 639</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient age, mean (min–max)</td>
<td>36 (0–95) years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%) of patients ≤18 years</td>
<td>1 206 (33.1%)</td>
<td>653 (54.1%)</td>
<td>855 (70.9%)</td>
</tr>
<tr>
<td>n (%) of patients 18–65 years</td>
<td>2 085 (57.3%)</td>
<td>1 079 (51.8%)</td>
<td>1 419 (68.1%)</td>
</tr>
<tr>
<td>n (%) of patients ≥65 years</td>
<td>474 (13.0%)</td>
<td>140 (29.5%)</td>
<td>240 (50.6%)</td>
</tr>
<tr>
<td>Male patients, n (%)</td>
<td>1 453 (39.9%)</td>
<td>713 (49.1%)</td>
<td>937 (64.5%)</td>
</tr>
<tr>
<td>Female patients, n (%)</td>
<td>2 186 (60.1%)</td>
<td>1 098 (50.2%)</td>
<td>1 498 (68.5%)</td>
</tr>
<tr>
<td>F-calprotectin, mean</td>
<td>242.1 µg/g</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pre-endoscopic F-calprotectin screening reduced the number of required colonoscopies by 49.7–66.9%. For more details on the distribution of patients in the testing strategy arms, see Figure 8. The cost avoidance, after deduction of the costs incurred by F-calprotectin screening, was 50.1–67.0%, corresponding to €1 569 989–2 131 669, depending on the cut-off used, see Table 7.

![Figure 8](image_url)

**Figure 8.** The distribution of patients in the sequential testing strategy applied when evaluating the use of F-calprotectin as a filter to minimize unnecessary colonoscopies by ruling out patients that most likely do not have IBD.

Almost twice as many tests were ordered for patients 10–19 years of age, than for patients in any other 10-year age span. These findings are in concordance with the large percentage of patients with IBD presenting before age 20 [169]. More women than men were investigated with an F-calprotectin test, yet the percentage of normal test results was higher for
women, which was likely a reflection of the findings of previous studies that more women than men suffer from IBS [170].

Table 7. Total costs for the respective testing strategy arms.

<table>
<thead>
<tr>
<th></th>
<th>Endoscopy</th>
<th>F-calprotectin</th>
<th>Total costs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nº of patients</td>
<td>Nº of patients</td>
<td>Nº of patients</td>
</tr>
<tr>
<td></td>
<td>≤18 years</td>
<td>&gt;18 years</td>
<td></td>
</tr>
<tr>
<td>Direct referral</td>
<td>1 206</td>
<td>2 433</td>
<td>0</td>
</tr>
<tr>
<td>Screening, 50 µg/g cut-off</td>
<td>553</td>
<td>1 275</td>
<td>3 639</td>
</tr>
<tr>
<td>Screening, 100 µg/g cut-off</td>
<td>351</td>
<td>853</td>
<td>3 639</td>
</tr>
</tbody>
</table>

Assuming the test ordering and morbidity patterns in Uppsala to be representative of those in Sweden as a whole, a cost avoidance of approximately €17 million–23 million could be achieved, as compared to direct referral for colonoscopy for all patients.

The study demonstrated that the use of a pre-endoscopic F-calprotectin screening test would clearly be favorable, from a cost-effectiveness point of view, to direct referral for colonoscopy. In addition to the costs of the diagnostic investigation itself, several attendant costs are associated with endoscopy. If these additional costs were to be factored into the equation, the potential savings associated with F-calprotectin screening would be even greater.

Paper IV. Longitudinal trends in laboratory test utilization at a large tertiary care university hospital in Sweden

The laboratories are often among the first disciplines to be targeted for budget reductions because their costs are easily discernable. However, as reduced test utilization produces disproportionately small true cost reductions [106], and test utilization is intimately related to other health care costs, it does not necessarily follow that a reduction in test utilization will lead to a decrease in the overall health care costs. Accurate and timely information on trends in test utilization is therefore essential to optimal financial management of clinical laboratories and hospitals.

