

# MEDICAL SCIENCE & PRACTICE

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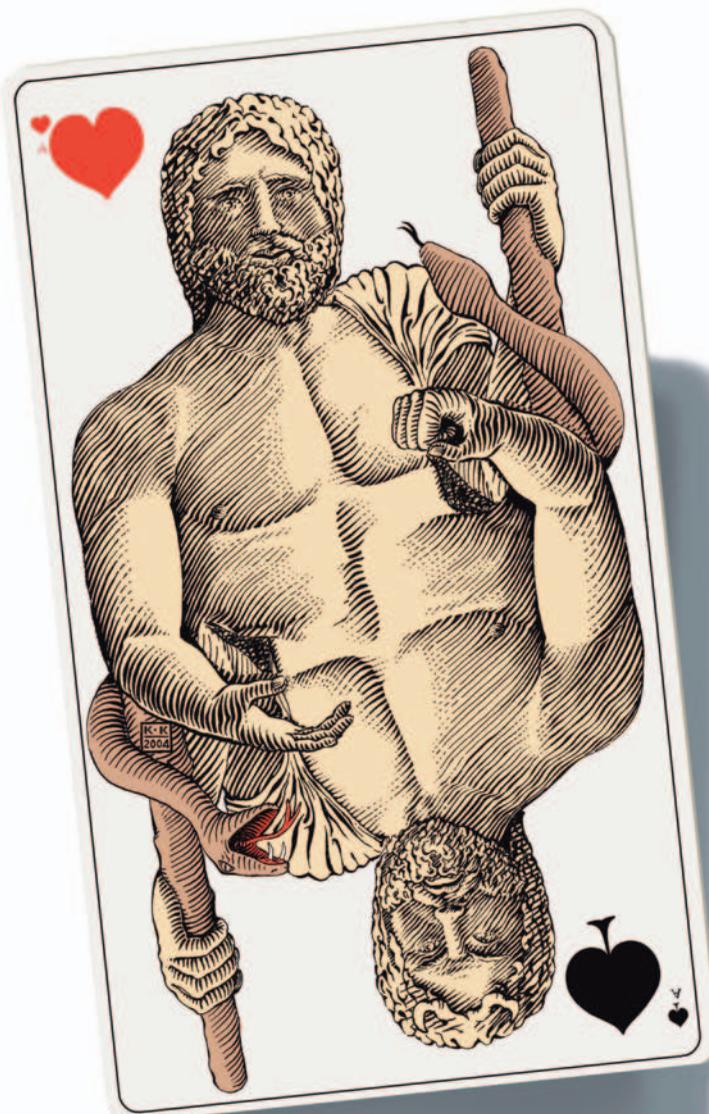


Illustration: Kenneth Karlsson. Concept: Ragnar Levi

## Helpful or harmful?

Nina Rehnqvist, SBU's new Executive Director, says that the first step toward evidence-based health care is monitoring your activities to determine what's working well and what isn't.

– To provide evidence-based health care, you have to keep track of the methods you use and the results they produce – in other words, create a mirror image of your activities.

Rehnqvist, professor of cardiology, has long experience of healthcare monitoring, which she regards as a vital first step in promoting clinical practice that rests on a firmer scientific foundation.

– It's not always pleasant to see yourself in the mirror. But only when we have scrutinized the current state of clinical practice can we make significant improvements.

## SBU'S NEWSLETTER SPECIAL EDITION

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## Cost-effective? Sure! But for whom?

When the worst bean counters get going – entrenched around meeting tables or barricaded behind podiums, far from the world of everyday health care – it's time to fasten your seatbelt. Before you know what's happening, they have thrown out important treatment methods by arguing that they are not cost-effective.

Just like other buzzwords, no matter how important their original meaning, this concept invites sweeping and careless use. Any method's cost-effectiveness should be judged as low or high relative to some other option. All methods that have any effect at all obviously have some degree of cost-effectiveness. Those who label a method "not cost-effective" are actually claiming that it isn't cost-effective enough – for instance, that its cost-effectiveness is lower than that of some alternative or lower than some boundary they have set. Such boundaries can and should be debated.

Solid knowledge about different methods' cost-effectiveness is key to managing health-care resources wisely – most people realize that. What isn't always made clear is that even such information isn't sufficient for intelligent priority-setting, partly because uncertainties are significant and partly because the numbers say nothing about certain important values.

Take equity, for instance. Health economists' calculations seldom account for how fairly health and quality of life are distributed in a population. A measure that makes life more pleasant for a great many people can, in fact, be more cost-effective than one that leads to great improvements for a few. For example, a pharmaceutical preparation that could cure the common cold could be more cost-effective than one that relieves pain in patients with chronic diseases. But that doesn't imply that a miracle-drug against runny noses should be given high priority. Improving the health and quality of life for those who already are living fairly well isn't the most urgent need. It should be much more important to improve conditions for those who are the sickest.

This is the sort of discussion that is crucial when healthcare priorities are to be set. No one can reduce priority-setting to a purely scientific matter. At the end of the day, resource distribution is about values. How crucial are different investments on the part of society and the healthcare system? What is a reasonable cost for a particular effect? What health care measures should be funded by tax-payers' money? What are various health outcomes seen to be worth?

The British assessment organization NICE (National Institute for Clinical Excellence) is now planning to poll a broad segment of the population to try to answer such questions. The intent is to make sure that future subsidy decisions more clearly mirror the public's values.

