

MS Dissertation Health Economics

Can physician laboratory-test requests be influenced by interventions?

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Preface

This master's thesis in health economics at the University of Iceland is valued as 30 credits (ECTS). The supervisor is Tinna Laufey Asgeirsdottir, an assistant professor and supervisor of the MS programme in health economics at the Department of Economics at the University of Iceland.

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Abstract

Background: Physicians order laboratory tests for various reasons during diagnoses and treatments. However, laboratory tests affect health-care costs and unnesseary test requests can thus be a concern. The objective in this study is to examine whether it is possible to influence physician laboratory-test requests using four different interventions; follow-up of clinical guidelines, education, feedback and reminder letters that have occurred at different times at Landspitali University Hospital compared to Akureyri Hospital, which is used as a control as no formal interventions were implemented there. Material and Methods: Six types of laboratory tests for which clinical guidelines have been made were analysed. The average number of tests per month before and after implementation of the guidelines was compared. The relative risk of a laboratory test being conducted at Landspitali University Hospital compared to Akureyri Hospital was calculated for various points in time, as well as the associated 95% confidence intervals. The primary estimates compare the pre and post intervention periods (2007-2009 vs. 2010-2013), but also on a monthly basis in order to observe the trend over the whole period from January 2007 to July 2013 in greater detail. Results: The multifaceted interventions at Landspitali University Hospital led to a significant reduction in the average number of laboratory tests (12-52%, p<0.001) compared with Akureyri Hospital. When the relative risk coefficients of laboratory tests at Landspitali University Hospital compared to Akureyri Hospital were calculated pre and post guidelines, the relative risk for ASAT, CRP and GGT fell markedly, while ALAT and ALP tests did not show a significant decrease. Relative risk for a blood culture test in the period after the guidelines was statistically significantly increased. Conclusion: It is possible to influence physician laboratory-test requests using multifaceted interventions that include continuous monitoring and follow-up. Compared to Akureyri Hospital, laboratory tests were statistically significantly reduced using interventions at Landspitali University Hospital and led to cost savings, under the assumption that the decrease did not cause increased costs elsewhere in the system. Hospitals can use multifaceted interventions to steer physician behavior, with continuous follow-up so as not to lose the effect.

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List of Abbreviations

AH Akureyri Hospital

ALP Alkaline phosphatase

ALAT Alanine aminotransferase

ASAT Aspartate aminotransferase

CBC Complete blood count

CI Confidence interval

CPOE Computer Provider Order Entry

CRP C-reactive protein

GDP Gross domestic product

ESR Erythrocyte sedimentation rate

GGT γ-glutamyltransferase

HbA1c Glycated haemoglobin

LIS Laboratory Information System

LUH Landspitali University Hospital

RaA Request and Answer system

RR Relative risk

1 Introduction

Attention was drawn to inappropriate laboratory utilization as early as 1975 (Lundberg, 1975) and subsequent estimate showed that up to 30% of laboratory tests were unnecessary (Rinsler, 1984). Unnecessary laboratory tests can cause the patient unnecessary concerns, phlebotomy and inconvenience, besides the cost for laboratory supplies, additional physician time, treatments and tests. Laboratory tests can also be underutilized, i.e. not used as they should be (Ming Zhi, 2013). Laboratory tests are necessary for optimal patient care as an essential part of diagnosis and management of a patient's condition (Houben et al., 2010; Whiting et al., 2007).

The purpose of this study is to look at the effect of interventions on laboratory tests. In the autumn of 2009, the executive management at Landspitali University Hospital (LUH) set the goal of a 15% reduction in laboratory tests in 2010, and a physician was appointed as the supervisor for the intervention project. This was partly triggered by known patterns of requests for many common laboratory tests. For example the total cost for Landspitali University Hospital and the Icelandic Health Insurance for four liverfunction laboratory tests in 2009 was ISK 125 million. The requests were almost identical between these four laboratory tests, indicating that all four of them were being requested together, but most specialists would agree that for most purposes the use of two of the four tests should suffice.

Hospitals in Iceland had also been under pressure to become more cost effective after the economic crisis in autumn 2008. The Icelandic state government pays for the majority of hospital costs. Expenditures on hospital care have fallen from 5.17% of GDP in 2006 to 4.84% of GDP in 2012 (Statistics Iceland, e.d.). The share of hospital budgets spent on laboratory services varies across countries and accounts for 4% in the United Kingdom (UK), 20% in the United States (US) and 7-10% in Canada. The nature of health-care systems has been one hypothesized determinant of those expenditures: the UK and Canadian systems are funded by the government while the US system relies on private insurance to a greater extent (McQueen, 2000).

At LUH the share of the total hospital budget spent on laboratory services has been 6% since 2008 (5% in 2007). The patient share of the laboratory service budget at LUH was 2% in 2009 but 3% from 2010-2012 (Soley S. Stefansdottir, personal communication, 2013, July 1st). Information from LUH for the previous years was not available because of a change in computer systems, and the information was not available from Akureyri Hospital (AH).

The hospital laboratories are financed by the government through the treasury, transactions with other health-care centres, contractual company services or specialist services, the patient's copayments, and grants. Laboratory tests for inpatients are paid by the hospital while tests for outpatients are a mixture of official health insurance and out-of-pocket payment (Icelandic Health Insurance, 2013). Laboratory tests are done in connection with treatment of inpatients and hospital outpatients or requested by general practioners and private specialists, but in this study the focus is only on inpatients and outpatients at LUH and AH.

The increased use of laboratory tests may be partly due to increased demands for efficiency in hospitals. Also, increased attention to health may result in increased demand for laboratory tests from patients. Between 2006 and 2012, life expectancy in Iceland has increased by 1 year and 4 months for women and by 9 months for men (Statistics Iceland, e.d.a.). Medical technology innovations are growing and the ageing population has increased the workload with corresponding increases in costs.

The testing process consists of five phases (pre-pre-analytical, pre-analytical, analytical, post-analytical and post-post-analytical. The phases in the testing process that are most likely to be error-prone are the pre-pre-analytical (outside the laboratory) phase which consists of the laboratory request, sample collection, container, handling, storage and transportation and the post-post-analytical phase, which consists of the physician's reaction to the laboratory results, interpretation and follow-up, possibly because these phases are not evaluated and monitored as well as the other phases (Plebani, 2009). The pre-pre-analytical phase which contains inappropriate laboratory-test requests is the phase that includes the most common cause of errors, or up to 68.2% in the total testing process (Plebani, 2009). A study on diagnostic errors in the

emergency department found that 58% of them occurred because of inappropriate laboratory-test requests (Kachalia et al., 2007).

The overuse of laboratory tests can be harmful for the quality of care in several ways. Physicians could receive too much information which can increase the risk of important results not being noticed (Bartlett, 1982). Increased use of laboratory tests can increase the laboratory turnaround time, which can have a negative effect on those patients who really need acute efficiency (Salinas, Lopez-Garrigos, & Uris, 2013), while increased sample volume can lead to false positive and false negative results which may lead to further treatment with associated increased costs. This problem can possibly be countered by the introduction of clinical guidelines for proper test use and proper interpretation of test data (Oosterhuis, Bruns, Watine, Sandberg, & Horvath, 2004).

The purpose of this study is to look at the effect of interventions on laboratory-test requests. Two hospitals are compared: LUH where interventions were made to reduce unnecessary laboratory tests and thereby costs, and AH where formal interventions were not made, with the exception of one educational intervention at the beginning of 2009 which aimed at decreasing the CRP tests. AH can therefore be used as a control hospital.

LUH covers a population of 205,675 in the greater capital area but also serves the whole country (pop. 325,010) as a tertiary referral hospital, while AH serves 36,297 people (Statistics Iceland, e.d.b.). Both hospitals are training and teaching hospitals. About 473 full-time and part-time physicians work at LUH (Landspitali University Hospital, e.d.), while 53 work at AH (Akureyri Hospital). Junior physicians and interns work at both hospitals under the supervision of medical specialists.

The four interventions at LUH occurred at different times, as seen in Figure 1, and the effects of all four will be examined. The interventions were:

- 1. Follow-up of clinical guidelines which were published at different times, sent to physicians at LUH and published on the LUH website.
- Education, the supervising physician for the proper laboratory-utilization project gave lectures on the use of laboratory tests, both at management meetings and medical meetings, as well as for medical students and junior physicians.
- 3. Feedback on laboratory-test use after the supervising physician had monitored their number and distribution amongst individual physicians from the Laboratory Portal.
- 4. Reminders, a letter was sent from the supervising physician to chief physicians, with instructions for the use of the Laboratory Portal and encouragement to take action.

The Directorate of Health publishes clinical guidelines on its website which are supposed to apply to all physicians in the country, but it is the responsibility of the health care institutions and individual physicians to follow them. Many clinical guidelines have been introduced, but they are not always followed as they should: 30-40% of patients do not get care based on evidence-based medicine and up to 25% of provided care is unnecessary (Grol & Grimshaw, 2003). One of the interventions examined at LUH was follow-up of clinical guidelines that are issued nationally; here, the focus will be on three different guidelines for laboratory tests that were published at different time points (Figure 1). The number of laboratory tests performed at LUH for those tests for which the follow-up of guidelines were tracked will be examined as to whether intervention by means of follow-up led to a reduction of laboratory tests compared with the situation at AH.

The three guidelines are for:

- 1. Liver function tests (ASAT, ALAT, GGT, ALP), published February 15, 2010.
- 2. C-reactive protein (CRP), published March 1, 2010.
- 3. Blood culture, published February 1, 2011.

Information about the laboratory tests may be found in Appendix 1 and the three guidelines in Appendix 2, 3 and 4.

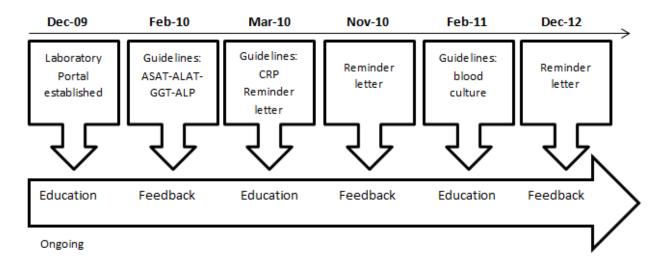


Figure 1: Timeline of interventions at Landspitali University Hospital (LUH)

A computerized laboratory management system, the Laboratory Portal, was launched in 2009 at LUH. The system contains information about the number of laboratory tests, the cost per month and year, the name of the physician requesting and his/her department. The supervisor has unlimited access and chief physicians have limited access to the system. The supervisor monitors laboratory use and contacts chief physicians as needed when use of laboratory requests in their department has increased or when an individual physician under their supervison differs substantially from others in terms of laboratory requests. Chief physicians are encouraged to monitor their physicians' laboratory habits and give them feedback if they seem to be requesting too many tests. The system thus requires the supervising and chief physicians to monitor and give feedback, since there are no automatic functions regarding feedback

or messages built into the system. It is relevant for medical students and interns to receive feedback as they seem to follow what specialists do rather than what they were taught at university (Grivell, Forgie, Fraser, & Berry, 1981).

In March 2010 all chief physicians were sent a reminder, which consisted of a letter with instructions for use of the Laboratory Portal. They were encouraged to take advantage of this in order to improve usage of laboratory tests in their department. The reminder letter was updated and reiterated in November 2010 and December 2012 (Appendix 5). An electronic or paper-based laboratory request form must be filled out and sent to the laboratory. Different electronic laboratory-test systems are in use by the two hospitals and the tests are documented in different systems, see Appendix 6.

Besides the scientific value, the result of this study can help predict which interventions are likely to affect physician behaviour. One of the first things to do towards a cost-effective health-care system is to reduce waste (Berwick & Hackbarth, 2012). This is not a field of study in which final answers will be provided in a single study. The interventions currently being used for influencing test requests are multiple and happen within varying contexts. Examination of each of them provides additional information until a pointallistic picture of results generates a valuable knowledge base for what works under which circumstances. We provide one such study, taking advantage of interventions that took place in Iceland. The results of the proposed analysis will not show whether the tests are misutilized, underutilized or overutilized. Instead, the study is meant to shed light on the determinants of physician behaviour and to shed light on whether their use of laboratory tests can be influenced by the interventions under examination.

2 Literature Review

Laboratory results have been shown to be the basis for 60-70% of medical decisions (like admittance, diagnosis, discharge, and use of medication) in a hospital and therefore have a big impact on costs (Forsman, 1996). However, a study from Australia found that up to 68% of laboratory-test requests for inpatients are avoidable without affecting the patients (Miyakis, Karamanof, Liontos, & Mountokalakis, 2006). Another study from the UK found that up to 25-40% of all hospital-based laboratory tests are unnecessary (Rao, Crook, & Tillyer, 2003). Increased testing can lead to false positive results which again can lead to more testing and discomfort for the patient (van Walraven & Naylor, 1998). Tests can also be repeated too frequently, as in one hospital where repeated blood culture tests were responsible for one-third of the blood culture tests. A repeated culture which was negative in the beginning was very unlikely to be positive when repeated (Tabriz, Riederer, Baran, & Khatib, 2004). A 15-year metaanalysis which looked at inappropriate laboratory testing has concluded that focusing on the correct test request in the beginning may have a bigger impact on improving care and errors than repeated laboratory tests (Ming Zhi, 2013). While low-volume laboratory tests can undoubtedly be improved upon, it is natural to concentrate on the high-volume, better-known laboratory tests as these have a greater total impact (Ming Zhi, 2013).

The reasons for inappropriate laboratory testing can for example be lack of experience, lack of knowledge (Cabana & et al., 1999), fear of uncertainty (Miyakis et al., 2006) and pressure from patients (Brett & McCullough, 2012). For overloaded doctors it can be more timesaving to order a laboratory test than speculating if the test might be unnecessary, and it can also be difficult for physicians to keep up with all the new tests available (Baron & Dighe, 2011). Physicians often do not know about the cost of laboratory tests (Allan & Lexchin, 2008). It can also be too easy to request laboratory tests, which could be changed by removing tests from standard forms and letting physicians justify the request instead. This can lead to a 20% reduction of laboratory tests (Zaat, van Eijk, & Bonte, 1992). The ageing of the population can affect the increased test volume.