The variables evaluated in this study and their inflation-values for 2002 and 2008, respectively, are presented in Table 8.
Table 8. Evaluated variables and their inflation-adjusted values.

<table>
<thead>
<tr>
<th>Generated test results&lt;sup&gt;a&lt;/sup&gt;</th>
<th>2002</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analyses offered</td>
<td>309</td>
<td>663</td>
</tr>
<tr>
<td>Mean price charged per test&lt;sup&gt;b&lt;/sup&gt;</td>
<td>€34.9</td>
<td>€37.5</td>
</tr>
<tr>
<td>Total laboratory expenditures</td>
<td>€10.4 million</td>
<td>€12.5 million</td>
</tr>
<tr>
<td>Testing expense&lt;sup&gt;c&lt;/sup&gt;</td>
<td>€2.8</td>
<td>€2.0</td>
</tr>
<tr>
<td>Primary health care visits with a physician</td>
<td>245 500</td>
<td>292 100</td>
</tr>
<tr>
<td>Admissions</td>
<td>53 504</td>
<td>58 001</td>
</tr>
<tr>
<td>Outpatient visits with a physician</td>
<td>291 000</td>
<td>419 213</td>
</tr>
<tr>
<td>Additional outpatient visits</td>
<td>329 000</td>
<td>419 213</td>
</tr>
<tr>
<td>Total hospital expenditures</td>
<td>€513 million</td>
<td>€629 million</td>
</tr>
</tbody>
</table>

<sup>a</sup>Includes non-chargeable test results such as calculations and ruined samples, <sup>b</sup>According to fee schedule, not volume adjusted, <sup>c</sup>Total laboratory expense/total number of generated test results.

From 2002 to 2008 the number of generated test results increased by over 70% with an average annual increase of 9.30%, see Figure 9.

![Figure 9](image.png)

*Figure 9.* The increase over time in laboratory test utilization as defined by the number of generated test results.

The 10, 20, and 30 most commonly ordered tests represented, on average, 46.9%, 66.9%, and 75.5%, respectively, of the total number of generated test results during the studied period, see Table 9.
Unlike the mean price charged per test, the testing expense decreased during the studied period, most likely due to a combination of increased automation and efficiency. The number of different analyses offered more than doubled during the studied period. Even so, the share of the total number of generated test results that was represented by the 10 most commonly ordered analyses was very stable at approximately 50% throughout the studied period, indicating that most of the new additions to the test menu were low-frequency tests.

Table 9. Percentage of the total number of tests represented by the most commonly ordered tests.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total number of ordered tests</th>
<th>10 most commonly ordered tests</th>
<th>20 most commonly ordered tests</th>
<th>30 most commonly ordered tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>3 760 508</td>
<td>40.4%</td>
<td>59.5%</td>
<td>67.6%</td>
</tr>
<tr>
<td>2003</td>
<td>3 983 149</td>
<td>47.7%</td>
<td>69.7%</td>
<td>78.7%</td>
</tr>
<tr>
<td>2004</td>
<td>4 218 082</td>
<td>47.6%</td>
<td>69.1%</td>
<td>77.6%</td>
</tr>
<tr>
<td>2005</td>
<td>4 614 524</td>
<td>48.8%</td>
<td>69.3%</td>
<td>77.1%</td>
</tr>
<tr>
<td>2006</td>
<td>5 100 550</td>
<td>48.0%</td>
<td>67.4%</td>
<td>75.8%</td>
</tr>
<tr>
<td>2007</td>
<td>5 766 947</td>
<td>47.9%</td>
<td>66.7%</td>
<td>76.2%</td>
</tr>
<tr>
<td>2008</td>
<td>6 402 617</td>
<td>47.8%</td>
<td>66.4%</td>
<td>75.7%</td>
</tr>
<tr>
<td>Mean</td>
<td>4 835 197</td>
<td>46.9%</td>
<td>66.9%</td>
<td>75.5%</td>
</tr>
</tbody>
</table>