In Sweden, a recent doctoral dissertation examines the gap between the expectations of patients and the public on one side and politicians and administrators on the other. In many places, different ways of reaching a better dialog between decision-makers and citizens are being tested. There's a crying need for more such initiatives.

RAGNAR LEVI, EDITOR



A stylized, handwritten signature of Ragnar Levi in black ink.



Photo: Anders Norderman

“We all tend to pay attention only to the findings that square with our own biases.”

The Swedish National Board of Health and Welfare's monitoring of health-care performance often reveals major discrepancies between various parts of the country. For some diseases, outcomes can vary as much as several hundred percent from one region to another.

– One obvious explanation is the wide variety of patients. But that's not the whole story. We also treat the same kinds of patients differently, and not all methods are equally effective.

### DISCREPANCIES

Rehnqvist points out that these discrepancies are inconsistent with the Swedish Health and Medical Services Act's promise of health care on equal terms for the entire population.

– Your survival odds and your risk of serious complications shouldn't be a function of where in Sweden you happen to live. Unfortunately, that's the way it works today.

Rehnqvist notes that introducing evidence-based health care is a complex process. While remaining skeptical of new approaches, the

medical profession must be willing to discard old methods when they no longer prove to be optimal. It's a balancing act. Knowledge is key to carrying out this widespread change, but sticks and carrots will also come into play.

#### MISLEADING GRAPHS

– I'll never forget when I was a relatively new doctor and a pharmaceutical company was launching a drug for heart failure, recalls Rehnqvist.

– They dumped a stack of studies and impressive graphs on our desk to prove that resistance in the peripheral blood vessels decreased and the coronary vessels dilated so that the heart could obtain more oxygen.

– Many of us trusted those surrogate endpoints – and besides, there were theoretical grounds for believing that the treatment would also make the heart pump more efficiently. But we were misled. The drug had an altogether unexpected effect in practice. Actually, I'm fairly certain that some patients died from the treatment.

– We should have demanded evidence of the drug's impact on morbidity and mortality, not only on blood vessels. But we simply focused on the studies that the company had selected and assumed that we had done our job.

In her new position at SBU, Rehnqvist plans to explore a number of ideas that she has discussed with Egon Jonsson, her predecessor.

#### MORE RAPID

– We've got to come up with faster ways of producing evidence, new procedures for communicating with key

members of our target groups, and fresh approaches to taking advantage of systematic reviews of literature by SBU's sister organizations in other countries.

– I can't be any more concrete at the moment, since I want to conduct internal discussions at SBU first. It's important for us to capitalize on SBU's 15 years of cumulative experience as we move forward.

Improving the use of evidence in health care is another major challenge.

– SBU enjoys enormous credibility, no doubt about it, says Rehnqvist.

– I'm thrilled at the opportunity to take over such a well-functioning organization. Our top-quality reports are in great demand.

– The problem is overcoming the resistance of many healthcare professionals who can't or won't change their working methods just because a new assessment has been released showing that new methods are more effective.

– We all tend to pay attention only to the findings that square with our own

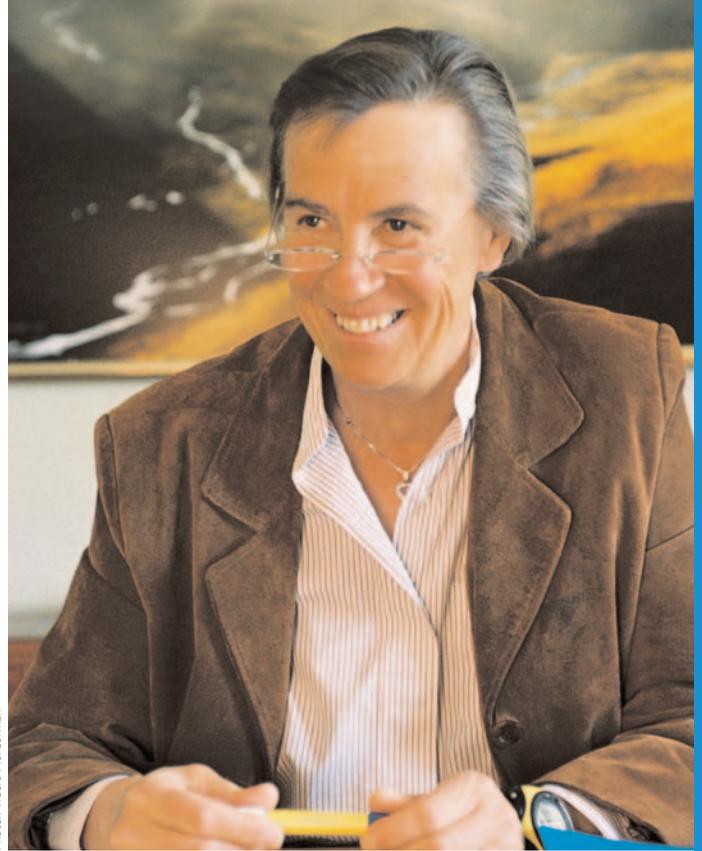


Photo: Anders Norderman

biases and ignore everything else. Such narrow-mindedness gets in the way of the re-evaluation and refocus on evidence-based practice that is so badly needed today.

#### CRITICAL THINKING

– This is not only a question of attitude, but also of knowledge, argues Rehnqvist.

– Some caregivers aren't used to systematic reviews and the critical analysis that they entail. Taking part in an

assessment project for the first time is a learning process.

– There was a time when I would base my scientific articles simply on research that supported my own hypothesis. We would find all kinds of errors in the other sources and figure that we could disregard them. Spinning our wheels in the same old rut was comfortable and painless. But it was also perilous...