2.1 Interventions to reduce laboratory tests

Several studies have been published about different interventions for improving laboratory-test requests (Bareford & Hayling, 1990; Cabana & et al., 1999; Fryer & Smellie, 2013; Grivell et al., 1981; Hutton, Drummond, & Fryer, 2009; Janssens, 2010; Kim, Dzik, Dighe, & Lewandrowski, 2011; W. S. A. Smellie, Lowrie, & Wilkinson, 2001; Solomon, 1998). However, little has been written about laboratory-test requests and costs in Iceland, except for one intervention study that was done in a Health Care Institution of South Iceland. In this study, the interventions were education, feedback about laboratory-request habits and change of the laboratory-request scheme. Laboratory tests removed from the request scheme decreased by 49% in one year and those that were not removed decreased by 23%. The study showed that the intervention was effective and cost saving (Reykdalsson, 2010).

The main interventions that have been used to influence laboratory tests are clinical guidelines (Driskell et al., 2012), changes in the laboratory request forms (Bailey, Jennings, & Parapia, 2005), education (Fryer & Smellie, 2013; Janssens, 2010), feedback (Jamtvedt, Young, Kristoffersen, O'Brien, & Oxman, 2006) and an electronic laboratory request system (Baron & Dighe, 2011). It has been shown that the design of the laboratory request and limiting the tests on the forms can influence physician test request habits and reduce inappropriate requests (Bailey et al., 2005; Kim et al., 2011).

2.1.1 Effect of clinical guidelines for laboratory tests

Clinical guidelines are a possible method for influencing physicians, but published guidelines have been shown to have a limited effect if not followed-up with other interventions (Lundberg, 1998). Many guidelines are published in journals or on websites and are not implemented with further interventions like education, feedback, detailing and workgroups (Gagliardi, 2012). Guidelines that are built on evidence and are straightforward, clear and uncontroversial may increase the probability of use (Grol et al., 1998). According to a study from 2001, to maintain up-to-date knowledge a general internist would need to read 20 articles a day the whole year (Shaneyfelt, 2001). Thus, physicians could save time by following guidelines, since they are supposed to be based on the best knowledge at the time and are presented in order to provide the best treatment with the least risk without excessive costs (Guyatt et al., 2000).

Adherence to clinical guidelines has been suggested to be only one-third in a study that looked at 11 studies with the Pathman awareness-to-adherence model (Mickan, Burls, & Glasziou, 2011). The study showed that strategies need to be in place to improve adherence and make physicians aware of the guidelines. Another systematic review of 76 studies showed that lack of awareness, knowledge, behaviour and attitude are some of the important factors regarding why physicians do not follow guidelines (Cabana & et al., 1999).

If the guidelines are complex, it is less likely that they will be followed compared to easily understood guidelines (Davis & Taylor-Vaisey, 1997; Francke, Smit, de Veer, & Mistiaen, 2008). An observational study including ten guidelines, where the aim was to determine which attributes of clinical guidelines influenced their use in clinical practice, showed that on average 61% of the general practioners followed the guidelines.

Multifaceted interventions have been shown to be more effective when implementing guidelines rather than single interventions (Francke et al., 2008) and education about clinical guidelines is more likely to succeed if it involves active participation of physicians, takes local circumstances into account, and includes reminders about specific patient cases (Davies, 1994). A multifaceted intervention, which included clinical guidelines at the bedside in the intensive care unit for laboratory-test requests as one of the interventions, decreased laboratory tests by 50% and led to substantial cost savings (Prat et al., 2009).

A UK study looked at the impact of clinical guidelines that were not followed up with any intervention after they had been published, regarding requests for the diabetes marker, glycated haemoglobin (HbA1c). The study showed that only 49% of requests were based on clinical guidelines, 51.2% of the repeated tests were inappropriate and under-requesting was more prevalent for the test, especially among general practitioners (Driskell et al., 2012).

Guidelines for prostate cancer routine screening in the US say that men 75 years and older should not undergo prostate-specific antigen testing. A national health survey published data that showed that guidelines for prostate cancer screening are not followed. The recommendations were published in 2008 but the screening rates were

unchanged from 2005 to 2010 in all groups, indicating that both patients and physicians had totally ignored the recommendations (Prasad, Drazer, Huo, Hu, & Eggener, 2012).

Tests were reduced by 85% in one acute and emergency unit after production of a memorandum about appropriate use of CRP tests, a protocol about when CRP could be requested, and a rule in the electronic system that identified unnecessary repeated tests within 24 hours (Hutton et al., 2009). Guidelines that restrict routine use have been shown to decrease cost (Kim et al., 2011), while tests on inpatients were reduced by 19% in one study that, together with education, restricted duplicate orders of several tests to a special department or required special approval for them (Calderon-Margalit, Mor-Yosef, Mayer, Adler, & Shapira, 2005).

2.1.2 Effect of education to reduce laboratory-test requests

Education has been used as an intervention to promote the correct utilization of laboratory tests and can, for example, improve clinical knowledge through lectures, educational material, guideline education, newsletters and reminders (Axt-Adam, van der Wouden, & van der Does, 1993; W. S. Smellie, 2012; Solomon, 1998). The effect of education on laboratory-test behaviour has varied (Fryer & Smellie, 2013; Janssens, 2010) and must be ongoing to increase effectiveness and to ensure the effects duration. It has been shown that the benefits are lost when the education stops (W. S. A. Smellie et al., 2001; Solomon, 1998; Zaat et al., 1992), which suggests the need for continuous follow-up.

Education as a single intervention has shown a limited effect, but it can be effective as a part of a multifaceted intervention (Fryer & Smellie, 2013; Grimshaw et al., 2004). One study examined the long-term effect of a two-day educational session for primary-care physicians, laboratory personnel and all new staff, during which they were shown, through scientific material, the benefits of changing their laboratory-test request habits. The study showed that the intervention managed to reduce the number of tests, save money and its effect was sustained after eight years (Larsson, Biom, Wernroth, Hulten, & Tryding, 1999; Mindemark & Larsson, 2009).

A study from Iceland (Reykdalsson, 2010) at the Health Care Institution of South Iceland had the same aim as LUH: to improve the quality of health care by reducing unnecessary laboratory tests, using two main interventions. The first intervention was

education for physicians about laboratory tests, which included the purpose, cost and nature of laboratory tests and also information about the use of laboratory tests by each physician compared to others at HCISI. The second intervention was a change in the electronic laboratory-test request forms, where fewer laboratory-test options were available. A change in laboratory request forms has been shown to reduce laboratory tests (Bailey et al., 2005). The first intervention, education, differs slightly from the education at LUH where the supervising physician gave lectures on the use of laboratory tests in general, although individual tests were mentioned to stress specific points, whereas at HCISI, a much smaller instituition, the education was about which test should be ordered for certain diseases and feedback was given about their laboratory request habits compared to others. A questionnaire was sent to the physicians at HCISI in which they were asked whether they thought the education had affected their laboratory-test request behaviour. All physicians participated; 91% thought it had a great effect and 86% thought they had decreased laboratory-test requests by 10-30% (Reykdalsson, 2010).

In the US, a campaign called Choosing Wisely from the American Board of Internal Medicine Foundation started in 2012 to educate both physicians and patients about unnecessary tests and treatments (Cassel & Guest, 2012). Studies have shown that 23 to 50% of interns are not confident in interpreting results from laboratory tests (Khromova & Gray, 2008; Stanfliet, Macauley, & Pillay, 2009). A study in an emergency department at a university hospital wanted to find out whether education about the correct use of CRP in the department could reduce the number of CRP tests. The medical staff worked as communicators to change the behaviour of interns and new students and managed to show a 48% decrease in CRP tests (Santos, Bensenor, Machado, Fedeli, & Lotufo, 2012).

Education about the price of CRP tests was given at a UK hospital to see whether it was possible to reduce the number of CRP test requests. The education resulted in a significant reduction of 32% and was greater for inpatients than outpatients. One possible reason suggested by the author was that junior physicians requested most of the inpatient tests and were possibly more open for feedback about costs (Fogarty, Sturrock, Premji, & Prinsloo, 2013).

These educational interventions show that it is possible to affect physician test request behaviour and reduce laboratory tests using inexpensive methods. Even printed educational material, which is relatively cheap, may be effective as part of multifaceted intervention (Grimshaw et al., 2004). A laboratory handbook which contains general information about each test, including which bottle should be used for blood samples, timing, fasting or not, reference values, retesting intervals and transporting conditions, should be easily accessible at both hospitals but is only accessible on the LUH website and not at AH. A laboratory handbook has been shown to change physician laboratory-test ordering routines by 36%, while 89% found it helpful in their daily work (Stakkestad, Sandberg, Bjerve, Runde, & Asberg, 1997).

2.1.3 Effect of feedback to reduce laboratory tests

Feedback about previous test behaviour and comparisons to others has been used as a method for changing physician laboratory-test behaviour. Audit and feedback are important factors for identifying problems and performance (Jamtvedt et al., 2006). The information can be obtained from a computer system like the Laboratory Portal at LUH or from medical records. The effect of feedback to reduce laboratory tests has shown mixed results (Ivers et al., 2012; Winkens et al., 1995).

To increase the effectiveness and permanence of feedback it should be ongoing (Beck, 1993; Miyakis et al., 2006; Tierney, Miller, & McDonald, 1990; Winkens, Pop, Grol, Kester, & Knottnerus, 1992), while feedback is also more likely to have an effect when physician behaviour is far from the optimal, in which case the feedback is given with high intensity (Jamtvedt et al., 2006).

A combination of feedback and education has been shown to be effective in changing physician behaviour only during the intervention (Miyakis et al., 2006; Tierney et al., 1990). One study has, though, managed to show a long-term effect after nine years, with feedback about laboratory-test behaviour to general practitioners which led to a permanent reduction (Winkens et al., 1996).

Some studies have shown that it can be more effective to use multifaceted interventions for behavioural change (Grimshaw et al., 2001; Solomon, 1998), as was done at LUH. A multifaceted intervention to improve test ordering in an emergency department, consisting of a protocol for laboratory-test requests, education of medical

staff and audit/feedback, showed a 40% decrease in all laboratory-test requests after 18 months (Stuart, Crooks, & Porton, 2002). Other studies have shown that this is not necessarily better (Grimshaw et al., 2004; Thomas, Croal, Ramsay, Eccles, & Grimshaw, 2006) and that a single intervention can decrease laboratory tests (Stuebing & Miner, 2011; Winkens et al., 1992).

A prospective observational study determined whether it was possible to make physicians aware of the phlebotomy cost every week for the patient and to reduce laboratory tests in a non-intensive care unit. This was shown to be an effective way for reducing tests and saved money after 11 weeks (Stuebing & Miner, 2011).

Another single interventional study on the effect of continuous feedback to general practitioners, based on the analysis of laboratory-test behaviour, reduced tests by 40% compared with no feedback (Winkens et al., 1992). Unnecessary repeated laboratory tests can be avoided by using monthly feedback of individual test use data in conjunction with physician data (Bareford & Hayling, 1990).

Multifaceted interventions using feedback on laboratory-test requests, in combination with education and educational reminder messages, were effective and did not differ among general practitioners compared with either of those parameters alone (Thomas et al., 2006). Interaction and social influence can be motivators for change: compared with classic feedback, a multifaceted intervention among general practitioners showed more success than a single intervention. The classic feedback was compared with group meetings where specific conditions and laboratory-test education was discussed instead of specific tests, since that was more likely to increase the interest. The number of laboratory-test requests decreased by 12% in the interactive group when compared with the group that received feedback only (Verstappen et al., 2004).

When testing is made more accessible, test requests are likely to increase. For instance, a UK hospital experienced an increase in test ordering after transferring measurements of CRP an acute phase reactant, from a specialist laboratory to a routine laboratory. Interventions to reduce the inappropriate tests included discussions with physicians and a disease-related protocol which led to an 85% overall reduction of test requests and cost savings (Hutton et al., 2009).

Feedback can aslo be electronic or automated. Electronic laboratory request systems or CPOE can contain templates that can make it easier for doctors to know what should be done and which tests to order for patients. Templates in an electronic system can contain clinical guidelines and are easy to update (Baron & Dighe, 2011; Wang et al., 2002). Incorporation of guidelines into computer admission templates and regular education for staff has been shown to reduce tests (Kim et al., 2011; Wang Tj & et al., 2002). It is also useful when more than two tests are available and physicians can be confused about which test to use (Kim et al., 2011).

When a doctor orders a special laboratory test, clinical guidelines for that test can be posted automatically as a reminder on the computer screen so the doctor can be aware of the advice. This has been shown to decrease tests by up to 71% (Kim et al., 2011). The computer flags tests that do not meet the criteria in the guidelines and sends an email to the director and the physician who ordered the test, with links to the key data on its use. Also, laboratory tests ordered beyond three days require an explanation (Kim et al., 2011).

This automatic function and incorporation of guidelines as a reminder is not in place within the laboratory systems in Iceland. Reminders have been shown to be more effective in changing physician behaviour when they are incorporated into clinical settings for different types of disease (Cheung et al., 2012). Reminders with information about the cost and total charge for laboratory tests resulted in a 27% reduction in costs in a paediatric department compared with the control period (Hampers, Cha, Gutglass, Krug, & Binns, 1999). Another system is the Laboratory Information System (LIS), which contains all information from the laboratory and is most effective when two systems (LIS and CPOE) are linked together (Baron & Dighe, 2011). This is like the Health Portal system at LUH and AH, where it is possible to both order tests and view results. The hospital structure is important for successful implementation of a CPOE and should include a group with key physicians and a respected clinical pathologist. The group should be responsible for monitoring, review and approval (Kim et al., 2011). The CPOE system has not yet been implemented in all hospitals in Europe and the US because of cost (Baron & Dighe, 2011).