The principal findings of this study were substantial increases in the number of generated test results and in the number of tests offered, despite a virtually unchanged share of the hospital’s total expenses represented by the costs of laboratory testing. The increase in patient throughput, as determined by the number of admissions, outpatient visits, and primary health care visits, could only explain less than one third of the increase in test utilization. The major part of the increase in test utilization is thus most likely due to intrinsic growth. The increase in workload in this study is in the range of average laboratory test growth rates reported in other countries during the period of 1970–2005 [20, 171-176]. The percentage of the total number of generated test results represented by the 30 most commonly ordered tests was similar to that reported in other studies [173, 175]. The data on the top-30 tests could be used as an indication of where small changes in test utilization may bring about considerable savings, as small technologies are likely to account for far more of the overutilization than big expensive technologies [98], and low-cost high-frequency tests have been demonstrated to account for the major proportion of laboratory costs [97].

Very little has thus far been published about changes in test utilization over time. This study provides insight into the utilization and economics of laboratory testing during a period that was characterized by tightened budget control and ever-growing concern about medical costs. The study defines trends and may thus have potential predictive values.
Conclusions

- CME can bring about long-lasting changes in the test ordering habits of primary health care physicians.
- CME can be used as a means of improving the cost-efficiency as well as the quality of test utilization.
- There are large regional differences in test utilization in primary health care in Sweden.
- Considerable inter-county variations indicate that large cost savings could be achieved alongside a quality improvement.
- Inter-county differences in test utilization are likely to be influenced by over- as well as under- and misutilization due to local traditions and habits.
- The savings associated with optimized test utilization are considerable.
- F-calprotectin has the potential to substantially reduce the number of invasive investigations necessary in the diagnostic work-up of patients with suspected IBD.
- F-calprotectin screening could lead to a cost avoidance of €17–23 million annually in Sweden as compared to direct referral for colonoscopy.
- The total number of test results generated at the Clinical Chemistry and Pharmacology Laboratory at Akademiska sjukhuset in Uppsala has increased by over 70% in 6 years.
- Even though the selection of tests has more than doubled, a very small number of tests account for a stable, and disproportionally large, share of the total number of generated test results.
- Despite the substantial increase in the number of generated test results, the laboratory’s share of the hospital’s total expenditures has remained virtually unchanged.
Laboratory analyses are essential in screening, diagnosis and monitoring of disease, and thus indispensable in the practice of health care, but proper utilization of tests is a balancing act. On the one hand, if too few are used, the direct costs of testing will admittedly decrease, but other health care costs may increase as a result of underutilization of tests. On the other hand, if too many are used, the direct costs of testing will inevitably increase, without it necessarily following that other health care costs will decrease as a result of the excessive diagnostic testing.

Laboratory tests are closely associated with other, greater, health care costs, but their indirect effects on other areas of medicine are difficult to discern and measure in monetary terms. It is therefore important to keep a wider perspective; a reduction of the direct analytical costs that increases the total costs of care is not desirable, but neither are increased analytical costs without adequately improved quality or outcomes of the care provided. Optimal utilization of laboratory tests in this context thus implies consideration of the clinical value of each test, by which the use of older, more unspecific analyses with reduced clinical values, or tests that provide redundant information should be abandoned on behalf of more specific up-to-date analyses with better diagnostic values. Although newer tests are often more expensive, this cost may be exceeded by the sum of costs for unnecessary follow-up tests and additional consultations that could result from the usage of unspecific tests. Regardless of the figure on the price tag, there should, simply put, always be a reason for any laboratory test ordered for a patient, and if the test selected cannot deliver the information needed, or the information yielded will not influence patient care, its use is unsound.

The physicians are, however, not alone at fault; the laboratories need to take responsibility for the extended use of laboratory analyses as well, as they have allowed their repertoires of tests to expand unrestrainedly through introduction of new assays as well as through failure to remove obsolete tests. To optimize laboratory testing it is consequently important for the laboratory, in consultation with the practicing physicians, to continuously evaluate the panel of offered tests in order to modify it over time to meet present and future clinical needs.

