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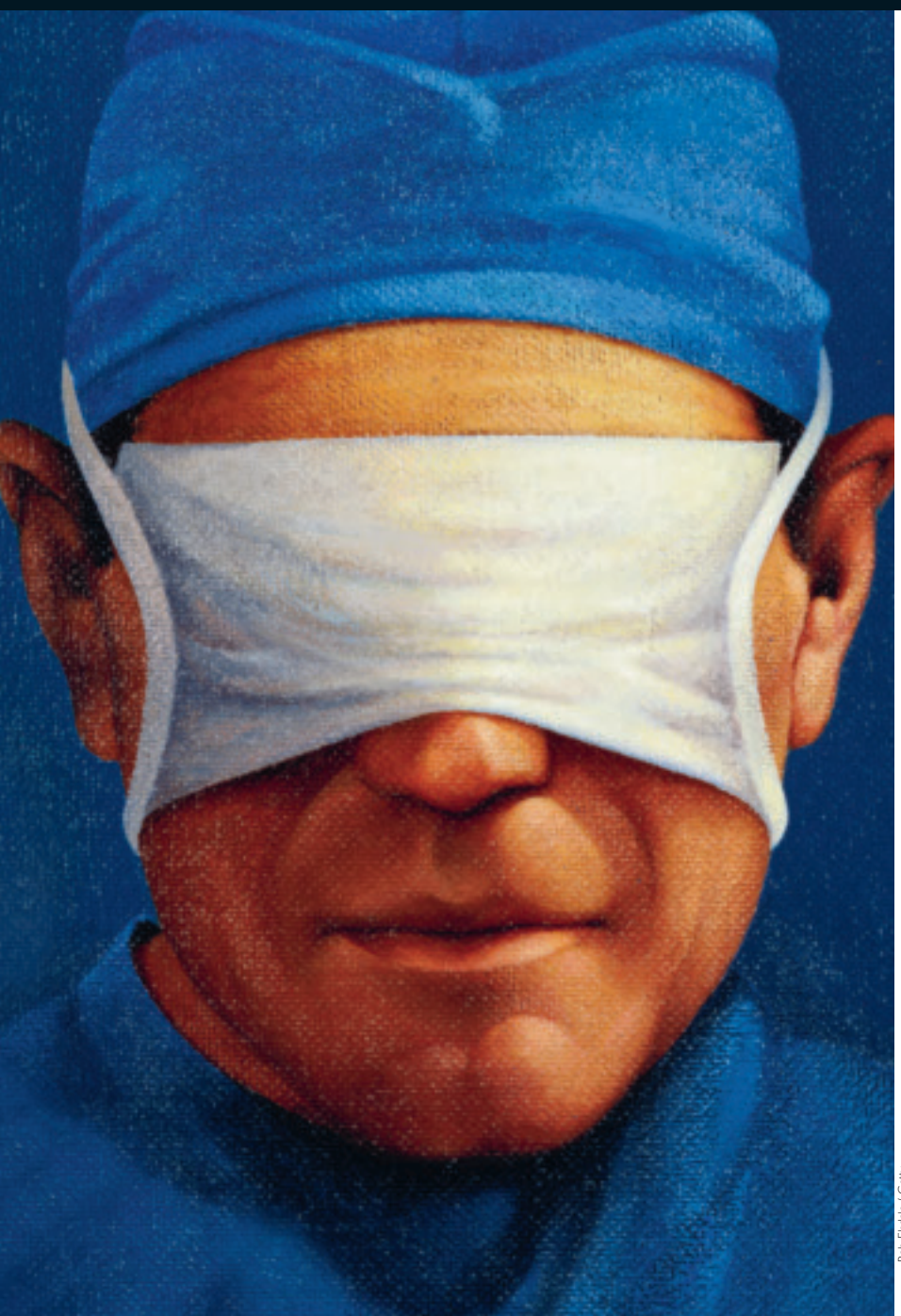
SBU – The Swedish Council on Technology Assessment in Health Care

MEDICAL SCIENCE & PRACTICE

NEW REPORTS SBU Results in Brief |10–15



Bob Elsdale / Getty

Showing Only Half the Truth

The choices that researchers make when they highlight certain findings and bury others can have critical consequences for health services and patients. Not telling the whole story is known as selective reporting.

Researchers face many choices when they conduct scientific studies. They must decide which questions are the most important to answer and how to analyze the findings. But they must also choose a fair and balanced way to present the results – and the scientific lit-.erature shows many examples to the contrary.