Computerised Laboratory Management System is a reimbursement system based on the diagnosis-treatment combination and allocates budget to those who request it. Like the Laboratory Portal at LUH, the system can monitor a doctor's laboratory habits but can also give automatic feedback when a test has already been done or give a message about a certain test that can automatically appear on the screen (Janssens, 2010). It has been shown that the design of the laboratory request and a limit to the number or type of tests on the forms can influence physician test request habits and reduce inappropriate requests (Bailey et al., 2005; Reykdalsson, 2010). Laboratory tests that were removed from the request scheme decreased in frequency by 49% in one year while those that were not removed decreased by 23% (Reykdalsson, 2010). Limiting orders to a fixed period and unbundling tests from a pre-specified panel so that physicians need to request individual tests has been shown to reduce the number of laboratory tests that were previous bundled by 51% (Neilson et al., 2004). Other studies have shown that as soon as doctors can choose to use the old request forms again, the benefits are lost (Zaat et al., 1992)

2.1.4 Effect of letters as a reminder to reduce laboratory tests

Reminders (paper-based or computerized) about clinical guidelines have been shown to be effective and lead to moderate improvements (Grimshaw et al., 2004).

In an intervention study, a paper-based letter was sent to physicians who ordered tests above a certain cost. The physicians were then asked for an explanation of the test within ten days; if no answer was provided, the test was cancelled. This was shown to be an easy and effective intervention which resulted in a 53% decrease in test requests and a 50% cost decrease in one year. This study did not discuss whether too many tests might have been cancelled, and it is possible that doctors thought it was time-consuming and extra work to give an explanation for tests (Liu et al., 2012). A controlled before-and-after study consisting of a mailing activity intervention (clinical guidelines, booklets, brochures, laboratory utilization report for each doctor and audit package), which was sent to general practitioners to increase awareness of guidelines, was shown to increase the quality of the requests according to guidelines and reduce cost by 23.5% (Tomlin, Dovey, Gauld, & Tilyard, 2011).

A systematic review with the aim of evaluating the effectiveness of reminders to change physician behaviour showed that reminders are more effective when they are incorporated into clinical settings for different types of disease (Cheung et al., 2012). A prospective, controlled and nonblinded study in a paediatric emergency department found that reminders with information about prices for requested laboratory tests reduced costs by 27% compared with the control period (Hampers et al., 1999).

3 Materials and Methods

A retrospective study was conducted using laboratory-test volume data from LUH and AH from January 1st, 2007 to July 1st, 2013 (6 years and 6 months). This period included a total of 1,366,275 hospital days at discharge and 2,596,672 ambulatory visits at LUH compared with 191,275 hospital days at discharge and 318,533 ambulatory visits at AH. From January 1st, 2007 to July 1st, 2013, LUH analysed 1,147,638 samples of the six laboratory tests under examination in this study (ASAT, ALAT, ALP, GGT, CRP and blood culture) while AH analysed 123,759 samples of the same tests.

From January 1st, 2007 to February 1st, 2010, LUH analysed 4,169,693 samples in haematological and clinical biochemistry and from January 1st, 2007 to January 1st, 2011, 242,877 microbiology samples. In the period after the guidelines from March 1st, 2010 to June 1st, 2013, LUH analysed 3,810,721 samples in haematological and clinical biochemistry and from February 1st, 2011 to June 1st, 2013, 117,561 microbiology samples. That amounts to a 9% decrease in haematological and clinical biochemistry samples and a 52% decrease in microbiology samples. The same data was not available from AH.

The frequency of the six laboratory tests focused on in this study from 2007 to 2013 at LUH and AH may be seen in Table 1. Seven other laboratory tests with no hospital specific guidelines at LUH were also studied to see whether the interventions had indirect effects on other tests (ESR, CBC, creatinine, sodium, potassium, glucose and HbA1c). For example, to identify and monitor inflammation, C-reactive protein (CRP), which is an acute phase protein, can be measured along with Erythrocyte Sedimentation Rate (ESR) to show acute phase response. CRP has been shown to rise and peak earlier in the inflammatory process and also returns faster to the normal level, while for ESR this takes longer and can be affected by several factors, for example age and pregnancy (Colombet et al., 2010). The number of tests, how they have evolved and the possible substitution effect of ESR instead of CRP when the guidelines were published will be presented graphically.

Data on operational figures (number of discharges per month, total hospital days at discharge per month and number of ambulant visits per month) was obtained from the finance departments at the hospitals. Data processing and statistical calculations were carried out in Microsoft Excel.

Table 1: Operational data and total number of tests per year at Landspitali University Hospital and Akureyri Hospital

LUH	2007	2008	2009	2010	2011	2012	2013*
Total hospital days at							
discharge	192,411	231,887	228,308	201,845	197,890	206,541	107,393
Ambulant visits	397,501	412,420	407,242	397,225	393,942	387,181	201,161
Tests with guidelines							
ALAT	34,199	36,183	33,985	28,000	30,502	31,556	16,666
ALP	33,863	35,220	32,296	26,434	29,006	30,054	15,342
ASAT	33,360	35,318	32,805	17,430	15,489	15,369	8,433
GGT	34,192	35,588	32,851	18,476	17,691	16,997	8,039
CRP	70,469	69,045	63,022	41,638	41,233	44,567	25,849
Blood culture	10,006	9,547	9,863	8,737	7,400	7,187	3,731
Total tests	216,089	220,901	204,822	140,715	141,321	145,730	78,060
Tests with no							
guidelines							
ESR	19,469	20,059	17,303	11,454	11,016	11,165	6,319
CBC	147108	150906	139493	127176	131704	130454	67112
Creatinine	109532	107798	108277	99691	107042	107957	56492
Sodium	104863	106752	103632	92269	99547	100772	53551
Potassium	105983	107849	104718	94185	101600	102203	53984
HbA1c	3685	4099	5189	6331	6543	7315	4052
Glucose	47407	48139	45108	42669	45735	46570	24660
Total tests	538,047	545,602	523,720	473,775	503,187	506,436	266,170
АН	2007	2008	2009	2010	2011	2012	2013*
Total hospital days at							
discharge	30,674	30,651	28,288	30,921	29,746	27,528	13,467
Ambulant visits	40,426	44,570	45,462	51,117	52,957	54,953	29,048
ALAT	3,641	3,945	3,319	3,452	3,564	3,917	1,891
ALP	3,126	3,352	2,711	2,951	3,017	3,399	1,784
ASAT	3,820	4,103	3,406	3,401	3,506	3,867	1,829
GGT	3,072	3,426	2,647	2,533	2,712	3,064	1,517
CRP	5,532	5,727	3,932	4,551	5,682	5,971	3.030
Blood culture	422	407	391	393	325	285	139
Total tests	19,613	20,960	16,406	17,281	18,806	20,503	10,190

^{*2013} data from the first six months

To measure the impact of the interventions on laboratory-test usage, the six laboratory tests in which clinical guidelines have been introduced were analysed graphically. The average number of laboratory tests was divided into periods, and differences in laboratory-test requests before (2007-2009) and after (2010-2013) the intervention were compared and tested for significance with a t-test. The year 2009 was chosen as the cut-off point since the Laboratory Portal was implemented in December 2009 and the interventions started after that. For blood cultures, the period before the guidelines (2007-2010) was compared with the period after they had been instigated (2011-2013).

The goal at LUH to reduce laboratory tests by 15% in 2010 is likely to have had an effect not only on specific laboratory tests where guidelines had been made but also a possible indirect (hereafter called spill-over) effect on several other laboratory tests (CBC, creatinine, potassium, sodium, glucose and Hba1_c), for which no clinical guidelines were introduced but which were studied for the same periods.

To account for trends unrelated to the interventions at LUH, the relative risk (RR) of a laboratory test being conducted at LUH compared to AH was calculated for various points in time, along with the associated 95% confidence intervals (CI). Specifically, this was done for the pre and post intervention periods separately (2007-2009 vs 2010-2013), but was also done on a monthly basis in order to observe the development of the effect over the whole period from January 2007 to July 2013 in greater detail.

One educational intervention took place at AH in February 2009 and was specifically designed to decrease CRP laboratory-test requests. This was before the CRP guidelines were published on March 1, 2010. AH thus serves as a control hospital to rule out the possibility that the observed changes over time are due to underlying trends in practice, disease prevalence or other confounders. It would have been possible to take an alternative strategy and calculate the RR of laboratory testing after the intervention compared to before the intervention at each hospital separately. However, measurement precision would have varied vastly between the two hospitals as they are very different in size. Using the RR as a measure across hospitals and subsequently evaluating those RRs over time provides consistent measures of precision throughout the calculations.

The RR of testing was calculated as risk per patient days at discharge and ambulant visits. An alternative strategy would have been to use the population living in the service area of each particular hospital. However, besides being theoretically more questionable, the uptake areas for each hospital are not well defined. The total hospital days at discharge and the number of ambulant visits at LUH and AH from 2007 to 2013 are listed in Table 1.

4 Results

An examination of a graphical representation of the unadjusted data reveals a clear decline in CRP, GGT and ASAT tests and a lesser decline in ALAT and ALP tests at LUH in mid-2010, as can be seen in Figure 2. The four liver function tests seem to have been ordered simultaniously pre guidelines, but post guidelines ALAT and ALP appear to be ordered together while ASAT and GGT are ordered together, but much less frequently. This is in line with the published guidelines. Blood-culture tests began to decrease slowly in 2010, before the clinical guidelines were published on February 1st, 2011, and continued to decrease post guidelines.

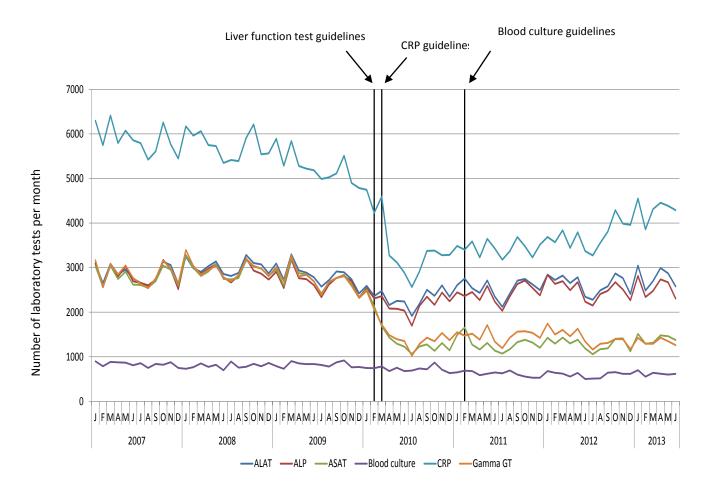


Figure 2: The time trend of laboratory-test frequencies at Landspitali University Hospital.

Examination of raw time lines from AH for comparison show that the development of laboratory tests at AH is noticeably different from the one at LUH, as can be seen in Figure 3. In early 2009, there is a clear decrease in CRP tests due to an educational intervention that AH arranged for doctors in February 2009, specifically to decrease CRP laboratory-test requests. This was before the CRP guidelines were published on March 1st, 2010 and appears to have produced only a temporary effect. At AH, ALP and GGT seem to be ordered together and ALAT and ASAT together. Blood-culture tests decreased slowly at AH from 2010-2013.

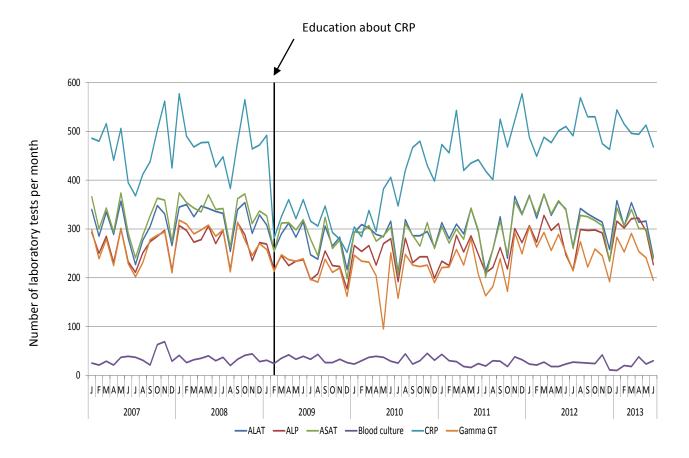


Figure 3: The time trend of laboratory-test frequencies at Akureyri Hospital.

When the time trend for the number of ESR and CRP tests at LUH is compared, a substitution towards ESR tests is not apparent, as can be seen in Figure 4.

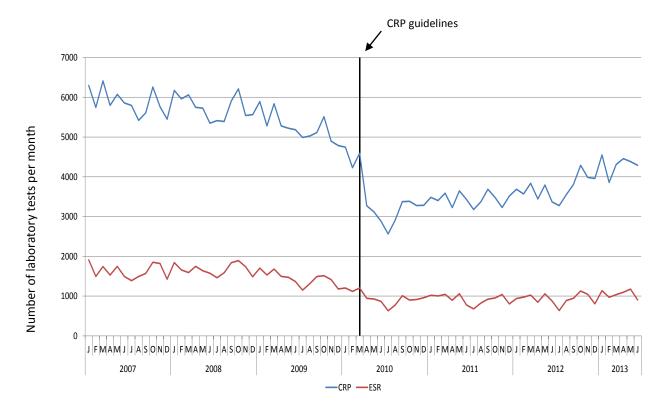


Figure 4: The time trend of Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) test frequencies at Landspitali University Hospital.

When the pre and post intervention periods are examined and the average number of laboratory tests per month in the period before the guidelines is compared with the average number of laboratory tests per month after the guidelines, a substantial (12-52%) and statistically significant (p<0.001) reduction is observed for all tests at LUH, as can be seen in Table 2. The biggest reduction from before the guidelines to afterwards was a 52% reduction for ASAT, while GGT decreased by 49%, CRP by 35%, blood culture by 23%, ALP by 15% and ALAT by 12%.

The same period was used for AH for comparison. Two tests showed a statistically significant decrease: blood culture tests by 26% (P<0.001) and GGT tests by 8% (p=0.038), while the average number of CRP tests increased by 9% (p=0.049), as can be seen in Table 2.