A very limited amount of research has so far been conducted regarding the utilization of laboratory tests, especially in relation to the cost-effectiveness of analyses and their influence on health outcomes, but it is
undoubtedly an area of growing importance and interest. Research on the impact of testing on health outcomes is, however, complicated by the remoteness between the two. The studies included in this thesis have, among other things, demonstrated a rapid increase and large variations in test utilization. This indicates that there is a vast potential for improvement in laboratory test utilization, in a quality as well as a cost-efficiency perspective. Furthermore, these studies suggest a method for improving test utilization and also illustrate how increased costs of laboratory testing can be used to reduce the total costs of care.

As variations in clinical practice have been shown to be an important determinant of expenditures for laboratory tests, this should be one of the main focuses for future research on laboratory testing. It would be interesting to extend our exploration of variations in test utilization to include intercountry differences, for example between the Scandinavian countries. Despite the close geographical proximity, the health care systems in the Scandinavian countries display differences. To evaluate if and how these differences impact on test utilization would be intriguing.

Another tempting investigation on the theme of variation in test utilization would be to examine differences in test panels, group tests, and bundled tests in terms of the tests included. On the basis of the disease spectrum being largely homogenous in, if not Europe, then at least in the Scandinavian countries, or within Sweden, one would expect the laboratory tests used in the diagnostic work-up of diseases to be chiefly the same. However, there are indications that this is not the case. A comprehensive evaluation of this phenomenon is needed to highlight the problem and to induce debate on optimal test utilization.

Another fascinating area of future research would be the impact of extensive POCT on health care, regional differences in extent of utilization, and the share of tests performed point-of-care versus centrally, respectively. POCT is an area of immensely rapid advancement. As it has been established to be more difficult to change physicians’ test ordering of well-established tests than of newly introduced ones, the impact of POCT on costs and outcomes of care should be evaluated as soon as possible. It is of utmost importance to establish whether the advantages of POCT outweigh the disadvantages, such as whether the potential shortening of TATs will offset the often heavily increased costs of POCT as compared to centralized testing.

Even though laboratory tests have been used for ages, biomedical laboratory science has been a neglected and largely unexplored area of research. This is bound to change in the future, as laboratory test utilization unfolds into a field of intriguing approaches and research points of attack.
Sammanfattning på svenska

Bakgrund

Besparingar är alltid aktuella inom sjukvården inte minst med tanke på att kostnaden för hälso- och sjukvården ökar i de flesta länder och att den i regel ökar snabbare än BNP. Då laboratorieanalyser används rutinmässigt i vården och antalet beställda tester ökar, stiger även kostnaderna för dessa snabbt. Eftersom det förefaller föga troligt att sjukvårdens resurser kraftigt kommer att öka inom en överskådlig framtid måste de medel som finns att tillgå användas på ett så effektivt sätt som möjligt för att leva upp till kraven på ökad kostnadseffektivitet med bibehållen vårdkvalitet. Även laboratorieanalyser, som är en av sjukvårdens viktigaste resurser, omfattas av sparkraven. Det har visats att många tester beställs i onödan. En överdriven användning av laboratorietester leder inte enbart till ökade laboratoriekostnader utan genererar också ett ökat antal falskt onormala testresultat. Om man på en patient till exempel beställer 20 analyser kommer dennes chanser att klassificeras som normal för samtliga analyser att minska till en på tre, enbart på grund av slumpen, även om personen i fråga är fullt frisk. För att ytterligare förvärra saken beställs ofta tilläggs tester som ett resultat av onormala testresultat; så många som 10% av begärda tester beställs på grund av ett tidigare resultat utanför angivet referensområde. Läkarna kan dock inte ensamma lastas för det överdrivna utnyttjandet av analyser; laboratorierna måste också ta sitt ansvar då de har tillåtit sina utbud av tester att växa kontinuerligt, såväl genom införande av nya analyser som genom underlåtenhet att avlägsna förlegade tester. För att utnyttja laboratorieanalyser optimalt, på ett sätt som gagnar både sjukvården och patienterna, kan man däremot inte heller bara minska antalet beställda analyser utan att överväga hur det påverkar prislappen för sjukvården som helhet. Optimering av användningen av laboratorieanalyser betyder alltså att den faktiska kliniska nytta av varje enskild analys måste tas i beaktande. Ett exempel är att begränsa användningen av äldre, mer ospecifika analysmetoder, vars kliniska värde minskat, till förmån för nyare, mer specifika analyser. Det är därför nödvändigt att kontinuerligt se över utbudet av analyser och modifiera detta efter de kliniska behoven i enlighet med aktuella kunskaper om analysernas diagnostiska värden. Om laboratorieanalyserna betraktas som en del i sjukvårdens kostnadsbesparing och kvalitetssatsning finns det också analyser som är underutnyttjade och vars an-
vändning därför bör öka. Det gäller exempelvis tester för att påvisa sjukdomar som är förhållandevis vanliga och behandlingsbara, men svåra att diagnostisera på annat sätt.