The problem fell under the spotlight when the *Journal of the American Medical*

Evidence Must Be Digested, Then Applied

Physicians are often viewed as scholars and intellectuals. But, in fact, how critically do physicians think and speak? Is it critical, scientific inquiry that their teachers, employers, and colleagues encourage? Or is it dogma?

A Swedish study asked 100 new doctors, straight from university, how much they had been encouraged to analyze and reflect on what they had learnt in their basic education. The results were distressing. Over half reported that critical thinking was seldom part of their preclinical education. And only 1 in 5 had been actively encouraged to reflect over causation and correlation in their clinical training.

My hypothesis is that today, the key to a clinical career is less about thinking independently and more about following instructions, memorizing rules of thumb, and conforming to standard practice. Stressed working conditions and demands for omnipotence hardly offer fertile ground for critical reflection. So perhaps we should not be surprised by the time it takes to achieve a self-examining approach in health care.

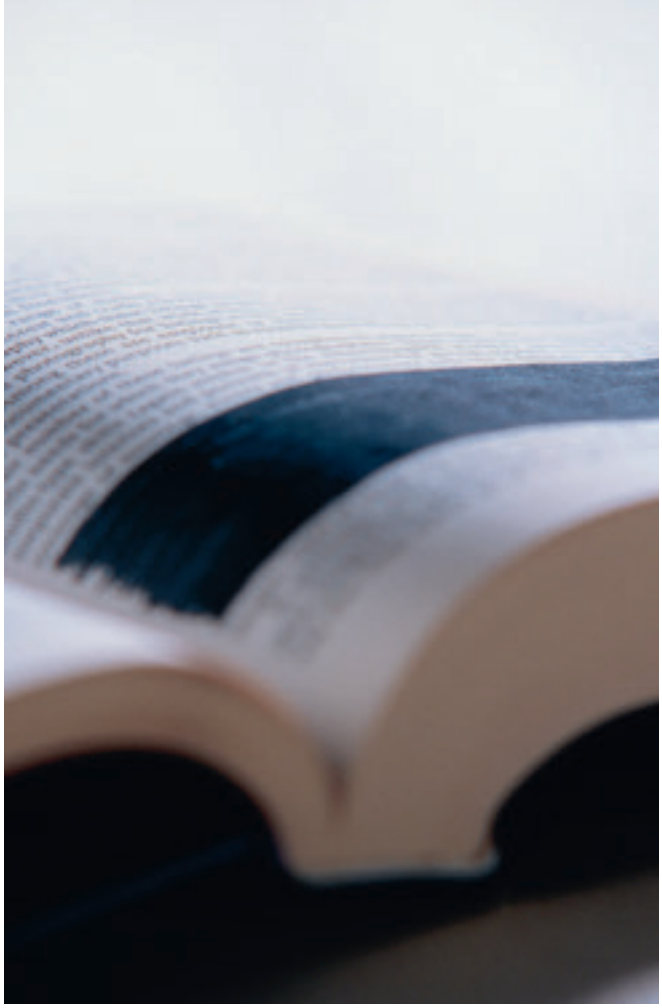
Do healthcare leaders fully realize the implications when they call for more knowledge-based health care? Are they really prepared to allocate resources to education, evaluation, and critical analysis – or do they focus only on production?

To integrate theoretical knowledge into their daily work, healthcare professionals must be able to reflect. Aristotle distinguished knowledge as *episteme*, scientific-theoretic knowledge, *techne*, practical-productive knowledge, and *phronesis*, practical wisdom. Today we refer to assertions, craftsmanship, and prudence. Assertions (theoretic knowledge) can be expressed in words and communicated to others, while craftsmanship (practical knowledge) and prudence (experiential knowledge) come from hands-on training and are not always easily formulated.

Central officials who want to steer health care by knowledge-based guidelines might not understand that all three types of knowledge must be involved. National agents can find the evidence, but local agents must interpret and apply it. Guidelines from above are not enough.

When SBU assesses research findings, scientifically trained reviewers with clinical experience do most of the work. There is a reason for this. Implementation projects consistently show that practitioners must be involved in interpreting and applying new knowledge. Managers must give clinicians and others on the frontline the encouragement, time, and opportunity to reflect on their routines. Force-feeding health professionals with guidelines is doomed to fail. Knowledge must be digested before it can be absorbed and applied.

RAGNAR LEVI, EDITOR



Nancy R Cohen / Getty

Association (JAMA) published a review of the situation in Denmark.

Before a clinical trial can begin, an ethics committee must approve the research protocol. The protocol specifies key questions that the researcher will investigate and the outcomes deemed to be most important, ie, primary endpoints.