Table 2: Average number of laboratory tests per month pre and post guidelines at Landspitali University Hospital (LUH) and Akureyri Hospital (AH)

	Before guidelines	After guidelines	p-value
	m(sd)	m(sd)	from a t-test
Landspitali University	/ Hospital		
ALAT	2899(211)	2541(247)	<0.001
ALP	2816(234)	2401(242)	<0.001
ASAT	2819(219)	1351(267)	<0.001
CRP	5626(418)	3650(501)	<0.001
GGT	2851(241)	1457(242)	<0.001
Blood culture*	795(69)	611(57)	<0.001
CBC	12153(815)	10868(828)	<0.001
S-Creatinine	9045(852)	8838(741)	0.255
S-Potassium	8849(510)	8380(693)	0.001
S-Sodium	8757(496)	8241(701)	<0.001
S-Glucose	3907(283)	3801(293)	<0.109
B-HbA1c	360(100)	577(120)	<0.001
Akureyri Hospital			
ALAT	303(39)	305(39)	0,787
ALP	255(36)	266(37)	0,221
ASAT	315(44)	300(40)	0,13
CRP	422(88)	458(71)	0,049
GGT	254(41)	234(42)	0,038
Blood culture*	34(10)	25(8)	<0.001

^{*} for blood culture the period is 2007-2010 and 2011-2013

To estimate possible indirect (spill-over) effects on other laboratory tests for which no hospital oriented clinical guidelines were introduced, several laboratory tests were studied at LUH and a less pronounced decrease was found. An 11% (p<0.001) decrease was found for complete blood count (CBC), which is the most common laboratory test requested at LUH, a 5% (p<0.001) decrease for potassium and a 6% (p<0.001) decrease for sodium. The number of glycated haemoglobin tests (Hba1c) increased by 60% (p<0.001).

When the relative risk coefficients of laboratory tests at LUH compared to AH were calculated pre and post guidelines, the RR for ALAT and ALP did not statistically significantly decrease in the period after the guidelines, but decreased statistically significantly for ASAT, CRP and GGT. The RR for a blood culture test in the period after the guidelines was statistically significantly increased, as can be seen in Table 3.

Table 3: Relative risk of laboratory tests at Landspitali University Hospital compared to Akureyri Hospital before the guidelines 2007-2009 and after the guidelines 2010-2013.

	Befor	e guidelines	Afte	er guidelines
	RR	CI	RR	CI
ALAT	1.126	(1.105 – 1.148)	1.152	(1.132 – 1.173)
ALP	1.299	(1.272 – 1.326)	1.252	(1.228 – 1.276)
ASAT	1.054	(1.035 – 1.074)	0.623	(0.611 – 0.635)
CRP	1.569	(1.545 – 1.594)	1.103	(1.087 – 1.119)
GGT	1.321	(1.294 – 1.349)	0.862	(0.844 – 0.880)
Blood culture*	2.894	(2.754 – 3.042)	3.400	(3.161 – 3.657)

^{*} for blood culture the period is 2007-2010 and 2011-2013

The relative risk of a laboratory-test request at LUH compared with AH on a monthly basis can be seen in Figure 5. Before 2010 the RR for a laboratory-test request was always higher at LUH, but in early 2010 the GGT and ASAT tests fell below 1 while ALP, ALAT and CRP are closer to 1 than before the interventions. Blood cultures are much more common at LUH than at AH, possibly because LUH has sicker patients and the difference increased in the post guideline period due to a slightly more pronounced decrease in blood cultures at AH.

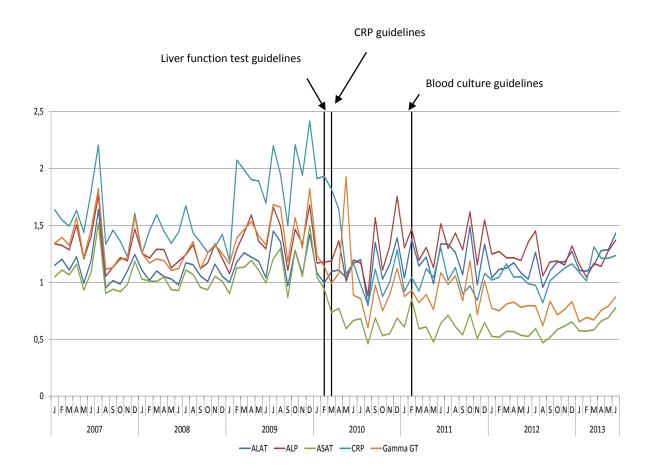


Figure 5: Relative risk of a laboratory-test request at Landspitali University Hospital compared to Akureyri Hospital.

5 Discussion

The study showed a positive and prolonged effect of the multifaceted interventions, follow-up of three guidelines, education, feedback and reminder letters at LUH compared to AH. It is possible to have an effect with only a modest increase in manpower and without much extra cost. The effect seems nevertheless to be slowly fading away for the CRP test, possibly because education and feedback have occurred less frequently recently.

One weakness in this study may be whether AH was a good control hospital since it is a much smaller institution and the case mix at the two hospitals is probably different. Akureyri Hospital did arrange a targeted intervention in February 2009, which was shown to have a great effect, but that effect was lost one year after the intervention and before the interventions began at LUH. This is in accordance with previous results showing that the benefits of an intervention are lost when it is stopped (Zaat et al., 1992). A further caveat is that the study lacks data, which was not accessible from AH, on the total number of laboratory tests to be taken into account along with the number of individual tests.

The data used in the study comes from the Laboratory Portal system at LUH and Technidata and ProClarity at AH and should be reliable since they are obtained directly from the hospital database. This study evaluated only the number of tests and not patient data. The saving through fewer laboratory tests was studied by using the unit price per test under the assumption that the price would remain unchanged. Also, it would have been interesting to view laboratory test orders from interns and junior doctors compared to specialists, as they have been shown to follow what specialists do rather than what they were taught in medical school (Grivell et al., 1981) and studies have shown that 23-50% of interns are not confident in interpreting laboratory tests (Khromova & Gray, 2008; Stanfliet et al., 2009). Unfortunately it was not possible to look at repeated tests, which probably represent a large part of the inappropriate tests (Driskell et al., 2012).

When the pre and post intervention periods were examined and the average number of laboratory tests per month in the period before the guidelines was compared with the average number of laboratory tests after the guidelines, a statistically significant 12-52% (p<0,001) reduction was observed for all six tests at LUH. Avoidable laboratory tests have been shown to account for up to 25-40% of all tests (Rao et al., 2003). It has also been shown that focus on high-volume tests can have a greater impact than tests that are rarely carried out (Ming Zhi, 2013) as could have been the case with CRP and CBC, which are among the most frequently requested tests at LUH and which were both reduced substantially after the interventions albeit much less so for CBC.

When the same period was used for the control AH, two tests showed a statistically significant decrease: blood-culture tests by 26% (P<0.001) and GGT tests by 8% (p=0.038). A possible reason for the decrease of blood-culture tests in Akureyri is that the guidelines for blood culture were made available on the meeting table in the physicians meeting room, and junior doctors were reminded about them in meetings (Nick Cariglia, personal communication, 2013, Nov 22nd).

In combination with education and feedback, the effect of the clinical guidelines for liver-function tests (ASAT, ALAT, GGT and ALP) and CRP in early 2010 was substantial. The four liver-function tests seemed to be unnecessarily ordered together before, but after the intervention ALAT and ALP were ordered together and ASAT and GGT together, but much less frequently as suggested by the clinical guidelines. A possible substitution effect at LUH of ESR instead of CRP was looked into graphically and ESR did not appear to be requested instead of CRP. This can indicate that interventions for certain tests can encourage physicians to change their behaviour and be more careful when ordering other tests as well.

A possible indirect (spill-over) effect from the interventions at LUH showed a less pronounced decrease in other laboratory tests which had no clinical guidelines, while tests for glycated haemoglobin (Hba1c) had even increased by 60% (p<0.001). This increase of the HbA1c test could possibly be linked to the rising prevalence of diabetes, which has coincided with a 50% increase of obesity in Iceland in the years 2000 to 2011 (OECD, e.d.a.). Another possible reason could be that the test was underutilized before.

The relative risk coefficients of laboratory tests at LUH compared to AH pre and post guidelines showed that the RR for ALAT and ALP tests was not statistically significantly decreased in the period after the guidelines, but was statistically significantly decreased for ASAT, CRP and GGT. These tests were almost certainly overused: for example, the ASAT test should only be requested when there is clinical suspicion of liver disease or alcoholic liver disease (Appendix 3). The RR for a blood culture test in the period after the guidelines was statistically significantly increased due to a more pronounced decrease in blood cultures at AH.

For each blood test, there may be multiple analysis possibilities, for example to test whether a certain blood sample contains a particular substance (e.g. bacteria in blood culture) or to find the concentration of a substance (e.g. for CRP). Each of those analytical methods or laboratory tests has a given unit and a given unit price. It was not possible to see in the Laboratory Portal when the tests were performed and therefore it was impossible to get the exact cost information from LUH. The reason for this is that the price for each test depends on when the test is requested. If laboratory tests are requested outside the usual working hours at LUH, an additional 70% is charged for the tests and a three-unit administrative fee is levied on each request, independent of how many analyses are requested on each order; this is not the case at AH. In Appendix 7 the price for the six tests is summarized and information is given about the number of units per test and the unit price from 2007 to 2013. This cost is according to a price list for services that have been contracted out to the hospitals (for example by healthcare centres) but departments asking for laboratory tests are not charged and do not receive special funding for tests.

The cost saving was calculated based on the reduction of laboratory tests and prices of tests in 2013. When the unit price per test was used and the period pre and post guidelines was compared for the six tests under study, the cost saving was ISK 67,400,021 per year at LUH while for the control, Akureyri hospital, the saving was ISK 343,627 based on the prices in 2013. Indirect costs must also be calculated, as although extra funds are not allocated for these interventions, laboratory staff cannot be performing other duties in the meantime.

It was assumed that all the tests were taken during normal working hours and therefore the cost-savings estimate is conservative. Unlike LUH, the laboratory at AH is not allowed to charge extra for tests ordered outside normal working hours.

Low-cost laboratory tests that are used often can account for the highest share of laboratory costs and are therefore a good target for improvement, compared to low-volume tests. The most common laboratory tests are relatively cheap, but the high volume of these makes the total cost high, even though low-volume tests are more frequently misutilized (Ming Zhi, 2013).

It was not possible to estimate the effect of fewer laboratory tests on patient outcomes, but increased awareness of proper utilization of laboratory tests will hopefully lead to improved patient care. However, previous findings have shown that it is possible to decrease unnecessary laboratory tests without affecting the diagnosis or treatment of patients (Attali et al., 2006; Wang et al., 2002). In one emergency department, feedback on physician laboratory-test behaviour, cost awareness of overuse of tests, and test request behaviour before and after led to a 68% reduction in laboratory tests without affecting the patient (Miyakis et al., 2006). As has been mentioned, the goal at LUH was to reduce laboratory tests by 15% in 2010. The question is whether it was appropriate to reduce the number of blood-culture tests further in 2011 since they were already decreasing and, according to the European Antimicrobial Resistance Surveillance System Annual Report in 2008 (EARSS, 2008), the use in Iceland was fairly low compared to other countries in Europe in 2008, and was substantially lower than the other Nordic countries (Norway, Finland and Sweden), as can be seen in Figure 6.

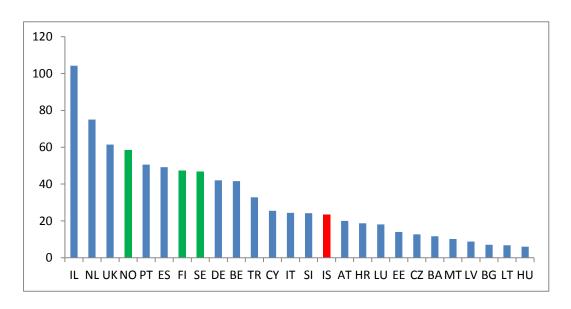


Figure 6: Number of blood culture sets per 1000 patient days. Data from the EARSS Annual Report 2008.

This study can contribute to our knowledge on to what extent interventions and clinical guidelines affect the number and cost of laboratory tests. It shows that it is possible to affect physician behaviour through the measures examined. Previous studies have shown reductions in laboratory tests of similar magnitude to those seen in this study. Stuart et al. found that with guidelines, feedback and education it was possible to reduce tests by 40% (Stuart et al., 2002) and Miyakis et al found that 68% of tests were avoidable with feedback and educational intervention (Miyakis et al., 2006).

The effect of interventions seems to be fragile and the request habits return to their previous level when the intervention is stopped (W. S. A. Smellie et al., 2001; Solomon, 1998; Tierney et al., 1990; Zaat et al., 1992). Therefore it is important to continuously monitor the use of laboratory tests and take action using interventions when needed, as can be done with the Laboratory Portal.

Landspitali University Hospital saw a significant decrease in all six laboratory tests for which clinical guidelines had been made as a part of a multifaceted intervention, and the interventions at LUH had a milder but noticeable spill-over effect on other tests at the hospital that did not have guidelines. Five of the laboratory tests (ASAT, ALAT, GGT, ALP and CRP) are still statistically significantly reduced, three and a half years after the intervention started, and the blood-culture test frequency is still statistically significantly decreased two years after the intervention started. A passive approach is

unlikely to be successful when introducing clinical guidelines, as may be seen in Akureyri hospital.

As noted in this study, only one other Icelandic study has been done on the effect of interventions on the use of laboratory tests (Reykdalsson, 2010). However, the present study has more data, looks at the effect over a longer period of time (2007-2013), and looks at different interventions. This study reaffirms the results of the other study, which shows the importance of continuous monitoring and follow-up that is needed for sustained effect. Further research is needed to answer whether the interventions on the use of laboratory tests have led to increased admissions and hospital stays.

Laboratory test improvements can contribute to better laboratory test utilization and have a positive impact on the budget which is under constant pressure, as well as providing better quality of care for the patient. Better utilization of laboratory tests will have both direct and indirect effects: direct effects on cost saving and indirect through fewer tests ordered that will minimize the risk for false-positive results, which will in turn reduce test frequency.