Det förekommer också stora variationer när det gäller hur och i vilken omfattning laboratorieanalyser används, såväl på en internationell, som på en nationell nivå, skillnader som inte enbart kan förklaras med olikheter i patientunderlag. Variationer i hur läkarer praktiserar har visats vara en avgörande faktor för kostnaderna för laboratorieanalyser i primärvården. Stora skillnader i nytjandet av laboratorieanalyser borde innebära att en optimering av användandet av testerna skulle kunna leda till tämligen stora besparingar för sjukvården.

Delarbete I

I delarbete I har vi visat att en effektiv metod att förbättra användningen av laboratorieanalyser i primärvården är fortbildning för primärvårdsläkare och laboratoriepersonal, där fortbildningen visats kunna åstadkomma kraftiga förändringar i beställningsmönstret, förbättra utnyttjandet av laboratorieanalyser och minska de totala kostnaderna. I fortbildningsprogrammet; ”Labore- ra rätt och lagom” i primärvården, som genomfördes hösten 1996, deltog 63 husläkare samt laboratoriepersonal från 19 vårdcentraler i Uppsala läns landsting. Syftet med fortbildningen var att optimera deltagarnas användande av kliniskt kemiska analyser. Förbättringarna i beställningsmönstret rekom-

En kortsiktig förändring i provtagningsmönstret säger dock ingenting om huruvida effekterna är bestående. De långsiktiga effekterna av den här typen av utbildning är givetvis centrala för om det skall vara meningsfullt att bedriva utbildning. Det är därför av stort värde att undersöka om förändringarna i husläkarnas beställningsmönster påverkades permanent av utbildningen, eller om trenden har varit att efterhand återgå till gamla vanor. Därför undersökte vi i delarbete I utbildningens långtidseffekter på husläkarnas beställningsmönster, med avsikten att ta reda på om utbildningens goda effekter är bestående eller om de varit övergående.

Precis som i korttidsuppföljningen undersökte utbildningens långtidseffekter med hjälp av analyskvoter, det vill säga kvoter mellan två analyser som ofta beställs tillsammans. Totalt undersökte 12 kvoter: 7 st som förväntades ligga kvar på samma nivå som vid korttidsuppföljningen eller minska ytterligare om utbildningens effekter var bestående, samt 5 kvoter som förväntades ligga kvar på samma nivå som vid korttidsuppföljningen eller öka om utbildningens effekter var bestående.

Utöver att undersöka förändringar i de deltagande läkarnas beställningsmönster undersökte vi också hur många av Uppsalas primärvårdsläkare som deltagit i utbildningskursen någon gång mellan 1996 och 2007, samt vad de ansåg om kursinnehållet och vikten av dylika utbildningsinsatser. En kort enkät bestående av följande fyra frågor skickades ut till samtliga Uppsalas primärvårdsläkare:

1. Har du deltagit i utbildningskursen “Laborera rätt och lagom”?
2. Om ja, när gick du kursen?
3. Tycker du att du har användning för det du fick lära dig under utbildningen i ditt dagliga arbete?
4. Anser du att man bör fortsätta med den här typen av vidareutbildning?
Sammanfattningsvis ansåg den absoluta majoriteten av deltagarna att de hade väldigt god användning av informationen som gavs vid kursen i sitt dagliga arbete, samt att den här typen av vidareutbildning borde genomföras regelbundet. Husläkarnas positiva inställning till kursen och den kunskap som förmedlades där är troligen en viktig orsak till att effekterna av utbildningen kvarstår.