ENDPOINTS CHANGED

The Danish study revealed obvious discrepancies in comparing 102 research protocols from the Copenhagen area with the 122 scientific articles later published by the researchers. Endpoints originally classified as primary endpoints in the research protocols had been excluded or reclassified as secondary endpoints. Two thirds of the 82 randomized trials that had specified a primary endpoint had either changed or excluded it when the results were published. Reasons given for excluding the endpoints were that statistical significance had not been achieved, that the results were clinically uninteresting, or the journal had not allowed sufficient space to fully present the results. Only 49 of the 102 researchers responded to a questionnaire about the excluded endpoints. Of those responding, the majority denied having measured effects that had gone unreported.

– In a single trial, researchers might perform between 20 and 40 different analyses of their data, notes Hans Melander, statistician at Sweden's Medical Product Agency.

– Of course, the results would be difficult to manage

if you reported everything in great detail. Of course, it can be difficult to recall your original intent with the study. And of course, you may have legitimate reasons to modify your plans during the study.

REASON TO WONDER

– But if researchers radically change their mind about which endpoints are most important, there is reason to wonder what they are actually trying to do. When a core question later falls on the periphery, or is completely ignored, this is remarkable, says Hans Melander.

An article in *The Lancet* reported on a similar problem. Reviewers had successfully obtained 37 of 67 protocols for randomized trials, all of which had been accepted for publication and were presented on the journal's website. But the 37 research protocols coincided poorly with the 50 articles that reported on findings from the studies. In 11 of 37 studies, the primary endpoints presented in the articles deviated substantially from the corresponding protocols: 5 studies did not include primary endpoints, 8 studies introduced new endpoints, and 2 studies had changed primary endpoints to secondary endpoints.

SKEW RESULTS

Reporting on a study at a different time than originally planned can be another way to skew the results. Often data are analyzed on several different occasions, and at times researchers publish data from only the most favorable one.

– An example, says Hans Melander, is a study that aimed to compare different non-steroidal antiinflammatory drugs, so-called NSAIDs, celecoxib among others. The study was designed to register symptomatic ulcers and complications in the gastrointestinal tract.

The researchers wanted to find which agent was the most tolerable and planned to follow the patients for 12 months. But halfway through the study they published their results as a 6-month trial showing that celecoxib was best.

– They never mentioned that the patients should have been followed twice as long, says Hans Melander. In fact, the 12-month results were already collected and analyzed at the time of publication, and showed no significant differences between the agents.

Furthermore, the endpoints presented at 6 months were not the primary endpoints, explains Hans Melander.

– It's an obvious case of selective reporting.

ANALYZE DROPOUT

Nearly all clinical trials experience some dropout, ie, participants leave the trial before it is finished. Different ways of analyzing dropout can have substantially different effects on the results.

– There's clearly a tendency to publish only the figures that show the most positive outcome, says Hans Melander. This overestimates the treatment's effect.

One example would be the meta-analyses of published studies on antidepressants, where we have shown that the overestimated effect is due largely to researchers choosing a particular type of dropout analysis.

SIDE EFFECTS

Another problem – perhaps the most serious – is that many articles present deficient information about side effects. Articles often report only the positive effects. A review of nearly 200 published studies in widely different areas of medicine shows that information on side effects was deficient in half the cases. Even more disturbing is an analysis of over 100 psychiatric studies, which showed that 75% reported poor information on side effects.

The question of what evidence is available must be followed by the question of what evidence is missing. [RL]

Additional reading

Chan AW, et al. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. JAMA 2004;291:2457-2465.

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SELECTIVE / BIASED REPORTING

EXAMPLES

- only some important (primary) endpoints are reported
- information on side effects is incomplete
- outcomes vary in subgroups of trial participants
- downplaying the effect of adjusting / not adjusting the results statistically
- downplaying the effect of including / ignoring risk factors among participants
- downplaying the effect of reporting the results based on the protocol or intention to treat (ITT)*
- downplaying the effect of statistical method for analyzing dropout