## SIX STEPS TO REVITALIZING CLINICAL PRACTICE

### 1. FORM A WORKING GROUP

Include people from different areas of expertise and representatives of the caregivers concerned.

### 2. EXAMINE THE CURRENT STATE OF PLAY

Explore current practice and healthcare performance. How should evidence-based practice improve current performance? What changes are needed to institute it? What would facilitate or thwart such changes?

### 3. PREPARE EVERYONE CONCERNED

Make sure that anyone affected by a change not only is motivated, but also has the knowledge and resources required to implement it. Assistance, time, commitment, straightforward communication, and various systems for providing reminders are vital to this effort.

### 4. DRAW UP A STRATEGY

Given the obstacles identified in Step 2, decide which methods of implementation are most suitable. Take advantage of research findings on the most effective approaches.\*

### 5. CONCRETE ACTION

Make sure that everyone concerned understands the purpose of the change and appoint a coordinator. Draw up a clear timetable and a preview of problems that may arise.

### 6. MONITOR AND REVISE

Monitor the process by keeping track of clinical practice and healthcare performance, and revise plans as needed. Communicate the results to everyone concerned. Implement the change slowly but surely, and invite feedback at each step along the way.

\*see Getting Evidence into Practice. Effective Health Care Bulletin no. 1, vol. 5, 1999. [www.york.ac.uk/inst/crd/ehc51.pdf](http://www.york.ac.uk/inst/crd/ehc51.pdf)

# Myths about assessment and evidence



## **MYTH 1: EVIDENCE-BASED HEALTH CARE MEANS DISCARDING EVERYTHING THAT HASN'T BEEN SCIENTIFICALLY ASSESSED**

False! Lack of evidence doesn't necessarily mean lack of effect. Treatments therefore shouldn't necessarily be abandoned just because their benefits haven't yet been scientifically assessed. However, additional research is called for in such cases.

When there are several methods for treating a given disease, top priority should be given to those that have been scientifically shown to provide benefit, and that carry acceptable costs and risks.

When there is only one conceivable treatment method – and that method is supported by experience and theory and entails no great costs or risks – its continued use can be justified until better scientific evidence is available.

In such cases, it is important to keep in mind that the benefit of the treatment has not been well documented, so as to ensure that it doesn't come to be accepted as standard practice before all the evidence is in.

Certain practices are so clearly and dramatically life-saving – for instance, stopping heavy bleeding – that their benefit is beyond ques-

tion. No research findings are required to confirm that some kind of treatment is crucial.

Nevertheless, a study identifying the most effective method may still be called for. The same holds true for procedures that help patients satisfy their basic needs, such as eating, drinking, sleeping, breathing, urinating and defecating.

Human solicitude – listening, understanding, monitoring and communicating about the patient's condition – can make treatment more effective. While no critical assessment is needed to establish the value of such thoughtfulness, finding out which approaches patients prefer may be an important research topic.



## **MYTH 2: RANDOMIZED TRIALS ALWAYS GENERATE THE BEST EVIDENCE**

False! The question a study poses determines which type of study design will yield the most reliable answer.

Since randomized trials minimize the risk of systematic errors, they are often most reliable for comparing the efficacy of different treatments.

However, randomized trials are not appropriate for addressing rare side effects, optimal diagnostic methods, the incidence of disease,

prognosis or risk factors.

What's more, small, poorly designed randomized trials may be less dependable than large, well-designed, non-randomized controlled trials.

Sometimes even the results of well-designed randomized trials cannot be reproduced when applied in clinical practice. For instance, researchers' selection of test subjects is sometimes so narrow that their findings do not apply to "typical" patients.

Certain key healthcare issues can be elucidated only by qualitative research methods. Such issues include how patients perceive their disease, interpret what the caregiver says, and make decisions about their health.

On the other hand, qualitative studies are of little value in demonstrating whether a new treatment saves lives or minimizes morbidity.



## **MYTH 3: THE SELECTION OF STUDIES AND ASSESSMENT OF THEIR QUALITY IS ARBITRARY**

False! Assessment and selection processes certainly affect the results of a systematic literature review.

But the criteria for selection and quality assessment are set in advance, before the review starts. This is to mini-

mize the risk that reviewers' biases will influence their analysis.

For the same reason, the reviewers (generally two, working independently of each other) proceed systematically, adhering to preset protocols.

Criteria for searching the literature, selection and quality assessment include the test methods, number of patients, follow-up period and choice of comparison group employed by the studies.

When publishing their results, the reviewers must present the criteria and protocols they have used.

Often they also specify which studies have been excluded from the review, and why. This helps the reader identify the conclusions' relevance to particular situations and allows other reviewers the chance to duplicate the effort and determine whether the conclusions hold.

Such approaches distinguish systematic reviews from documents more susceptible to bias or caprice.



## **MYTH 4: SCIENTIFIC ASSESSMENTS DELAY NEW TREATMENTS**

Most "promising" methods eventually turn out to provide only modest gains in patient health. Moreover, a look at

history shows that many untested methods, which have later been shown to do more harm than good, have been quickly adopted. Thus, introducing promising but untested methods into routine health care can be harmful for patients, while at the same time depleting resources that could have offered genuine benefit.

It doesn't follow that new, untested treatments should be rejected out of hand. But there are good reasons for early scientific assessment of their utility. SBU Alert performs such early assessments.

The golden rule should be to employ untested methods only within a frame-

work of scientific protocols that can be assessed. That is the only way to speed up the process of recommending or discarding such methods.