6 Conclusion

It is possible to influence physician laboratory-test requests using multifaceted interventions that include continuous monitoring and follow-up. The involvement of senior physicians and continuous monitoring and feedback will increase the likelihood of success. Compared to Akureyri Hospital, laboratory tests were statistically significantly reduced using interventions at Landspitali University Hospital and led to cost savings, under the assumption that the decrease did not cause increased costs elsewhere in the system. Laboratory tests account for a relatively small part of the health-care cost, but the results lead to further medical decisions that can have a big impact on patient care and how the money is spent. Hospitals can use multifaceted interventions to steer physician behavior, with continuous follow-up so as not to lose the effect. A passive approach when introducing clinical guidelines is less effective, as may be seen in the case of Akureyri Hospital.

References

- Akureyri Hospital. Akureyri Hospital Annual Report 2012 Retrieved July 19, 2013, from http://www.fsa.is/static/files/arskyrslur/Arsskyrsla2012.pdf
- Allan, G. M., & Lexchin, J. (2008). Physician awareness of diagnostic and nondrug therapeutic costs: a systematic review. *Int J Technol Assess Health Care*, *24*(2), 158-165. doi: 10.1017/s0266462308080227
- Attali, M., Barel, Y., Somin, M., Beilinson, N., Shankman, M., Ackerman, A., & Malnick, S. D. (2006). A cost-effective method for reducing the volume of laboratory tests in a university-associated teaching hospital. *Mt Sinai J Med*, *73*(5), 787-794.
- Axt-Adam, P., van der Wouden, J. C., & van der Does, E. (1993). Influencing behavior of physicians ordering laboratory tests: a literature study. *Med Care*, *31*(9), 784-794.
- Bailey, J., Jennings, A., & Parapia, L. (2005). Change of pathology request forms can reduce unwanted requests and tests. *J Clin Pathol*, *58*(8), 853-855. doi: 10.1136/jcp.2004.023101
- Bareford, D., & Hayling, A. (1990). Inappropriate use of laboratory services: long term combined approach to modify request patterns. *BMJ*, 301(6764), 1305-1307.
- Baron, J. M., & Dighe, A. S. (2011). Computerized provider order entry in the clinical laboratory. *J Pathol Inform, 2*, 35. doi: 10.4103/2153-3539.83740
- Bartlett, R. C. (1982). Making optimum use of the microbiology laboratory. II. Urine, respiratory, wound, and cervicovaginal exudate. *JAMA*, *247*(9), 1336-1338.
- Beck, J. R. (1993). Does feedback reduce inappropriate test ordering? *Arch Pathol Lab Med*, 117(1), 33-34.
- Berwick, D. M., & Hackbarth, A. D. (2012). Eliminating waste in US health care. *JAMA*, 307(14), 1513-1516. doi: 10.1001/jama.2012.362
- Brett, A. S., & McCullough, L. B. (2012). Addressing requests by patients for nonbeneficial interventions. *JAMA*, *307*(2), 149-150. doi: 10.1001/jama.2011.1999
- Cabana, M., Rand, C. S., Powe N. R.,, & et al. (1999). Why don't physicians follow clinical guidelines? A framework for improvement. *JAMA*, 282(15).
- Calderon-Margalit, R., Mor-Yosef, S., Mayer, M., Adler, B., & Shapira, S. C. (2005). An administrative intervention to improve the utilization of laboratory tests within a university hospital. *Int J Qual Health Care*, *17*(3), 243-248. doi: 10.1093/intqhc/mzi025

- Cassel, C. K., & Guest, J. A. (2012). Choosing wisely: helping physicians and patients make smart decisions about their care. *JAMA, 307*(17), 1801-1802. doi: 10.1001/jama.2012.476
- Cheung, A., Weir, M., Mayhew, A., Kozloff, N., Brown, K., & Grimshaw, J. (2012). Overview of systematic reviews of the effectiveness of reminders in improving healthcare professional behavior. *Syst Rev, 1*, 36. doi: 10.1186/2046-4053-1-36
- Davies, J., Freemantle, N., Grimshaw, J., Hurwitz, B., Long, A., Russell, IT. (1994). Implementing clinical practice guidelines: Can guidelines
- be used to improve clinical practice? Effective Health Care Bulletin, 1, 1-12.
- Davis, D. A., & Taylor-Vaisey, A. (1997). Translating guidelines into practice. A systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical practice guidelines. *CMAJ*, 157(4), 408-416.
- Driskell, O. J., Holland, D., Hanna, F. W., Jones, P. W., Pemberton, R. J., Tran, M., & Fryer, A. A. (2012). Inappropriate requesting of glycated hemoglobin (Hb A1c) is widespread: assessment of prevalence, impact of national guidance, and practice-to-practice variability. *Clin Chem*, *58*(5), 906-915. doi: 10.1373/clinchem.2011.176487
- EARSS. (2008). European Antimicrobial Resistance Surveillance System Annual Report 2008.
- Fogarty, A. W., Sturrock, N., Premji, K., & Prinsloo, P. (2013). Hospital Clinicians' Responsiveness to Assay Cost Feedback: A Prospective Blinded Controlled Intervention Study. *JAMA Intern Med.* doi: 10.1001/jamainternmed.2013.8211
- Forsman, R. W. (1996). Why is the laboratory an afterthought for managed care organizations? *Clin Chem*, 42(5), 813-816.
- Francke, A. L., Smit, M. C., de Veer, A. J., & Mistiaen, P. (2008). Factors influencing the implementation of clinical guidelines for health care professionals: a systematic meta-review. *BMC Med Inform Decis Mak, 8*, 38. doi: 10.1186/1472-6947-8-38
- Fryer, A. A., & Smellie, W. S. (2013). Managing demand for laboratory tests: a laboratory toolkit. *J Clin Pathol*, 66(1), 62-72. doi: 10.1136/jclinpath-2011-200524
- Gagliardi, A. R. (2012). "More bang for the buck": exploring optimal approaches for guideline implementation through interviews with international developers. *BMC Health Serv Res, 12*, 404. doi: 10.1186/1472-6963-12-404
- Grimshaw, J. M., Shirran, L., Thomas, R., Mowatt, G., Fraser, C., Bero, L., . . . O'Brien, M. A. (2001). Changing provider behavior: an overview of systematic reviews of interventions. *Med Care*, *39*(8 Suppl 2), II2-45.

- Grimshaw, J. M., Thomas, R. E., MacLennan, G., Fraser, C., Ramsay, C. R., Vale, L., . . . Donaldson, C. (2004). Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technol Assess*, 8(6), iii-iv, 1-72.
- Grivell, A. R., Forgie, H. J., Fraser, C. G., & Berry, M. N. (1981). Effect of feedback to clinical staff of information on clinical biochemistry requesting patterns. *Clin Chem,* 27(10), 1717-1720.
- Grol, R., Dalhuijsen, J., Thomas, S., Veld, C., Rutten, G., & Mokkink, H. (1998). Attributes of clinical guidelines that influence use of guidelines in general practice: observational study. *BMJ*, *317*(7162), 858-861.
- Grol, R., & Grimshaw, J. (2003). From best evidence to best practice: effective implementation of change in patients' care. *Lancet, 362*(9391), 1225-1230. doi: 10.1016/s0140-6736(03)14546-1
- Guyatt, G. H., Haynes, R. B., Jaeschke, R. Z., Cook, D. J., Green, L., Naylor, C. D., . . . Richardson, W. S. (2000). Users' Guides to the Medical Literature: XXV. Evidence-based medicine: principles for applying the Users' Guides to patient care. Evidence-Based Medicine Working Group. *JAMA*, 284(10), 1290-1296.
- Hampers, L. C., Cha, S., Gutglass, D. J., Krug, S. E., & Binns, H. J. (1999). The effect of price information on test-ordering behavior and patient outcomes in a pediatric emergency department. *Pediatrics*, 103(4 Pt 2), 877-882.
- Houben, P. H., Winkens, R. A., van der Weijden, T., Vossen, R. C., Naus, A. J., & Grol, R. P. (2010). Reasons for ordering laboratory tests and relationship with frequency of abnormal results. *Scand J Prim Health Care*, *28*(1), 18-23. doi: 10.3109/02813430903281758
- Hutton, H. D., Drummond, H. S., & Fryer, A. A. (2009). The rise and fall of C-reactive protein: managing demand within clinical biochemistry. *Ann Clin Biochem, 46*(Pt 2), 155-158. doi: 10.1258/acb.2008.008126
- Icelandic Health Insurance. (2013). Regulation of the share of health insurance costs for health care Retrieved July 10, 2013, from http://www.stjornartidindi.is/Advert.aspx?ID=366c43d0-b826-43ce-aa0d-ee607a9561b5
- Ivers, N., Jamtvedt, G., Flottorp, S., Young, J. M., Odgaard-Jensen, J., French, S. D., . . . Oxman, A. D. (2012). Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev, 6*, CD000259. doi: 10.1002/14651858.CD000259.pub3
- Jamtvedt, G., Young, J. M., Kristoffersen, D. T., O'Brien, M. A., & Oxman, A. D. (2006). Does telling people what they have been doing change what they do? A systematic review of the effects of audit and feedback. *Qual Saf Health Care*, 15(6), 433-436. doi: 10.1136/qshc.2006.018549

- Janssens, P. M. W. (2010). Managing the demand for laboratory testing: Options and opportunities. *Clinica Chimica Acta, 411*(21–22), 1596-1602. doi: http://dx.doi.org/10.1016/j.cca.2010.07.022
- Kachalia, A., Gandhi, T. K., Puopolo, A. L., Yoon, C., Thomas, E. J., Griffey, R., . . . Studdert, D. M. (2007). Missed and delayed diagnoses in the emergency department: a study of closed malpractice claims from 4 liability insurers. *Ann Emerg Med*, 49(2), 196-205. doi: 10.1016/j.annemergmed.2006.06.035
- Khromova, V., & Gray, T. A. (2008). Learning needs in clinical biochemistry for doctors in foundation years. *Ann Clin Biochem*, 45(Pt 1), 33-38. doi: 10.1258/acb.2007.007122
- Kim, J. Y., Dzik, W. H., Dighe, A. S., & Lewandrowski, K. B. (2011). Utilization management in a large urban academic medical center: a 10-year experience. *Am J Clin Pathol*, 135(1), 108-118. doi: 10.1309/ajcp4gs7ksbdbacf
- Landspitali University Hospital. (e.d.). Operational information Retrieved July 19, 2013, from http://www.landspitali.is/library/Sameiginlegar-skrar/Gagnasafn/Rit-og-skyrslur/Starfsemisupplysingar-LSH/2012/starfsemisupplysingar uppgjor 2012.pdf?download=true
- Landspitali University Hospital. (e.d.a.). Clinical biochemical user manual for laboratory tests Retrieved August 14, 2013, from https://kaldur.landspitali.is/gaeda/gnhsykla.nsf/5e27f2e5a88c898e00256500003c9 8c2/97cc2b29dd6857270025783200530edd?OpenDocument
- Landspitali University Hospital. (e.d.b.). Microbiology testing Retrieved August 14, 2013, from https://kaldur.landspitali.is/gaeda/gnhsykla.nsf/0/e4914586bbccb33d00256d57006 1aef4?OpenDocument&ExpandSection=4%2C1.2%2C1.1%2C2.3#_Section4
- Larsson, A., Biom, S., Wernroth, M. L., Hulten, G., & Tryding, N. (1999). Effects of an education programme to change clinical laboratory testing habits in primary care. *Scand J Prim Health Care*, *17*(4), 238-243.
- Liu, Z., Abdullah, A., Baskin, L., Lewis, G., Kelter, G., & Naugler, C. (2012). An intervention to reduce laboratory utilization of referred-out tests. *Lab Medicine*, *43*(5), 164-167. doi: 10.1309/LMSPKPZEX602NOKS
- Lundberg, G. D. (1975). The modern clinical laboratory; Justification, scope, and directions. *JAMA*, *232*(5), 528-529.
- Lundberg, G. D. (1998). Changing physician behavior in ordering diagnostic tests. *JAMA*, 280(23), 2036.
- McQueen, M. J. (2000). Evidence-based medicine: its application to laboratory medicine. *Ther Drug Monit*, 22(1), 1-9.

- Mickan, S., Burls, A., & Glasziou, P. (2011). Patterns of 'leakage' in the utilisation of clinical guidelines: a systematic review. *Postgrad Med J, 87*(1032), 670-679. doi: 10.1136/pgmj.2010.116012
- Mindemark, M., & Larsson, A. (2009). Long-term effects of an education programme on the optimal use of clinical chemistry testing in primary health care. *Scand J Clin Lab Invest*, 69(4), 481-486. doi: 10.1080/00365510902749123
- Ming Zhi, E. L. D., Jesse Theisen-Toupal, Julia Whelan, Ramy Arnaout. (2013). The Landscape of Inappropriate Laboratory Testing: A 15-Year Meta-Analysis. *PLoS ONE,* 8(11). doi: DOI: 10.1371/journal.pone.0078962
- Miyakis, S., Karamanof, G., Liontos, M., & Mountokalakis, T. D. (2006). Factors contributing to inappropriate ordering of tests in an academic medical department and the effect of an educational feedback strategy. *Postgrad Med J, 82*(974), 823-829. doi: 10.1136/pgmj.2006.049551
- Neilson, E. G., Johnson, K. B., Rosenbloom, S. T., Dupont, W. D., Talbert, D., Giuse, D. A., . . . Miller, R. A. (2004). The impact of peer management on test-ordering behavior. *Ann Intern Med*, 141(3), 196-204.
- OECD. (e.d.a.). Health at a Glance 2013: OECD Publishing.
- Oosterhuis, W. P., Bruns, D. E., Watine, J., Sandberg, S., & Horvath, A. R. (2004). Evidence-based guidelines in laboratory medicine: principles and methods. *Clin Chem*, *50*(5), 806-818. doi: 10.1373/clinchem.2003.025528
- Plebani, M. (2009). Exploring the iceberg of errors in laboratory medicine. *Clin Chim Acta*, 404(1), 16-23. doi: 10.1016/j.cca.2009.03.022
- Prasad, S. M., Drazer, M. W., Huo, D., Hu, J. C., & Eggener, S. E. (2012). 2008 US Preventive Services Task Force recommendations and prostate cancer screening rates. *JAMA*, *307*(16), 1692-1694. doi: 10.1001/jama.2012.534
- Prat, G., Lefevre, M., Nowak, E., Tonnelier, J. M., Renault, A., L'Her, E., & Boles, J. M. (2009). Impact of clinical guidelines to improve appropriateness of laboratory tests and chest radiographs. *Intensive Care Med*, *35*(6), 1047-1053. doi: 10.1007/s00134-009-1438-z
- Rao, G. G., Crook, M., & Tillyer, M. L. (2003). Pathology tests: is the time for demand management ripe at last? *J Clin Pathol*, *56*(4), 243-248.
- Reykdalsson, Ó. (2010). Er hægt að breyta rannsóknarvenjum lækna? *Læknablaðið,* 96(4), 291-295.
- Rinsler, M. G. (1984). The appropriate use of diagnostic services. (1) Introduction to the series. *Health Trends*, 16(4), 73.