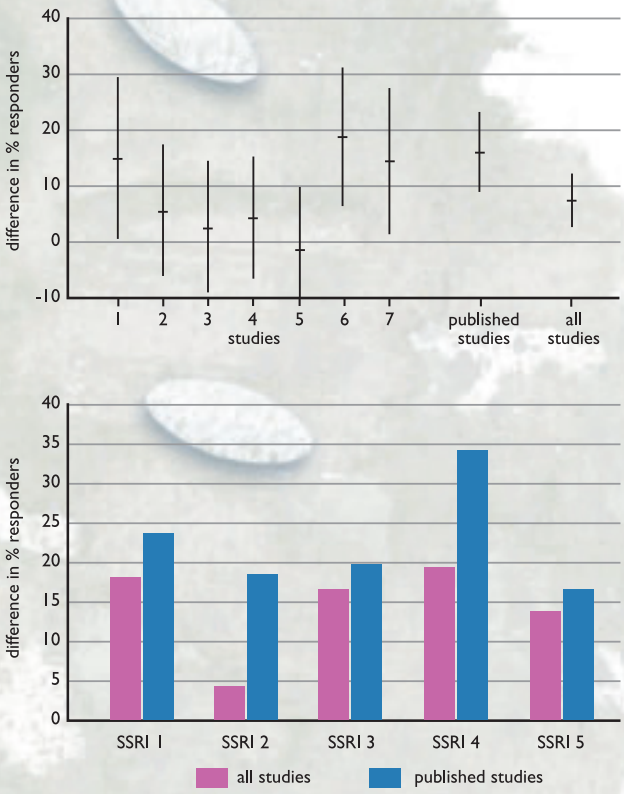
* The results from all trial participants are included, even those that did not follow the protocol (eg, ended treatment prematurely). ITT analysis is desirable – otherwise the results from some participants could be excluded on insufficient or inadequate grounds.

Biased Publication May Distort Overall Picture

When scientific journals publish only certain studies, the full picture can be skewed, writes Professor Björn Beermann, member of SBU's Scientific Advisory Committee.

The effects of a drug often differ from one study to the next. Even treatments with proven effects show wide variations between trials – particularly if the trials are relatively small. Hence, among the total number of studies on a drug we can find a mix of trials: some with positive outcomes showing statistically significant effects, and some trials with negative outcomes, where statistical power is insufficient or where there is no tendency toward effects.

Upper diagram: Different studies (1–7) of the antidepressant agomelatine. When considering only published studies, the effects tend to be overestimated compared to considering all studies, even unpublished ones.
Lower diagram: A similar tendency is also apparent for different SSRI agents (1–5).
Source: Swedish Medical Products Agency



HALF THE CHANCE

Several investigations have shown that, compared to positive studies, negative studies have half the chance of being published; even years after the trials have been completed. [1,2,3]

Another problem is that some positive studies are published in more than one version, which is not always easy to detect. [2,4]

Several actors can influence the decision to publish – researchers, sponsoring corporations, journal editors, and reviewers. Studies sponsored by the drug industry report negative results less often than studies funded by other sources. [13,14]

But regardless of who stands in the way of publication, the consequences are the same – the conclusions on treatment effects are incorrect, which can harm patients or lead to misuse of resources.

An example would be the use of magnesium to treat acute myocardial infarction. A meta-analysis of all published studies (which were relatively small) suggested that the treatment substantially reduced mortality. [5] Several years later, two large studies [6,7] showed that the treatment had no effect on mortality.

The difference in outcomes between the meta-analysis and the two large studies is probably due to the fact that several negative studies had been conducted, but were never published. Wide differences in the outcomes of meta-analyses and large controlled trials have also been observed for other treatments. [8]

FINDINGS DIFFER

Another example concerns the percentage of patients that respond to five different antidepressant drugs used in treating depression (see diagram, left). The findings differ depending on whether they include published studies only, or all studies submitted by drug companies before approval. [2] Meta-analyses that include only published studies show a substantial effect for all of the drugs. Whether or not patients benefit when we choose treatment based on such analyses is not clear.

In some cases, the selection of studies for a meta-analysis is consciously skewed to include only the most

Todd Davidson / Getty

positive studies. The diagram (left) shows the outcomes of all studies on the effects of agomelatine, a new antidepressant, and the outcomes of studies selected for a meta-analysis.[9]

Time factors can also play a role in skewing the evidence presented in published studies. When a new drug is approved and introduced in the marketplace, generally it is supported by only a few published studies, mostly positive ones. This exaggerates the drug's positive profile for those who prescribe it. Drug monographs published by pharmaceutical regulators present more comprehensive, balanced information and can be found in European Public Assessment Reports (EPARs) at www.emea.europa.eu, and at www.lakemedelsverket.se.