Any new method must be weighed by comparing its efficacy with established methods and analyzing its cost-effectiveness. Such information is key to the optimal allocation of health-care resources.



**MYTH 5: MY PATIENTS ARE NOT AT ALL COMPATIBLE TO TEST SUBJECTS**

Research that weighs different treatment methods against each other typically

seeks a valid answer to the question "Which one is best?" However, an individual caregiver can generalize from a study's findings about a particular group of subjects only if that group accurately represents the patient to be treated.

That is why a narrow selection of participants in a clinical trial can cause problems when translating the results into practice. For that reason, some randomized trials should include a broader and thereby more representative sample of the patient population with respect to age, sex and health status.

A method that has been shown to be effective for most patients will not necessarily work for every patient. Thus, caregivers must always bear in mind whether a patient is undergoing other treatments or is suffering from other diseases that may affect the outcome.

In some cases, the differences among patients with the same disease may be more relevant than the similarities.

But instead of assuming that the existing evidence does not apply to their own patients, caregivers should ask themselves if there are specific reasons why it shouldn't. For instance, do these patient suffer from more than one disease, and/or are they undergoing other treatments that may affect the outcome?

Finally, the difficulty of generalizing is not peculiar to scientific evidence.



**MYTH 6: EVIDENCE-BASED HEALTH CARE IS INCOMPATIBLE WITH TRUSTING PRACTITIONER-PATIENT RELATIONSHIPS.**

False again! There's no conflict here. On the contrary, evidence is an important ingredient of effective health care. Caregivers who ignore evidence of the benefits and risks of different methods jeopardize their relationships with patients. Their patients will be misinformed about the benefits and risks associated with various diagnostic methods or treatments.

A solid evidence base is necessary but certainly not sufficient for good medical practice. A practitioner who has all the expertise but who is unable to communicate with patients cannot provide good health care.

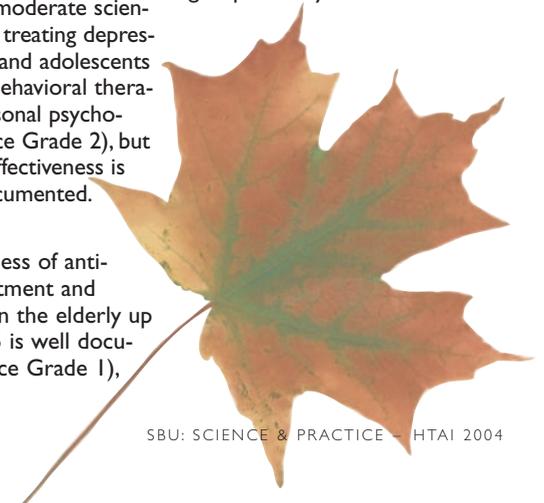
Evidence-based medicine is decidedly not "cookbook medicine." Patients must have the chance to actively participate in decisions that affect their health. It is in dialog between the caretaker and the patient that such decisions should be made.

The capacity to discuss crucial health decisions, considering the best available evidence and individual variations, is essential to good clinical practice.