Långtidsuppföljningens resultat visar att effekterna av utbildningen är kvarstående. Majoriteten av de undersökta kvoterna ligger kvar på ungefär samma nivåer som vid tillfället för korttidsuppföljningen 1997. Detta innebär att det är möjligt att även med begränsade utbildningsinsatser förändra beställningsrutinerna i primärvården långsiktigt, vilket resulterar såväl i besparingar som i optimerat användande av laboratorieanalyser; det vill säga ökad kostnadseffektivitet med förbättrad kvalitet.

Delarbete II

Laboratorieanalyser används rutinmässigt i primärvården, och det snabbt ökande antalet tester medför stigande kostnader. Många av testerna som beställs är onödiga, och 25–40% av alla beställda tester samt 20–95% av vissa utvalda tester anses vara överflödiga. Felaktig användning av tester måste åtgärdas av flera anledningar. Överdriven användning av tester leder inte bara till ökade direkta och indirekta kostnader, utan åsamkar också patienterna onödigt lidande och ökar risken att generera falskt positiva testresultat, vilket i sin tur kan leda till onödig oro, fortsatta undersökningar och kan dessutom vara till skada för patienterna. Optimerad användning av laboratorieanalyser har framförs som ett sätt att kontrollera kostnaderna samtidigt som kvaliteten på vården som tillhandahålls bibehålls. Ansvaret för kostnadskontroll och korrekt användning av laboratorietester har sagts kunna vara särskilt viktigt för primärvårdsläkare, vilka ofta är de första att träffa och undersöka patienten, och därmed också avgör det initiala antalet prover som beställs. För att kunna avgöra om och i så fall vilka förändringar i användningen av laboratorieanalyser som behöver göras, samt för att kunna uppskatta storleken på eventuella besparingar, måste man först ta reda på hur analyserna används i utgångsläget. Målet med delarbete II var att utvärdera svenska primärvårdsläkares användning av ett antal utvalda kliniskt kemiska laboratorieanalyser. Studiens syfte var tredelat. Först och främst att fastställa förekomsten och omfattningen av regionala variationer i användningen av laboratorietester i åtta landsting i Sverige. För det andra att undersöka den eventuella inverkan på dessa variationer av faktorer som tidigare visats kunna vara bakomliggande orsaker till variationer i testanvändning. För det tredje att beräkna de eventuella besparingar som en förbättrad testanvändning skulle kunna resultera i.
Information om vilka och hur många analyser som beställdes av primärvårdsläkarna i de studerade landstingen under 2004 samlades in från 223 vårdcentraler fördelade i åtta landsting i Sverige. Samtliga vårdcentraler i respektive landsting inkludерades, och totalantalet vårdcentraler per landsting varierade mellan 21–41. Studien fokuserade på analyser utförda på centrala laboratorier i motsats till patientnära, eftersom tillgången till patientnära analysinstrument varierar mellan olika vårdcentraler och landsting, vilket i sig kan påverka valet av tester som används och även omfattningen av testanvändningen. Två grupper av analysekoffer jämfördes i studien. I grupp A ingick kvoter där användningen av analyserna generellt rekommenderades minska på grund av deras begränsade kliniska nytta eller omotiverade användning i primärvården. Grupp B bestod av kvoter där användningen av analyserna generellt rekommenderades öka tack vare deras användbarhet vid tidig upptäckt av behandlingsbara sjukdomar eller för att följa ett sjuksomsförlopp och därigenom förhindra eller minimera risken för komplikationer.

Vi studerade huruvida eventuella variationer i testanvändning skulle kunna härledas till ett antal olika faktorer som tidigare har visats kunna orsaka variationer i analysbeställningsmönstret. Hur stora besparingar som skulle kunna åstadkommas om man minskade användningen av analyserna i grupp A, samt hur mycket kostnaderna skulle öka vid utökad användning av testerna i grupp B beräknades också.