- Salinas, M., Lopez-Garrigos, M., & Uris, J. (2013). Differences in laboratory requesting patterns in emergency department in Spain. *Ann Clin Biochem*, *50*(Pt 4), 353-359. doi: 10.1177/0004563212474568
- Santos, I. S., Bensenor, I. M., Machado, J. B., Fedeli, L. M., & Lotufo, P. A. (2012). Intervention to reduce C-reactive protein determination requests for acute infections at an emergency department. *Emerg Med J, 29*(12), 965-968. doi: 10.1136/emermed-2011-200787
- Shaneyfelt, T. M. (2001). Building bridges to quality. JAMA, 286(20), 2600-2601.
- Smellie, W. S. (2012). Demand management and test request rationalization. *Ann Clin Biochem*, 49(Pt 4), 323-336. doi: 10.1258/acb.2011.011149
- Smellie, W. S. A., Lowrie, R., & Wilkinson, E. (2001). A laboratory based intervention to improve appropriateness of lipid tests and audit cholesterol lowering in primary care. *BMJ*, 323(7323), 1224-1227. doi: 10.1136/bmj.323.7323.1224
- Solomon, D. H., Hashimoto, H., Daltroy, L., Liang, M.H. (1998). Techniques to improve physicians' use of diagnostic tests. A new conceptual framework. *JAMA*, 280, 2020-2027.
- Stakkestad, J. A., Sandberg, S., Bjerve, K. S., Runde, I., & Asberg, A. (1997). Use and usefulness of laboratory handbooks. *Scand J Clin Lab Invest*, *57*(7), 647-653.
- Stanfliet, J. C., Macauley, J., & Pillay, T. S. (2009). Quality of teaching in chemical pathology: ability of interns to order and interpret laboratory tests. *J Clin Pathol*, 62(7), 664-666. doi: 10.1136/jcp.2009.064824
- Statistics Iceland. (e.d.). Total expenditure on health care, breakdown 1998-2012.
- Statistics Iceland. (e.d.a.). Life expectancy and number of survivors 1971-2012.

 Retrieved June 13, 2013, from

 http://www.statice.is/?PageID=1175&src=https://rannsokn.hagstofa.is/pxen/Dialog/varval.asp?ma=MAN05401%26ti=Life+expectancy+and+number+of+survivors+1971%2D2012++++++++++**

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- Statistics Iceland. (e.d.b.). Population by urban nuclei, age and sex 1 January 2011-2013 Retrieved July 9, 2013, from http://www.statice.is/?PageID=1173&src=https://rannsokn.hagstofa.is/pxen/Dialog/varval.asp?ma=MAN03106%26ti=Population+by+urban+nuclei%2C+age+and+sex+1+Janu

- ary+2011%2D2013%26path=../Database/mannfjoldi/Byggdakjarnar/%26lang=1%26units=Data
- Stuart, P. J., Crooks, S., & Porton, M. (2002). An interventional program for diagnostic testing in the emergency department. *Med J Aust, 177*(3), 131-134.
- Stuebing, E. A., & Miner, T. J. (2011). Surgical vampires and rising health care expenditure: reducing the cost of daily phlebotomy. *Arch Surg*, *146*(5), 524-527. doi: 10.1001/archsurg.2011.103
- Tabriz, M. S., Riederer, K., Baran, J., Jr., & Khatib, R. (2004). Repeating blood cultures during hospital stay: practice pattern at a teaching hospital and a proposal for guidelines. *Clin Microbiol Infect*, *10*(7), 624-627. doi: 10.1111/j.1469-0691.2004.00893.x
- Thomas, R. E., Croal, B. L., Ramsay, C., Eccles, M., & Grimshaw, J. (2006). Effect of enhanced feedback and brief educational reminder messages on laboratory test requesting in primary care: a cluster randomised trial. *Lancet*, *367*(9527), 1990-1996. doi: 10.1016/s0140-6736(06)68888-0
- Tierney, W. M., Miller, M. E., & McDonald, C. J. (1990). The effect on test ordering of informing physicians of the charges for outpatient diagnostic tests. *N Engl J Med*, 322(21), 1499-1504. doi: 10.1056/nejm199005243222105
- Tomlin, A., Dovey, S., Gauld, R., & Tilyard, M. (2011). Better use of primary care laboratory services following interventions to 'market' clinical guidelines in New Zealand: a controlled before-and-after study. *BMJ Qual Saf, 20*(3), 282-290. doi: 10.1136/bmjqs.2010.048124
- van Walraven, C., & Naylor, C. D. (1998). Do we know what inappropriate laboratory utilization is? A systematic review of laboratory clinical audits. *JAMA*, *280*(6), 550-558.
- Verstappen, W. H., van der Weijden, T., Dubois, W. I., Smeele, I., Hermsen, J., Tan, F. E., & Grol, R. P. (2004). Improving test ordering in primary care: the added value of a small-group quality improvement strategy compared with classic feedback only. *Ann Fam Med*, *2*(6), 569-575. doi: 10.1370/afm.244
- Wang Tj, M. E. A. N. P., & et al. (2002). A utilization management intervention to reduce unnecessary testing in the coronary care unit. *Arch Intern Med*, *162*, 1885-1890.
- Wang, T. J., Mort, E. A., Nordberg, P., Chang, Y., Cadigan, M. E., Mylott, L., . . . Fifer, M. A. (2002). A utilization management intervention to reduce unnecessary testing in the coronary care unit. *Arch Intern Med*, *162*(16), 1885-1890.
- Whiting, P., Toerien, M., de Salis, I., Sterne, J. A., Dieppe, P., Egger, M., & Fahey, T. (2007). A review identifies and classifies reasons for ordering diagnostic tests. *J Clin Epidemiol*, 60(10), 981-989. doi: 10.1016/j.jclinepi.2007.01.012

- Winkens, R. A., Pop, P., Bugter-Maessen, A. M., Grol, R. P., Kester, A. D., Beusmans, G. H., & Knottnerus, J. A. (1995). Randomised controlled trial of routine individual feedback to improve rationality and reduce numbers of test requests. *Lancet*, *345*(8948), 498-502.
- Winkens, R. A., Pop, P., Grol, R. P., Bugter-Maessen, A. M., Kester, A. D., Beusmans, G. H., & Knottnerus, J. A. (1996). Effects of routine individual feedback over nine years on general practitioners' requests for tests. *BMJ*, *312*(7029), 490.
- Winkens, R. A., Pop, P., Grol, R. P., Kester, A. D., & Knottnerus, J. A. (1992). Effect of feedback on test ordering behaviour of general practitioners. *BMJ*, 304(6834), 1093-1096.
- Zaat, J. O., van Eijk, J. T., & Bonte, H. A. (1992). Laboratory test form design influences test ordering by general practitioners in The Netherlands. *Med Care*, 30(3), 189-198.

Appendix 1 - Information about the six laboratory tests in the three guidelines focused on in this study

The three clinical guidelines for laboratory tests focused on in this study were for:

- 1) Liver function tests (ASAT, ALAT, GGT, ALP)
- 2) C-reactive protein (CRP)
- 3) Blood cultures

Information about the tests was obtained from the Clinical Biochemistry Laboratory Handbook (Landspitali University Hospital, e.d.a.) and for bloodculture from the Microbiology Quality Manual (Landspitali University Hospital, e.d.b.).

Aspartate aminotransferase (ASAT) is an enzyme which catalyzes the transfer of amino groups and is found in high levels in heart, liver and muscle cells. Elevated levels are an indicator of tissue damage with increased permeability of the cell membrane and/ or cell death. With infarction the levels increase up to 20-fold the upper limit of normal. The greater the cell damage, the greater the increase. Increased levels are found in various liver diseases, particularly hepatitis caused by infection and liver damage caused by medications. Muscle diseases also cause an increase in ASAT.

Alanine aminotransferase (ALAT) is an enzyme in the cytoplasm and catalyzes the transfer of amino groups. ALAT is found in large quantities in hepatocytes but also in substantial quantities in the kidney, heart and muscle cells. Elevated levels are an indicator of tissue damage with increased permeability of cell membranes and/ or cell death. A sharp rise is seen in acute hepatitis ($10-100 \times 100 \times$

γ-Glutamyltransferase (GGT) function is unknown but it is found mainly in the liver, kidney, prostate and pancreas, though GGT levels come largely from the liver. Elevation occurs mainly in liver disease, when it increases together with alkaline phosphatase (ALP). GGT is not found in bones. If the level of alkaline phosphatase (ALP) is elevated due to bone disease, there will be no change in GGT. GGT increases significantly with gallstones (>1000) and toxic damage to the liver, and is commonly used to screen for alcoholism. A smaller increase in GGT is seen in hepatitis, pancreatitis and kidney disease.

Alkaline phosphatase (ALP) is an enzyme which is found in most cells of the body. Most ALP is found in serum liver and bones, and levels are much higher in children and adolescents than in adults. High values are seen during periods of rapid growth, and ALP levels also increase somewhat in those aged >70 years. ALP can increase significantly after a high-fat meal. During the third trimester of pregnancy, ALP increases because the placenta contributes much of the enzyme which enters maternal blood. ALP levels are higher in those with liver disease with cholestatis and liver metastasis, and in bone disease with increased bone synthesis.

C-reactive protein (CRP) is a plasma protein produced by the liver. It is an acute-phase protein that increases rapidly with inflammatory processes and is increased in bacterial infections, aseptic necrosis and malignant tumors, as well as after major surgery.

Blood culture is a test to detect for bacteria (sepsis or endocarditis), fungi (often done in patients with impaired defenses, such as immune suppression caused by chemotherapy) or mycobacteria in the blood. It is also used to monitor resonse to treatment.

Appendix 2 - Clinical guidelines for the use of CRP

Tilmæli um verklag við notkun greiningarrannsókna á LSH

<u>Umfang</u>: Mæling á CRP (C-Reactive Protein) í sermi við skimun, greiningu og eftirlit hjá fullorðnum

<u>Markhópur</u>: Læknar LSH sem annast greiningu, meðferð og eftirlit fullorðinna einstaklinga Höfundar: Bryndís Sigurðardóttir læknir, Kristín Huld Haraldsdóttir læknir, Steingerður Gunnarsdóttir læknir

Eigandi: Ari Jóhannesson læknir fyrir hönd framkvæmdastjóra lækninga

Dagsetning: Mars 2010

<u>Kveikja</u>: Árið 2009 var samanlagður kostnaður við mælingar á CRP á LSH 73 milljónir kr. og fjöldi beiðna var 63.000. Telja má víst að draga megi verulega úr mælingum á CRP án þess að sjúkdómsgreiningu eða meðferð sjúklinga sé teflt í tvísýnu.

Tilmæli

Mælst er til þess að eftirfarandi verklag verði viðhaft við mælingar á CRP en klínískt mat skal þó ávallt vera í fyrirrúmi.

CRP sem rútínupróf.

CRP er ekki rútínupróf við komu á bráðamóttöku eða við innlögn. Undantekning frá þessari reglu eru kviðverkir. Við mat á óljósu sjúkdómsástandi þar sem sýking eða bólgusjúkdómur koma til greina kemur til álita að mæla CRP en þar skal klínískt mat þó ætíð ráða.

CRP við greiningu og eftirlit í sýkingum.

Þegar sterkur grunur er um sýkingu eða sýking staðfest er í mörgum tilfellum óþarft að mæla CRP. Á það sérstaklega við þegar ólíklegt er að niðurstöður mælingarinnar muni hafa áhrif á klíníska ákvarðanatöku.

Í alvarlegum sýkingum þar sem CRP er mælt í upphafi skal hafa í huga að <u>daglegar</u> CRP mælingar í eftirlitsskyni eru ekki viðeigandi.

Við óljósan grun um sýkingu, getur lágt eða eðlilegt CRP stutt við ákvarðanatöku, en alltaf þarf að hafa klínískt ástand sjúklings í huga.

Við langvinnar sýkingar sem þurfa lengri sýklayfjagjafir, svo sem liðsýkingar, beinsýkingar eða hjartaþelsbólga, er CRP mælt u.þ.b.. vikulega til að fylgjast með sjúkdómsgangi.

Fylgst verður reglulega með mælingum á CRP á sjúkrahúsinu og ef breytingar verða ekki í takt við framangreind tilmæli, kemur til greina að framkvæmdastjóri lækninga gefi út

takmarkandi fyrirmæli um notkun þeirra í samráði við höfunda.