# DEPRESSION

## SBU's conclusions

- Treatment of depression should aim at full recovery, i.e., that the patient is not only free from symptoms but also able to function as usual socially and at work. That objective can be achieved for the great majority of patients if available treatment options are consistently exploited (Evidence Grade 1).
- There are a large number of antidepressants and several types of psychotherapy that have been shown to be effective for treating major depression in adults (Evidence Grade 1).
- For the acute treatment of mild or moderate depression in adults, several types of psychotherapy are as effective as tricyclic antidepressants (TCAs) (Evidence Grade 1) and probably as effective as selective serotonin reuptake inhibitors (SSRIs) (Evidence Grade 2).
- Antidepressants and electroconvulsive therapy (ECT) have proven to be most effective for severe depression, such as melancholia and psychotic depression (Evidence Grade 2).
- Antidepressants and ECT produce more rapid results than psychotherapy (Evidence Grade 2).
- Maintenance psychotherapy reduces or delays relapses, particularly in cases where acute antidepressant treatment or psychotherapy has not rendered the patient symptom-free (Evidence Grade 1).
- No significant differences have emerged in the effectiveness of various antidepressants for the treatment of mild and moderate depression (Evidence Grade 1).
- Due to either side-effects or lack of effectiveness, initial antidepressant treatment produces unsatisfactory results in an average of one-third of the patients (Evidence Grade 1).
- Once antidepressant treatment has resulted in remission, there is a high risk of relapse unless the same dosage is prescribed for at least another 6 months (Evidence Grade 1). Extension of the treatment to 1 year further reduces the risk of relapse.
- Prophylactic antidepressant treatment for as long as 3 years reduces the risk of recurrence with 50 percent in patients who suffer frequent or particularly severe depressive episodes (Evidence Grade 1).
- Sudden discontinuation of treatment with SSRIs, or TCAs that affect serotonin uptake, can cause severe withdrawal symptoms (Evidence Grade 2). But these symptoms do not indicate dependence given that its classic signs – such as a significant dosage increase, preoccupation with tablet intake, or neglect of work, friends and normal interests – are absent.
- Antidepressants are more effective than psychotherapy for the treatment of chronic low-grade depression (dysthymia) (Evidence Grade 1).
- ECT is safe and effective, both more rapid and more effective than antidepressant treatment (Evidence Grade 1). But there is a high probability of relapse, and only limited knowledge is available about which antidepressants are effective to prevent relapse (Evidence Grade 2).
- Transcranial magnetic stimulation (TMS) and vagus nerve stimulation (VNS) are experimental treatments that lack sufficient scientific basis for use in routine medical care.
- Light therapy has not been shown to be significantly more effective than placebos for treating seasonal affective disorder.
- St. John's Wort (*hypericum perforatum*) has been shown to be effective for short-term and mild depression (Evidence Grade 2), but its effectiveness in long-term treatment has not been studied. The preparation accelerates the metabolism of many common medications (including cholesterol lowering drugs, anticoagulants, oral contraceptives and immunosuppressive drugs following organ transplants), as a result of which their effectiveness may be reduced or eliminated.
- Primary care studies in several countries produced better results than routine medical care when the provider offered patient instruction, telephone support and computerized reminders about treatment protocols, as well as ready access to psychiatrists and psychologists trained in short-term psychotherapy (Evidence Grade 1).
- One antidepressant, (fluoxetine), has been shown to be effective for short-term treatment of depression in children and adolescents (Evidence Grade 2). No antidepressant has been approved in Sweden for treating that age group. Controlled long-term trials are completely lacking, though the risk of relapse after short-term treatment is just as high as in adults. There is moderate scientific support for treating depression in children and adolescents with cognitive-behavioral therapy and interpersonal psychotherapy (Evidence Grade 2), but the long-term effectiveness is insufficiently documented.
- The effectiveness of antidepressant treatment and psychotherapy in the elderly up to the age of 75 is well documented (Evidence Grade 1), but there are no studies of people over 80.
- Research on effective treatments for bipolar disorder has been very limited, and the results of the numerous trials now under way are not expected for several years. Lithium has been proven to be the most effective drug for the acute treatment of both manic and depressive episodes, as well as for preventive treatment (Evidence Grade 1). Several new antipsychotic drugs have also been proven to be effective with acute manic episodes (Evidence Grade 1), but there is only moderately strong scientific evidence for their preventive effect (Evidence Grade 2). Although some drugs originally developed to treat epilepsy are effective with both mania and depression (Evidence Grade 1), only lamotrigine has been shown to have a preventive effect, primarily against depressive episodes (Evidence Grade 1).
- There are several key areas in which research provides no basis for choosing a particular treatment. Studies are totally lacking when it comes to treating depression in people over 80. There are no studies of antidepressant treatment in children and adolescents that have lasted longer than 10 weeks, and documentation of the long-term effectiveness of psychotherapy in these age groups is very limited.





# FINDINGS

## SBU Alert

### SCREENING

#### Universal newborn hearing screening

##### ■ Technology and target group

More than 1 out of every 1 000 children are born with permanent hearing impairment that calls for habilitation. Early detection of hearing loss and commencement of habilitation can improve the language development of such children. Most industrialized countries have programs for detecting hearing impairment in infants. The most common approach is for children to undergo a screening test just before the age of 1. Swedish child health centers have used two distraction methods – BOEL (Gaze Orients By Sound) and the Infant Distraction Test. But flaws have emerged in these screening approaches and it has been shown that only 5.4 percent of all hearing impairment in Sweden is detected before the age of 6 months. Otoacoustic Emissions (OAEs) and Auditory Automated Brainstem Response (aABR), two new methods that offer fresh opportunities for hearing screening of the newborn, can be performed while the baby is still at the maternity ward. A two-step approach is often employed, i.e., a second test is performed within a few days unless the initial results are negative in both ears. Habilitation measures – such as the fitting of hearing aids, support for the family and sign language training – can commence as soon as hearing loss is detected. The potential target group for newborn hearing screening consists of the approximately 100 000 children born in Sweden each year.

##### ■ Patient benefit and risks

A number of studies and reviews of the literature indicate that screening during the neonatal period (the first month of life), using OAEs and/or aABR, results in earlier detection of congenital hearing impairment than traditional distraction tests. The only controlled (non-randomized) trial, which included 54 000 children, compared newborn with traditional screening. The number of children with bilateral hearing impairment (40 dB or greater hearing loss in the better ear) who were referred to further examination before the age of 6 months was 94 per 100 000 in the group screened during the neonatal period, as opposed to 32 per 100 000 with traditional screening. The number of false negatives was significantly lower for neonatal (4 percent) than traditional (27 percent) screening. Habilitation commenced before the age of 10 months for 59 per 100 000 of the children who underwent neonatal screening, as opposed to 25 per 100 000 of those who were screened in the traditional manner. A number of studies based on thorough observations suggest that early detection and commencement of habilitation measures improved communicative and linguistic development. There is no evidence that the actual assessment of hearing has a negative impact on the child.

##### ■ Ethical aspects

For screening to be ethically acceptable, any hearing impairment that is detected must be followed up by an organization that can provide rapid, effective habilitation. False positive screening results, and even early diagnosis, can upset parents during a sensitive period in the relationship with their child. Proper information, short assessment periods and

the fewest possible number of false positives can minimize that risk.

##### ■ Economic aspects

Universal screening of the newborn, including diagnostic assessments, costs approximately SEK 240 per child. The adoption of such a program throughout Sweden would add approximately SEK 19 million to annual healthcare costs, i.e., SEK 300 000 per additional case detected. Since hearing impairment is detected with traditional screening methods in a considerably smaller percentage of children than in Britain – the country from which the data for making the calculation was taken – the estimated cost in Sweden is approximately 30 percent less. To assess the program's cost-effectiveness, the costs of providing earlier habilitation must also be taken into consideration, as well as the financial resources that society frees up by virtue of better language development among the children affected and improved health-related quality of life for both them and their parents. No data is currently available for calculating either the lifetime costs or the health benefits of universal screening.