I delarbete II visade vi att det fanns stora skillnader mellan samtliga studerade landsting för alla undersökta kvoter. Separat tycks ingen av de undersökta faktorerna helt och hållet kunna förklara variationerna, men det kan inte uteslutas att deras sammanlagda effekt skulle kunna ha större inverkan på testanvändningen än de verkar ha var för sig. Variationerna mellan landsting funna i den här studien påverkas troligen av såväl över-, som under- och felanvändning av tester, och besparingspotentialen var betydande. De uppskattade totala besparingarna som skulle kunna åstadkommas över en ettårsperiod per 100 000 invånare beräknades till mellan 14 000–185 000 euro (€1 = 10 kr).

Sammanfattningsvis visade studien att det finns stora regionala skillnader i testanvändning i primärvården i Sverige, och att de totala årliga kostnaderna för laboratorieanalyser skulle kunna minska avsevärt. Optimerad användning av laboratorieanalyser kommer troligen också ha effekter bortom de direkta besparingarna för laboratorieterester. När antalet beställda tester sjunker minskar också risken att generera falskt positiva testresultat som behöver kontrolleras och följas upp. Sådana indirekta effekter kan vara nog så viktiga som de direkta kostnadsbesparingarna och deras ekonomiska effekter är troligen lika stora som eller större än de direkta besparingarna. De avsevärdare variationer vi fann i testanvändning mellan landstingen tillsammans med de uppskattade besparingar som skulle kunna åstadkommas genom optimerad testanvändning visar således att stora besparingar skulle kunna göras med en samtidig kvalitetsförbättring.
Delarbete III

När det gäller sjukdomar i magen och tarmen skiljer man bland annat på sådana sjukdomar där tarmen är inflammaderad och sådana där det inte finns någon inflammation, till de olika grupperna räknas framförallt IBD respektive IBS. Båda typerna har dock ett antal centrala symptom gemensamt, bland andra magsmärtor och diarré, och det kan därför vara svårt att skilja sjukdomarna åt bara genom att patienten berättar hur han eller hon mår. Standardförfarandet vid diagnostisering av IBD är att låta patienten genomgå någon typ av diagnostisk undersökning, vanligtvis en koloskopi, för att läkaren ska kunna ställa rätt diagnos. Koloskopi är en undersökning av tjocktarmen där man för in en slang med en lampa och en liten kamera på från ändtarmen upp i tjocktarmen. Via kameran är det möjligt att på en TV-skärm se om tarmslemhinnorna ser friska ut, eller om de till exempel är inflammaderade. Man tar också ofta små prover av tarmvävnaden som man sedan undersöker närmare i mikroskop. Eftersom det är svårt att skilja patienter som har IBD från patienter som har IBS enbart utifrån symptom genomgår många patienter med IBS ofta koloskopi i onödan för att utesluta att de har IBD. Koloskopier är inte bara invasiva, utan också dyra, potentiellt riskfyllda, obehagliga för patienten och de kräver förberedelse av patienten innan undersökningen. Därför vore det en fördel, såväl för patienterna som rent ekonomiskt, om ett enkelt laboratorieprov skulle kunna användas för att sålla bort patienter hos vilka inflammation i tarmen är mycket osannolikt, och som därför inte skulle behöva genomgå en koloskopi. Den främsta skillnaden mellan IBD och IBS är som sagt att patienterna med IBD har en inflammation i tarmen. En möjlighet att skilja de två sjukdomstillstånden åt vore därför att mäta en markör för tarminflammation. Fekalt calprotectin (F-calprotectin) är ett enkelt, billigt och smärtfritt avföringsprov som kan visa om man har en inflammation i tarmen. Ett högt calprotectinvärde tyder på att man har IBD, vilket behöver utredas vidare med en koloskopi.