Appendix 3 - Clinical guidelines for the use of liver function tests



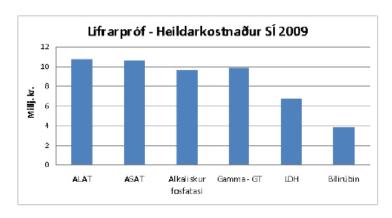




Tilmæli um verklag við notkun lifrarfrumu- og gallstíflublóðprófa

Kveikja: Árið 2009 var samanlægður kostnaður Landspítala og Sjúkratrygginga Íslands (SÍ)* við mælingar á ASAT, ALAT, GGT og ALP (alkalískum fosfatasa) 125 milljónir kr. Verð mælinga á ASAT, ALAT, GGT og ALP er svipað. Af mynd 1 er ljóst að beiðnir skiptust nánast jafnt á þessar fjórar rannsóknir og líklegt að oftast sé beðið um þær allar í einu. Svipað rannsóknarmynstur sást á Landspítala.

*Vegna sérfræðilækna og heilsugæslulækna utan heilsugæslustöðva (HUH).



Ekki er hægt að greina notkun einstakra prófa m.t.t. ábendinga og ljóst að sumar mælingar eru notaðar við mat á öðrum sjúkdómum en í lifur og gallvegum t.d. LDH. Þó virðist sem mæling á ASAT, ALAT, GGT,ALP, LDH og bilirúbín samtímis sé algeng.

Tilmæli:

Mælst er til þess að eftirfarandi verklag verði viðhaft við mælingu á lifrarprófum, en klínískt mat skal þó ávallt vera í fyrirrúmi.

ı

Skimun fyrir röskun á lifrarstarfsemi

- Skimun hjá einkennalausum þegar ekki er rökstuddur grunur um skerta lifrarstarfsemi eða lifrarsjúkdóm er ekki réttlætanleg. Þetta gildir jafnt um einstaklinga sem leita til sérgreinalækna, heilsugæslulækna, á bráðamóttökur og legusjúklinga. Lifrarpróf eru ekki rútín upróf við komu á bráðamóttökur eða við innlögn.
- 2. Hjá einstaklingum þegar lítill grunur er um skerta lífrarstarfsemi eða lífrarsjúkdóm en talið rétt að útiloka slíkt t.d. við notkun lyfja* sem geta valdið lífrarskemmdum, vegna sjúkdóma í öðrum líffærum eða almennra og/eða óljósra einkenna nægir að mæla ALAT og ALP (ALAT og GGT hjá börnum). Ef þessi próf reyn æt hækkuð er eftir þörfum hægt að bæta við öðrum prófum sem hægt er að nota sem mælikvarða á starfsemi.

*Fjölmörg lyf geta valdið lifrarskaða. Mikilvægt er að læknar hafi lágan þröskuld fyrir að mæla lifrarpróf þegar óljós ein kenni koma í ljós hjá sjúklingum sem eru á lyfjameðferð s. s. nýtilkominn slappleiki, ógleði eða ónot í kviðarholi. Þetta á sérstaklega við ef sjúklingur hefur nýlega hafið lyfjameðferð. Flest lyf sem valda lifrarskaða gera það hjá litlum hluta þeirra sem taka lyfið og í fæstum tilfellum er þörf á að mæla lifrarpróf nema um klínískan grun um lifrarskaða sé að ræða. Ekki talinn ávinningur af skimun fyrir hækkunum hjá einkennalausum.

Mat á lifrarstarfsemi hjá einstaklingum þegar <u>klínískur grunur er um lifrarsjúkdóm</u> Sé klínískur grunur um lifrarsjúkdóm, til dæmis við gulu skal mæla ASAT, ALAT, ALP, bílirúbín og INR. Æskilegt er að haft sé samráð við meltingarlækni til mats á því hvaða tegundgulu er um að ræða. Við bráðan lifrarsjúkdóm með gulu skal það vera mat sérfræðilæknis hversu oft og með hve löngu millibili prófin eru mæld. Mælt er með því að læknar sem eru ekki vanir að túlka niðurstöður lifrarprófa leiti álits meltingarlæknis þegar um er að ræða aðra bráða lifrarsjúkdóma eða eftirlit vegna brenglaðra lifrarprófa án staðfests lifrarsjúkdóms. Sjúklingar með langvinna lifrarsjúkdóma eiga að vera undir eftirliti meltingarlækna eða fylgt eftir í samráði við þá.

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Ábendingar fyrir einstök lifrarpróf

Ábendirg fyrir mælirgu á **GGT hjá fullorðnum**: Einangruð hækkun á ALP. Ef GGT reynist hækkað má gera ráð fyrir lifraruppruna á ALP. GGT gefur yfirleitt ekki viðbótarupplýsingar þegar bæði ALP og ALAT eru hækkuð. GGT er mjög ósértækt próf og væg hækkun er algerg við marga sjúkdóma utan lifrar. **GGT getur vissulega hækkað við ofneyslu áfengis en aðrar orsakir eru fitulifur sem ekki tengist áfengisneyslu og ýmis lyfjameðferð. Ekki er því hægt að mæla með GGT mælingu sem skimun fyrir ofnotkun á fengis nema sterkur klínískur grunur sé um slíkt en saga sjúklings gefur það ekki til kynna.**

Ábending fyrir mælingu á ASAT: Grunur um lifrarsjúkdóm af völdum áfengisneyslu

Fyrirvari:

Í öllum tilvikum er eftirlit einstaklingsbundið og á ábyrgð þess sem annast meðferð sjúklingsins og tekur mið af ástandi sem verið er að meðhöndla, öðrum sjúkómum og annarri lyfjameðferð. Þessir þættir geta haft afgerandi þýðingu við ákvörðun um tíðni eftirlits og hvaða rannsóknir eru framkvæmdar. Blóðrannsóknir eru eingöngu lítill hluti af eftirliti með lyfjameðferð og er gert ráð fyrir að fylgst sé með einkennum, framvindu sjúkdómsins og aukaverkunum m.a.. Sjá einnig fylgiseðil á vef Lyfjastofnunar www.lyfjastofnun.is eða SPC á t.d. http://ema.medicines.org.uk/.

Útgefið á vef LSH 15. febrúar 2010 en endurútgefið með minni háttar breytingum og viðbótum á vef LSH og Landlæknisembættisins í október 2010

Höfundar: Einar S. Björnsson, Ari Jóhannesson, Sigurður Helgason.

Umsagnaraðilar: Jóhann Ág. Sigurðsson, Óskar Reykdalsson, Stefán Þórarinsson,Tryggvi Egilsson og Þórir B. Kalbeinsson

Tilvitnun: Björnsson ES, Jóhannesson A. Helgason S. Notkun lifrarfrumu- og gallstíflublóðprófa. Tilmæli um verklag. Landlæknisembættið, 2010 [skoðað dd/mm/yyyy]. Sótt á: http://www.landlaeknir.is/Kliniskarleidbeiningar

Heimildir:

- London and South East Medicines Information Service, South West Medicines Information Service and Croydon Primary Care Trust (August 2008) Suggestions for drug monitoring in adults in primary care. National Electronic Library for Medicines. Sótt 18 apríl 2010 á vef: http://www.nelm.nhs.uk/en/NeLM-Area/Evidence/Drug-Monitoring/
- NHS. Derbyshire JAPC. Monitoring Drug Therapy (August 2009). Sótt 11 apríl 2010 á vef: http://www.derbyshirecountypct.nhs.uk/content/files/Ginical%20Guidelines/Drug%20Monit-oring%20Aug%2009.pdf
- AGA Technical Review on the Evaluation of Liver Chemistry Tests. Gastroenterology. 2002;123:1367-84.
- American Gastroenterological Association Medical Position Statement: Evaluation of Liver Chemistry Tests. Gastroenterology 2002;123: 1364-66.
- 5. Svensk Förening för Klinisk kemi. http://www3.svls.se/sektioner/sfkk/nyckel/toc.htm
- Guidelines and Protocols Advisory Committee. British Columbia Medical Association. Liver chemistry abnormalities in adulst – Evaluation and Interpretation. July 2004. Sótt 21 júlí 2010 ávef: http://www.boguidelines.ca/gpac/guideline-liver.html
- Giannini GE, Testa R, and Savarino V. Liver enzyme alteration: a guide for clinicians.CMAJ 2005;172:367-79.
- 8 Health Benchmarks. Clinical Quality Indicator Specification 2009. HEPATIC ENZYME MONITORING FOR STATIN USE AFTER INITIATING THERAPY.
 http://www.bdbsal.org/providers/physicianqualityandtransparencyprogram/qualityIndicators/Additional/hepaticEnzymeMonitoringForStatinUseAfterInitiatingTherapy.pdf
- Canadian Association of Gastroenterology practice guidelines. Evaluation of abnormal Liver enzyme tests. Can J Gastroenterol 1998;12:417-21.
- Bjornsson, E. and R. Olsson, Suspected drug-induced liver fatalities reported to the WHO
 database. Dig Liver Dis, 2006. 38(1): p. 33-8.

Appendix 4 - Clinical guidelines for blood cultures

Tilmæli um verklag við blóðræktanir á Landspítala

Inngangur

Blóðræktanir eru ómetanlegar til að greina blóðsýkingar, en líkt og með aðrar greiningarrannsóknir er mikilvægt að ákvörðun um sýnatökuna sé vel studd faglegum rökum og að verklag við sjálfa sýnatökuna sé vandað. Petta á bæði við um upphaflegar og endurteknar ræktanir. U.þ.b. 12% blóðræktana reynast jákvæðar, en þar af er um þriðjungur talinn mengun. Það er mjög bægalegt þegar ekki er vandað til verka við sýnatöku því mengun í kolbum leiðir til óþæginda fyrir sjúklinga og mikils kostnaðarauka vegna óþarfa sýklalyfjægjafa, endurtekinna ræktana, aukinnar vinnu starfsfólks og lengri sjúkrahúsdvala. Árið 2010 voru gerðar rúmlega 9.000 blóðræktanir á Landspítala. Kostnaður við hverja ræktun er 5500 kr og heildarkostnaður því um 50 milljónir.

Aldrei er hægt að gefa nákvæm fyrirmæli um ábendingar og frábendingar fyrir blóðræktunum. Eins og ávallt er einstaklingsbundin nálgun nauðsynleg og klínískt mat í fyrirrúmi.

Vinnuleiðbeiningar um sýnatöku við blóðræktanir er að finna í gæðahandbók sýklafræðideildar.

Blóðræktanir við nokkrar algengar sýkingar

Húðsýkingar (heimakoma (erysipelas), netjubólga (cellulitis))

Algengustu sýklar eru *S. aure u*s og streptókokkar GrA. Hlutfall jákvæðra blóðræktana er lágt (1-3%) og er þá reyndar oft um mengun að ræða. Sýklalyf sem virk erugegn Gram jákvæðum bakteríum eru oftast notuð frá upphafi, og ólíklegt að ræktunarniðurstöður breyti meðferðinni. Því er ekki mælt með blóðræktunum þegar verið er að vinna upp dæmigerða húðsýkingu nema sjúklingur leggist inn á gjörgæslu, grunur sé um dýpri sýkingu eða drep eða sýking komi í kjölfar meiri háttar skurðaðgerðar.

Þvagfærasýkingar (urosepsis, nýrnaskjóðubólga (pyelonephritis))

Algengasti sýkillinn er E coli. Nýrnaskjóðubólga veldur gjarnan hita í allt að 5-7 daga, þrátt fyrir viðeigandi meðferð. Langflestir sjúklingar sýna lækkandi sýkingarvísa, þ.e. hvít blóðkorn og tilhneigingu til lægri hitatoppa, ásamt almennt batnandi líðan á fyrstu dögum meðferðar. Ekki er þörf á endurteknum blóðræktunum ef þvag- og /eða blóðræktanir við komu hafa sýnt fram á líklegan sýkingarvald.

Lungnabólga

Blóðræktanir eru sjaldan jákvæðar, en það er þó háð sýkingarvaldi. Um 6-10% sjúklinga sem þarfnast innlagnar eru með jákvæðar blóðræktanir (60% eru *S. pneumoniæ*). Rannsóknir hafa sýnt að niðurstöður breyta ekki meðferð og leiða til breytinga á sýklalyfjum í < 1% tilfella. Ekki er mælt með blóðræktunum við samfélagslungnabólgu, nema sjúklingur sé mjög meðtekinn (hiti > 39°C. möguleg sýklasótt, gjörgæsla). Rétt er að klínískt mat ráði því hvort beðið er um þvagmótefnavakaleit gegn *Legionella pneumophila* og/eða *Streptococcus pneumoniae* (kr. 5300 hvor).

Beina- og liðsýkingar

Hlutfall jákvæðra blóðræktana hjá einstaklingum með beina og liðsýkingar er háð áhættuþáttum og eðli sýkingarinnar (hærra hjá börnum og sprautufíklum). Í sumum tilfellum er sýkillinn eingöngu greindur með blóðræktunum, sérstaklega við beinsýkingu í hrygg og ekki næst gott sýni til ræktunar. Mælt er með blóðræktunum í upphafi meðferðar hjá völdum einstaklingum, einkum þeim sem eru með einkenni bráðrar sýkingar. Ef sýkingin er langvinn og sjúklingur er hitalaus eru sáralitlar líkur á að blóðræktanir séu jákvæðar.

Sýklasótt

Um 50% blóðræktana eru jákvæðar hjá sjúklingum með svæsna sýklasótt (severe sepsis). Sjúklinga sem uppfylla skilyrði um hana á skilyrðislaust að blóðrækta. Skilgreiningin á sýklasótt (sepsis) er almenn; bólgusótt ásamt einkennum/teiknum um sýkingu, en sjúklingar með margvíslega sjúkdóma geta uppfyllt þessi skilyrði í upphafi veikinda (tafla1). Því skal klínískt mat ráða við val á rannsóknum, en í vafatilvikum er þó ávallt rétt að taka blóðræktun.

Tafla I. Skilgreiningar á sýklasótt, svæsinni sýklasótt og sýklasóttarlosti.