##### ■ Scientific evidence

There is scientific evidence that newborn screening, using either OAEs or aABR, results in earlier detection of congenital hearing impairment and commencement of habilitation (Evidence grade 2). Limited evidence exists that earlier detection and commencement of habilitation promotes improved communication and language development in the child (Evidence grade 3). The evidence is satisfactory with respect to costs per case detected but insufficient when it comes to the method's cost effectiveness.

### SCREENING

#### Abdominal aortic aneurysms

##### ■ Technology and target group

Abdominal aortic aneurysms (permanent localized dilatation of the abdominal aorta) are common, particularly in older men. The generally accepted definition of an abdominal aortic aneurysm is that the aorta's maximum diameter exceeds 30 mm. The risk of rupture increases as the aneurysm expands, a condition which often leads to death. Since aneurysms generally are asymptomatic, they are currently detected either by chance following computed tomography or by ultrasound screening of the abdomen upon suspicion of another disease, or when a rupture occurs. While an aneurysm can be treated with preventive surgery, the associated mortality risk is 4–5 percent. Thus, such a procedure is not performed until the risk of rupture exceeds that figure. One way to reduce the mortality rate is to detect aneurysms early by means of a screening method that involves ultrasound scanning of the abdomen. Since abdominal aortic aneurysms are considerably less common in women, most of the discussion has focused on the screening of men. Screening all men at the age of 65 appears to be the optimal approach. In line with such a model, approximately 40 000 Swedish men would be invited to undergo a scan each year. An estimated 5 percent of these men would have aneurysms. Since previous screening studies suggest that approximately 75 percent of the men would choose to undergo the scan, approximately 1 500 new cases of abdominal aortic aneurysm would be detected on an annual basis. An estimated 150 aneurysms would be large



enough to require immediate surgery, while periodic follow-up screening would be called for in the remaining cases. An estimated 600 Swedish men die each year of aneurysm-related causes.

#### ■ Patient benefit

The findings of three controlled trials, which involved screening programs for a total of 87 000 men aged 65–80, suggest that both the incidence of ruptures and the consequent aneurysm-related mortality rate can be reduced. The men were randomized to either screening and, if necessary, surgery or to a control group. The Multicentre Aneurysm Screening Study (MASS), the biggest trial, was carried out in Britain among 67 800 men aged 65–74. Results from the four-year follow-up period indicated that aneurysm-related mortality was 42 percent less in the study group than the control group. The absolute risk decreased from 0.33 percent to 0.19 percent. In other words, approximately 700 men had to be invited for screening in order to prevent one aneurysm-related death. The other two trials reported similar results.

#### ■ Economic aspects

Adoption of a screening program for abdominal aortic aneurysms would entail costs for both ultrasound scanning and a greater number of elective surgical interventions. However, costs for emergency surgery would decline. A number of studies based on conditions outside of Sweden have assessed the cost-effectiveness of screening for abdominal aortic aneurysms. An analysis of the MASS data found that the mean incremental cost-effectiveness ratio was 28 400 pounds per life year gained over a four-year follow-up period. While based on considerably smaller efficacy studies,

several other analyses suggest substantially lower costs per life year gained.

#### ■ Ethical aspects

Screening a symptom-free population for a condition, the available treatment for which carries a mortality risk of 4–5 percent and a certain measure of morbidity following surgery, poses several ethical issues. Although screening would reduce the incidence of aneurysm-related deaths, a number of patients would die prematurely as a result of the treatment itself. Furthermore, the majority of the aneurysms that are detected would not be large enough to justify preventive surgery. The knowledge that one has an aneurysm that will remain untreated until it has become larger may be difficult to live with. Such issues must be clearly explained to the prospective participants in a screening program.

#### ■ Scientific evidence

There is strong scientific evidence (Evidence Grade 1)\* that screening reduces abdominal aortic aneurysm-related mortality in men. Limited scientific evidence (Evidence Grade 3)\* exists with regard to the method's cost-effectiveness. No evaluation study has been conducted in Sweden concerning screening for abdominal aortic aneurysms. No randomized study has examined total effects and costs of screening all men, when screening began at the age of 65. A number of ethical considerations require further examination. Any kind of screening program for abdominal aortic aneurysms that is contemplated in Sweden should fall within the scope of a scientific study that evaluates all potential consequences.

## HEART

### Drug eluting stents in coronary arteries

#### ■ Technology and target group

Percutaneous coronary intervention (PCI) is a general concept covering procedures in the coronary arteries carried out via a catheter, eg, balloon angioplasty, for the purpose of widening a narrowed part of a vessel (stenosis). However, narrowing may later recur in a stenosis that has been widened (restenosis). Insertion of a thin, net-shaped, metal prosthesis (stent) has been shown to reduce the risk for restenosis by nearly half in comparison to balloon angioplasty alone. In comparing balloon angioplasty alone versus balloon angioplasty with stents, no differences have been found in the risks for mortality or myocardial infarction. During 2003, approximately 13 000 PCI procedures were performed in Sweden, whereof most involved the use of stents. A continuing problem is that symptoms may return due to tissue growing from the vascular wall in the stent (in-stent restenosis). Methods that involve coating the stent surface with drugs to prevent the growth of tissue in the stent (Drug Eluting Stents, DES) are currently being tested.