I delarbete III har vi visat användning av F-calprotectin före koloskopi vid misstanke om IBD skulle kunna minska antalet koloskopier vid IBD-diagnostisering i Sverige med mellan hälften och två tredjedelar, samt sjukvårdskostnaderna med ca 17–23 miljoner euro. Olika tarmssjukdomar är en mycket vanlig frågeställning i primärvården, men det finns varken kapacitet eller resurser att utföra koloskopi på alla patienter där man misstänker IBD. Att använda sig av ett enkelt avföringsprov för att sålla bort de patienter som med största sannolikhet inte har IBD skulle innebära en möjlighet att snabbare kunna bekräfta eller utesluta diagnosen IBD, och det skulle också innebära att man skulle kunna undvika ett betydande antal koloskopier och därigenom minska obehaget för patienterna som slipper genomgå koloskopi samtiget som man minskar väntetiden till koloskopi för de patienter som är i störst behov av undersökningen. Korrekt utredning och diagnos är viktigt för att fokusera på rätt åtgärder för den individuella patienten, och för att fördela resurserna på bästa möjliga sätt.
Delarbete IV


Det totala antalet utförda tester hade under studieperioden ökat med över 70%. Baserat på tidigare beställningsmönster beräknades ökningen i antalet inskrivningar på sjukhuset samt antalet öppenvårds- och primärvårdsbesök bara kunna svara för knappt en tredjedel av ökningen i användningen av laboratorietester. Totalkostnaden för laboratoriet fördelat per test minskade under studieperioden, troligen till följd av en ökad automatisering samt en ökad effektivitet. Antalet olika analyser som erbjuds vid laboratoriet mer än fördubblades mellan 2002 och 2008. Trots detta svarade de 10 vanligast beställda analyserna för nästan 50% av alla beställda tester genom hela studieperioden, vilket tyder på att majoriteten av de nytillkomna testerna utgjordes av analyser som används i liten utsträckning. Ett litet antal tester svarade för en oproportionerligt stor andel av det totala antalet utförda analyser: de 30 vanligaste testerna utgjorde i genomsnitt mer än 75% av totalantalet beställda tester. Detta är vital information då den största besparings- och förbättringspotentialen tenderar att ligga just hos de vanligast använda analyserna.

Sammanfattningsvis ökade antalet beställda tester med mer än 70% på mindre än ett decennium samtidigt som ett mycket litet antal olika tester utgjorde majoriteten av totalantalet beställda analyser. Trots att antalet utförda analyser ökade kraftigt var laboratoriets andel av sjukhusets totala kostnader nästintill oförändrad.
Slutsats

Sammanfattningsvis har vi i den här avhandlingen visat att det finns stora regionala skillnader i analysanvändning i primärvården i Sverige, vilka trotsligtvis till stor del beror på över-, under-, och felanvändning av laboratorieanalyser, samt på traditioner och vanor i beställningsmönstret. Vidare har vi påvisat att optimerad testanvändning potentiellt skulle resultera i avsevärda besparingar och en samtidig kvalitetsförbättring.

Vi har också demonstrerat att det är möjligt att även med begränsade vidareutbildningsinsatser förändra beställningsrutinerna i primärvården långsiktigt, vilket resulterar såväl i besparingar som i optimerat användande av laboratorieanalyser; det vill säga ökad kostnadseffektivitet med förbättrad kvalitet.

Utöver det har vi i ett illustrativt exempel av hur laboratorieanalyser kan påverka andra vårdkostnader visat på stora besparingspotentialer och patientfördelar vid användning av F-calprotectin för att utesluta diagnosen inflammatorisk tarmsjukdom.

Slutligen har vi också visat att analysanvändningen vid Akademiska sjukhuset ökat kraftigt under de senaste åren, dock utan att laboratoriets kostnader för den skull ökat i förhållande till sjukhusets totala kostnader, samt att ett litet antal tester utgör en oproportionerligt stor andel av det totala antalet utförda analyser.
Tänk så mycket i livet som aldrig blir som man hade tänkt sig, och tänk så bra det ändå oftast blir till slut. Förutfattade meningar är ju oftast precis det – förutfattade.

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