Sýklasótt (sepsis)

Sjúklingurinn sýnir tvö eða fleiri neðantalinna einkenna í tengslum við sýkingu:

(Þessi einkenni geta verið til staðar án þess að um sýkingu sé að ræða og er þá talað um heilkenni almennra bólguviðbragða eða bólgusótt (systemic inflammatory response syndrome, SIRS)

- 1. Likamshiti >38°C eða <36°C
- Hjartsláttartíðni >90 slög/mínútu
- Öndunartíðni >20 andartök/mínútu eða hlutþrýstingur koltvísýrings í blóði (PaCO₃) <32 mmHg
- Fjöldi hvítra blóðkorna >12,000/mm³, <4000/ mm³, eða >10% óþroskuð hvít blóðkorn

Svæsin sýklasótt (severe sepsis)

Auk sýklasóttar hefur sjúklingurinn einkenni um vanstarfsemi á líffærum, teikn um minnkað gegnflæði um líffæri eða lágan blóðþrýsting. Einkenni um minnkað gegnflæði geta verið sýring í blóði, minnkaður þvagútskilnaður eða nýtilkomnar breytingar á meðvitund.

Sýklasóttarlost (septic shock)

Sjúklingurinn hefur svæsna sýklasótt og lágan blóðþrýsting og/eða teikn um minnkað gegnflæði um líffæri þrátt fyrir fullnægjandi vökvameðferð. Sjúklingar sem hafa þörf fyrir æðavirk lyf falla undir þessa skilgreiningu.

Hiti og hvítkornafæð

Blóðræktanir hafa áhrif á meðferð og leiða oft til breytinga á henni. Sjúklinga með hita og hvítkornafæð (HVBK< 1 x 10°/L) skal blóðrækta, þó ekki oftar en á 24-48 klst fresti, eftir einkennum.

Ónæmisbæling

Ónæmisbæling er af ýmsum toga (áunnir og meðfæddir sjúkdómar, lyf, HIV, aldur, næringarskortur) og sjúklingar misnæmir fyrir sýkingum af völdum baktería. Því er ógerlegt er að flokka þá alla saman m.t.t bælingar. Mælt er með blóðræktunum ef hiti >38°C, og/eða breyting verður á almennri líðan sem gæti bent til sýkingar.

Útgefið í febrúar 2011

Höfundar: Bryndís Sigurðardóttir læknir, Ari J. Jóhannesson læknir

Heimildir

Shapiro NI erial. Who needs a blood culture? A prospectively derived and validated prediction rule. J Emerg Med 2008;35:255-64

Marrie TJ. Community-acquired pneumonia. Clin Infect Dis 1994;18:501-513

Bone RC et al. Sepsis syndrome: a valid clinical entity. Crit Care Med 1989;17:789-93

Hummel M et al. Diagnostic yield of blood cultures from antibiotically-naive and antibiotically treated patients with haemotological malignancies and high risk neutropenia. Scand J Infect Dis 2009;41:650-5

Sigurdsson GH, Möller AD. Sigrumst á sýklasótt. Læknablaðið 2004;90:855-60

Appendix 5 - Letter to physicians at LUH

The following is a paragraph from the letters to physicians sent in March 2010, November 2010 and December 2012:

"Using the Laboratory Portal is necessary, but of course is not a sufficient prerequisite to make the use of laboratory requests more effective and thereby increase their value. In the Laboratory Portal the following points need to be kept in mind:

- Review regularly laboratory-test routines, some of which have remained unchanged for years, even though the original indications are no longer available.
- Stop using laboratory tests in situations where a test is unlikely to change the results of the diagnosis, treatment and prediction of prognosis.
- Have a consistent approach to the diagnosis and treatment of diseases common in your specialty, in collaboration with others as appropriate. The same shall apply to those rare diseases for which laboratory tests are very expensive.

Finally, it is worth pointing out various clinical guidelines that can be found on the LUH website of clinical guidelines under the heading 'Investigations'."

Appendix 6 - Electronic laboratory-test systems

Electronic laboratory-test systems in use by the two hospitals:

Electronic laboratory-test systems at Landspitali University Hospital and Akureyri Hospital

System	Biochemistry tests (ASAT, ALAT, GGT, ALP, CRP) LUH and AH	Microbiology tests (Blood culture) LUH	Microbiology tests (Blood culture) AH	
Laboratory Information System (LIS)	FlexLab	Glims	Technidata	
Request and answer system (RaA)	RaA	Cyberlab	Technidata web	
Request and answer system + Electronic Health Record	Health Portal Saga	Health Portal Saga	Health Portal Saga	
Statistical system	ProClarity for FlexLab			

The name of the laboratory information system in use for biochemistry tests at LUH is the FlexLab system, which was set up in 2007 and implemented at AH in May 2010, but for microbiology Glims is used at LUH and Technidata at AH. Before the Flexlab system was implemented at AH, the Technidata system, which is still used today for microbiology tests, was used to document all tests. The reason for the different systems is that one laboratory information system suits one type of laboratory and a specific request system from each manufacturer fits that system.

The electronic laboratory request system is a computer system whereby physicians can order laboratory tests and view information about previous tests and results. The electronic laboratory request system in use for biochemistry tests at both LUH and AH is the Request and Answer system (RaA) and is used in combination with the Flexlab to order laboratory tests and view results. When a biochemistry test is ordered, a physician can either order a test by opening the RaA system or open RaA through the Saga system.

Different systems are in use at LUH and AH for the microbiology tests: the Request and Answer system in use at LUH is Cyberlab while Technidata web is used at AH. When a microbiology test is ordered, the physician can either choose to open Cyberlab at LUH (Technidata web at AH) or open Cyberlab through Saga.

A replacement called Health Portal RaA (HRaA) is being developed for the RaA system and is part of the Health Portal system. Health Portal and Saga are in use at both hospitals and gather all information about a patient in one place, from where it is possible to open the HRaA to order a laboratory test and view all results. The system is supposed to be more user-friendly and contain fewer request steps. When the system has been fully implemented by the end of 2013, the old RaA system will be replaced. Physicians today order half of the laboratory tests from RaA and half from HRaA. CPOE has been shown to improve laboratory utilization, save time, avoid errors and lead to better staff utilization (since there are fewer manual steps) and to decreased costs (Baron & Dighe, 2011). At LUH and AH the Saga system has a link to clinical guidelines, which can be useful for physicians when ordering tests.

Appendix 7 - Cost of laboratory tests

Price (ISK) per test at LUH and AH from 2007-2013.

Landspitali University Hospital (LUH)	CRP	ASAT	ALAT	ALP	GGT	Bloodculture
Jan 2007 – Feb 28 2007	870	435	435	435	435	4,785
March 1 2007- Jan 31 2008	870	435	435	435	435	4,785
Feb 1 2008 – Jan 31 2009	906	453	453	453	453	4,983
Feb 1 2009- Dec 31 2010	1,006	503	503	503	503	5,531
Jan 1 2011- Dec 31 2012	1,051	525	525	525	525	5,780
Jan 1 2012- Dec 31 2013	1,107	553	553	553	553	6,088
Jan 1 2013-	1,169	584	584	584	584	6,428
LUH with extra 70% charge plus 3						
units						
Jan 2007 – Feb 28 2007	4,089	2,045	2,045	2,045	2,045	22,490
March 1 2007- Jan 31 2008	4,089	2,045	2,045	2,045	2,045	22,490
Feb 1 2008 – Jan 31 2009	4,258	2,129	2,129	2,129	2,129	23,420
Feb 1 2009- Dec 31 2010	4,727	2,363	2,363	2,363	2,363	25,996
Jan 1 2011- Dec 31 2012	4,939	2,470	2,470	2,470	2,470	27,166
Jan 1 2012- Dec 31 2013	5,202	2,601	2,601	2,601	2,601	28,611
Jan 1 2013-	5,493	2,747	2,747	2,747	2,747	30,213
Akureyri Hospital (AH)						
Jan 2007 – Feb 28 2007	840	420	420	420	420	4,622
March 1 2007- Jan 31 2008	855	428	428	428	428	4,703
Feb 1 2008 – Jan 31 2009	883	442	442	442	442	4,858
Feb 1 2009- Dec 31 2010	1,006	503	503	503	503	5,531
Jan 1 2011- Dec 31 2012	1,053	527	527	527	527	5,792
Jan 1 2012- Dec 31 2013	1,109	554	554	554	554	6,098
Jan 1st 2013-	1,169	584	584	584	584	6,428

Laboratory test	Number of units			
CRP	6			
ASAT	3			
ALAT	3			
ALP	3			
GGT	3			
Bloodculture	33			

Period	LUH unit cost	AH unit cost	
Jan 2007 – Feb 28 2007	145.00	140.05	
March 1 2007- Jan 31 2008	145,00	142.50	
Feb 1 2008 – Jan 31 2009	151.00	147.20	
Feb 1 2009- Dec 31 2010	167.61	167.60	
Jan 1 2011- Dec 31 2012	175.15	175.50	
Jan 1 2012- Dec 31 2013	184.47	184.80	
Jan 1 2013-	194.80	194.80	

Appendix 8 - Approval from the National Bioethics Committee



Háskóli Íslands, Hagfræðideild, Tinna Laufey Ásgeirsdóttir, lektor Oddi v/Suðurgötu 101 Reykjavík Hafnarhúsið, Tryggvagata 17 101 Reykjavík,

Sími: 551 7100, Bréfsími: 551 1444 netfang: visindasidanefnd@vsn.stjr.is

> Reykjavík 7. maí 2013 Tilv.: VSNb2013040021/03.07

Efni: Varðar: 13-074-afg Áhrif íhlutandi aðgerða á notkun greiningarrannsókna.

Umsókn þinni til Vísindasiðanefndar hefur verið gefið númerið VSN-13-074. Við förum vinsamlegast fram á að það númer verði notað í samskiptum vegna þessarar umsóknar.

Á fundi sínum 07.05.2013 fjallaði Vísindasiðanefnd um umsókn þína. Meðrannsakandi þinn er Helga Erlingsdóttir, Mastersnemi í heilsuhagfræði við HÍ.

Eftir að hafa farið vandlega yfir umsókn þína og innsend gögn gerir Vísindasiðanefnd ekki athugasemdir við framkvæmd rannsóknarinnar. Rannsóknaráætlunin er endanlega samþykkt. Vísindasiðanefnd bendir rannsákendum vinsamlegast á að birta VSN tilvísunarnúmer rannsóknarinnar þar sem vitnað er í leyfi nefndarinnar í birtum greinum um rannsóknina. Jafnframt fer Vísindasiðanefnd fram á að fá send afrit af, eða tilvísun í, birtar greinar um rannsóknina. Rannsakendur eru minntir á að tilkynna rannsóknarlok til nefndarinnar.

Áréttað er að allar fyrirhugaðar breytingar á þegar samþykktri rannsóknaráætlun þurfa að koma inn til nefndarinnar til umfjöllunar. Jafnframt ber ábyrgðarmanni að láta stofnanir, sem veitt hafa leyfi vegna framkvæmdar rannsóknarinnar eða öflunar gagna vita af fyrirhugðum breytingum.

> Með kveðju og ósk um gott rannsóknargengi, f.h. Vísindasiðanefndar,

> > Gisli Ragnarsson, Waraformaour

Appendix 9 - Approval from Managing Medical Director at LUH



Helga Erlingsdóttir, mastersnemi í heilsuhagfræði við HÍ

> Reykjavík, 6. maí 2013 Tilv. 16 ÓB/eí

Efni: Áhrif íhlutandi aðgerða á notkun greiningarrannsókna (Effect of intervention on the use of laboratory tests)

Ágæta Helga.

Vísað er til erindis þíns til framkvæmdastjóra lækninga sem dagsett var 28. apríl sl. þar sem óskað er heimildar til að ofangreind rannsókn fari fram m.a. á Landspítala. Fram kom að rannsóknin er hluti af meistaraverkefni þínu við Háskóla Íslands. Ábyrgðarmaður rannsóknarinnar er Tinna Laufey Ásgeirsdóttir, lektor við HÍ og aðrir rannsakendur eru auk þín Ari Jóhannesson, sérfræðilæknir við LSH og Ólöf Sigurðardóttir, yfirlæknir við FSA.

Hér með er veitt heimild til að ofangreind rannsókn fari fram á Landspítala. Jafnframt er veittur aðgangur að sjúkraskrám sem tengjast rannsókninni. Leyfi þetta er háð því að fyrir liggi samþykki Vísindasiðanefndar og Persónuverndar og mun aðgangur að sjúkraskrám verða opnaður þegar þær heimildir liggja fyrir.

Með kveðju og ósk um gott rannsóknargengi,

Ólafur Baldursson, framkvæmdastjóri lækninga

Afrit:

Kristján Erlendsson, formaður Vísindasiðanefndar Sigrún Jóhannesdóttir, forstjóri Persónuverndar Tinna Laufey Ásgeirsdóttir, lektor við HÍ Ásbjörn Jónsson, framkvæmdastjóri Magnús Gottfreðsson, yfirlæknir vísindadeildar

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Appendix 10 - Approval from Managing Medical Director at AH



Tinna Laufey Ásgeirsdóttir, Lektor í hagfræði við Háskóla Íslands, Sæmundargötu 2, 101 Reykjavík.

Akureyri 26. apríl 2013.

Efni: Beiðni um aðgang að gögnum vegna rannsóknar "Áhrif íhlutandi aðgerða á notkun greiningarrannsókna".

Óskað hefur verið eftir aðgengi að rannsóknargátt vegna ofannefndrar rannsóknar og er fyrirhugað að skoða rannsóknir sem gerðar hafa verið á Sjúkrahúsinu á Akureyri. Tengiliður við rannsóknina á Sjúkrahúsinu á Akureyri er Ólöf Sigurðardóttir, rannsóknalæknir og yfirlæknir rannsóknadeild sjúkrahússins. Rannsóknin er hluti af mastersverkefni Helgu Erlingsdóttur, mastersnema í heilsuhagfræði við Háskóla Íslands.

Undirritaður veitir hér með leyfi til ofannefnds aðgangs. Ekki er ætlast til að skoðaðir séu persónugreinanlegir hlutir. Vinsamlegast hafið samband við tengilið sjúkrahússins við upphaf rannsóknar.

Gangi ykkur vel með rannsóknina.

Sigurður E. Sigurðsson,

framkvæmdastjóri lækninga og handlækningasviðs,

Sjúkrahúsinu á Akureyri.

Afrit: Ólöf Sigurðardóttir, yfirlæknir

SES/JR