#### ■ Patient benefits and risks

Seven randomized trials, covering 3 559 patients with narrowing in a single vessel, have compared treatment with drug eluting stents (DES) versus treatment with noncoated stents (Bare Metal Stents – BMS). Followup (up to one year) has shown that, on average, 4 percent of the patients treated with DES had undergone at least one repeat intervention in the stenosis. The corresponding

percentage in the group treated with BMS varied among the studies, ranging from 11 percent to 21 percent. Some of the restenoses that led to repeat interventions were detected via the followup angiography specified by the protocol. Hence, it is unknown how many of these would have led to repeat intervention if the decision had been based solely on the recurrence of symptoms in the patient. Analysis of a registry of 958 consecutive patients from the Netherlands compared the results from routine treatment using DES and BMS respectively. When patients' symptoms were used as the indication for re-intervention, the results showed that 3.7 percent of those receiving DES versus 10.9 percent of those receiving BMS had undergone at least one repeat intervention, eg, PCI or CABG (bypass surgery), within one year. No comparisons between DES and BMS treatment groups have been reported with respect to symptoms, quality of life, or use of medication following intervention. In followup lasting up to one year, no difference was found in mortality or the occurrence of myocardial infarction between groups treated with DES or BMS, either in randomized trials or the registry. In the randomized trials, the risk for subacute thrombosis was less than 1 percent for both DES and BMS. Compared to BMS, the use of DES is thought to be associated with a higher rate of malapposition ie, on followup examination the entire surface area of the stent was not attached to the vessel wall. At 18-month followup, this was not found to result in any complications.

#### ■ Economic aspects

A drug eluting stent costs, on average, about 11 000 Swedish kronor (SEK) more than a stent that is not drug eluting. The additional cost to the Swedish health services of changing to



DES, at the current volume of PCI, is estimated to be approximately 220 million SEK per year. Part of this cost would be offset by a decrease in the need for repeat procedures to treat restenosis. An analysis has shown cost savings of approximately 8 million SEK per year for every percentage point of decline in the need for repeat procedures. No studies were identified that investigated the cost effectiveness of changing to DES.

#### ■ Scientific evidence

There is strong scientific evidence that DES treatment – in comparison to BMS – reduces the risk for restenosis in the stent (Evidence Grade 1). Followup lasting up to one year has shown that fewer repeat interventions have been performed in patients treated with DES in comparison to patients treated with BMS (Evidence Grade 1). The extent to which this has affected patients' symp-

toms, well being, or the use of medication has not been reported. Followup lasting up to one year provides no support for differences in risks of myocardial infarction or death between DES and BMS. Likewise, there is no support for differences in side-effects and complications between DES and BMS.

## STROKE

### Thrombolysis with plasminogen activator (rtPA) in

#### ■ Technology and target group

Although stroke affects approximately 30 000 individuals in Sweden annually, options for treatment in the acute phase have been limited. However, an acute treatment method is now available to dissolve clots (thrombolysis) using recombi-

nant tissue plasminogen activator (rtPA) in patients with cerebral infarction, the most common type of stroke. The method has been tested only in younger stroke patients (<80 years) where treatment has been initiated shortly after onset. The Medical Products Agency has approved thrombolysis with rtPA for patients up to 80 years of age and within 3 hours following the onset of symptoms. Based on current estimates, the target group is limited to approximately 1 500 patients per year in Sweden.

#### ■ Patient benefit and risks

Eight randomized controlled studies involving 2 955 patients have been conducted where treatment with rtPA was initiated within 6 hours following onset. The most serious risk of treatment is the risk for cerebral hemorrhage. An increase in symptomatic (including fatal) cerebral hemorrhage has been found in 62 of 1 000 patients treated. Nevertheless, a net gain in overall outcome has been shown, namely that an additional 55 of 1 000 patients survived or were not dependent of the help of others if they were treated with rtPA. The highest percentage of positive effects was found in the 957 patients where treatment was initiated within the first 3 hours following onset. Of these, 110 of 1 000 patients treated avoided death or dependency on others.

#### ■ Economic aspects

There are no studies on cost or cost-effectiveness except for a model study with unconfirmed results.

#### ■ Scientific evidence

Thrombolysis with rtPA within 3 hours of onset in patients up to 80 years of age yields a generally positive result

(Evidence grade 2) despite the increase in severe brain hemorrhages (Evidence grade 1). Relatively few patients were included in the studies, and the studies were conducted at specialized centers. Therefore, it is important to follow up the results in general health services by using quality registries (SITS-MOST, Riks-Stroke). Effect size and risk must also be presented with greater precision. Sweden needs to participate in large international randomized trials to acquire further knowledge about which patients benefit, eg, regarding age and longer time periods following onset, and which patients are at higher risk. Knowledge concerning cost-effectiveness is greatly limited (Evidence grade 4), and further studies are needed.



## EVIDENCE GRADES

Grading of the level of scientific evidence for conclusions. The grading scale includes four levels;  
1 = strong scientific evidence,  
2 = moderately strong scientific evidence,  
3 = limited scientific evidence,  
4 = insufficient scientific evidence.

See [www.sbu.se](http://www.sbu.se) for full English summaries.

# The force of habit in health care

The sooner solid evidence is brought to bear on clinical practice, the better health care will be, writes Dr. Jörgen Malmquist. History shows that when caregivers continue in the same old rut, regardless of the evidence, patients pay the price.

Sometimes there are good reasons for holding off on a change. For instance, methods that have proven effective but have serious

side effects may have to be introduced in a controlled manner. Old-fashioned but established routines may have to be retained until organizational and financial circumstances are conducive to adopting new practices.

## GOES ON AS BEFORE

But history demonstrates that clinical practice often takes too long to adapt to scientific evidence – both when discarding unproven, ineffective methods and when adopting new, effective ones. Practice goes on as

before. As a result, patients suffer unnecessarily.

For instance, many years passed<sup>1,2</sup> before health care professionals accepted the evidence showing that aspirin can prevent heart attacks and strokes in people with a high risk of arterial thrombosis.<sup>3</sup>

## BED REST AND HEART

Another long-lived misconception was that 3–4 weeks of bed rest are required following a heart attack. That practice survived until the late 1960s. Nobody questioned the assumption that a damaged heart muscle benefits from such respite.

But a systematic review of the matter showed that most patients could get up after a day or two and leave the hospital within a week. Those who did so not only got to go home sooner but also avoided the adverse effects of inactivity, including the risk of blood clots.

## REST AND BACKACHE

According to an equally tenacious and erroneous belief, acute lower-back pain goes away most quickly if the patient lies still in bed and rests. Such recommendations predominated well into the 1980s.

The idea goes back to the 19th-century precept that rest is required whenever a part of the body has been injured, torn or broken.<sup>4</sup>



Illustration: Kenneth Karlsson  
Concept: Ragnar Lev

However, as demonstrated by the SBU report Back and Neck Pain, there is strong evidence that such an approach is ineffective and even harmful.<sup>5</sup>

#### ACID INHIBITORS

Upper abdominal discomfort that persists after a thorough examination ruling out any specific cause is called functional dyspepsia.<sup>6</sup> In 2000, SBU concluded that ulcer drugs such as H2 blockers and proton pump inhibitors are often prescribed, despite the lack of scientific evidence that they are effective for functional dyspepsia without heartburn.<sup>6</sup> SBU concluded that prescribing such drugs for functional dyspepsia cost some 500 million SEK a year.

#### HEART ATTACKS

Retrospective analyses have demonstrated that lives could have been saved, unnecessary suffering avoided, and resources utilized more effectively if caregivers had taken systematic advantage of research findings.

A case in point is thrombolytic therapy to dissolve blood clots after acute myocardial infarct.

More than 20 trials studied the method from the mid-1950s to the early 1980s. No single study was large enough to convincingly demonstrate any benefit. Since the treatment could produce serious side effects, the healthcare profession held off.

But when researchers finally re-examined the previous findings, they found that a statistically significant effect could have been detected more than 20

years earlier if the studies had been compiled in a meta-analysis.

If routine thrombolytic therapy had been adopted as soon as the evidence was clear, hundreds of thousands of lives might have been saved.<sup>7</sup>

The use of beta blockers following heart attacks has a similar history. From 1967 to 1997, more than 30 trials investigated the protective effect of beta-blocking agents in heart attack patients. According to subsequent analyses, the conclusion that the treatment reduces mortality by 20 percent could have been reached back in 1981 if existing research findings had been taken into account<sup>8</sup> through a cumulative meta-analysis. Instead, trials were conducted on an additional 15,000 patients before the same conclusion was reached.

#### SMOKING CESSATION

Not even half of all Swedish general practitioners ask their patients whether they smoke unless specific symptoms are present. Fewer than 50 percent of nurses in out-patient care and 20 percent in in-patient care ever actively help people quit smoking. Nevertheless, there is scientific evidence that brief, structured counseling, combined with nicotine replacement products, is relatively effective. The approach is cost-effective when used routinely – it can save lives and should be adopted by both primary and dental caregivers.<sup>9</sup>

#### ALCOHOL ABUSE

Scientific studies have shown that structured, psychosocial

methods, sometimes combined with medication, are effective for treating alcohol abuse.<sup>10</sup>

But the best methods are not used. Many of the approaches currently employed in Swedish alcohol abuse treatment lack scientific support. In some cases, they have even been scientifically shown to be ineffective.

Hindsight is always easy, and the history of medicine is no exception. However, the purpose of looking back and shedding light on the gaps between medical science and clinical practice is not to pass judgment – but to learn. Previous errors are meaningful only if we learn from them.

*Jörgen Malmquist  
M.D. and freelance writer*

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## WHEN CLINICAL PRACTICE FALLS VICTIM TO INERTIA

### METHODS THAT TOOK TOO LONG TO DISCARD

Bed rest after heart attack  
Protracted rest for acute, uncomplicated back pain  
Premature X-ray of acute backache without suspicion of other disease  
Acid inhibitors for functional dyspepsia  
Surgery (nephropexy) for floating kidney  
Appendectomy for vague abdominal discomfort (chronic appendicitis)  
Preventive extraction of wisdom teeth that have not erupted  
Neuroleptics for anxiety in non-psychotic elderly  
Routine chest X-ray or ECG before surgery

### METHODS THAT WERE ADOPTED TOO SLOWLY

Aspirin treatment following heart attack or stroke  
ACE inhibitors after heart failure or heart attack  
Treatment to prevent blood clotting before major surgery  
Thrombolytic therapy to dissolve blood clots after acute myocardial infarct  
Beta blockers after heart attack  
Counseling to help patients quit smoking  
Brief intervention for at-risk drinkers  
Structured psychosocial treatment of alcohol abuse  
Advice about fluoride toothpaste to prevent tooth decay

Examples taken from Jörgen Malmquist, Lars Werkö, Mona Britton, Thomas Ihre, Susanna Axelsson, Ingegerd Mejäre, Juliette Säwe, and Åke Andrén-Sandberg

# MEDICAL SCIENCE & PRACTICE

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