STUDIES OVERLOOKED

In many instances, meta-analyses are based only on studies published in English. This means that relevant studies are overlooked at times. German journals, for example, publish negative studies on a much larger scale than English language journals do. [10]

Late or excluded publications of trials showing harmful effects in patients can lead to similar trials, possibly resulting in harmful or fatal outcomes for no reason. The most serious example of this involved the use of certain types of drugs to treat cardiac arrhythmias, ie, antiarrhythmics. In the 1980s, researchers found that people with extra ventricular beats after myocardial infarction ran a higher risk of dying compared to those without extra beats. A large trial investigated whether or not antiarrhythmics would reduce mortality. The trial was stopped in 1989 when the drug was found to increase mortality by two and a half times, corresponding to 34 extra deaths in the trial. [13]

Four years later a similar study was published and showed similar results. [14] That trial had been stopped already in 1980. However, it was not approved for publication because the results were not accepted as credible. Consequently, a harmful study was repeated, leading to 34 unnecessary deaths.

PROBLEM REMAINS

The problem of publication bias has received greater attention in recent years, leading to the creation of several openly accessible databases[15, 16] containing study protocols and summaries of outcomes. Although this has improved the situation, information on unpublished trials conducted up to a few years ago are probably missing from the databases. As long as the databases contain only trial abstracts, the problem of selective reporting remains.

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Can the Sick Choose Appropriate Care?

Swedish law empowers patients to influence their care. But expecting patients to make choices about their care without the necessary knowledge can make health care inequitable and ineffective.

For health services to be truly effective, patients need to participate in their care and take some responsibility themselves. This might involve seeking the right kind of help, describing their problems fairly, learning about the treatment options offered, participating in treatment decisions, and complying with prescriptions. But in patient care, where does the responsibility of the individual end and the responsibility of the health services begin?

CONSUMER POWER

For the Swedish Consumers Association, consumer power is a concept with positive overtones even when it comes to health services. In the Association's magazine *Consumer Power*, Louise Ekström, Director of Communications, writes:

"More (researchers) should compare patients and consumers. When we shop in a supermarket we are informed of dietary fiber content, nutrition content, chemical substances, ecological goods, price comparisons, and quality differences. We compare electricity prices and demand simple and understandable labeling of goods. I wish there were greater consumer awareness even in health services. So we know where we can turn with our complaints, make contact by phone, be able to select for quality, and have the right to buy on a sale-or-return basis."

REQUIRES KNOWLEDGE

However, consumer empowerment requires knowledge. Patients who are not aware of the potentials and risks associated with different therapies cannot be informed consumers and weigh advantages against disadvantages before making informed choices.

Lars-Åke Levin is a health economist in Linköping and member of the Swedish Pharmaceutical Benefits Board.

– Of course, as economists some of us dream about a perfect market even in the healthcare sector, where patients choose treatment just as consumers do in any market, Levin remarks.

– But most realize, however, that this is rather unrealistic since medicine is such a complex field. Patients do not know nearly as much about the different alternatives as the providers do.

– It's hardly possible to make rational choices when you have only superficial knowledge, or no knowledge, about the implications of the different choices, says Lars-Åke Levin.

From yesterday's paternalistic health services, where physicians usually made decisions without patient input, the pendulum has now swung so that patients are often expected to act as active care consumers who are full of initiative and take on heavy responsibility. Many welcome the trend toward more patient power, but some point out that it also has its problems.

SAFETY NET NEEDED

Marie-Jeanette Bergvall is a member of SBU's Lay Advisory Committee and is the executive director of Brain Power (Hjärnkraft), an organization for individuals with acquired brain injury. She has worked toward further empowering patients in health care – but emphasizes that a safety net is also needed for the weakest patients.

– Even if it's important to have the possibility to influence your treatment, for those patients who can and want to, there is clearly a risk that this right can quietly change into an obligation, and the demands from health services

Ragnar Levi / Robert Nyberg

Simon Roberts / Getty

can become too great, says Marie-Jeanette Bergvall.

– Then the patients with the weakest resources and those who are less verbal and less informed will receive poorer care than others. And this bodes ill for our society's goal of equitable care.

SUIT THE ACTIVE

Health services today are often geared to the active healthcare consumers, she notes.

– For instance, some of our members couldn't remember what their meeting with their doctor was about, or forgot a doctor's appointment, and the health services just left them high and dry.

– They have fallen out of the system. This is not at all how it should be. You shouldn't need to be healthy to receive appropriate care for your illness.

Occasionally we hear about a medically astute patient who surfs the Internet and might even be more updated than the doctor. But in reality such patients are rare, and seldom are they severely ill, suggests Marie-Jeanette Bergvall.

– Health services cannot, in fact, expect patients on their own to identify the various potential treatment options and ask relevant questions about the advantages and disadvantages of these methods. Actively informing patients about these options must remain an obligation of the attending physician, she says.

ETHICAL PROBLEMS

Tore Nilstun, Professor of Medical Ethics at Lund University, notes that ethical problems can also arise when health services turn over the choice of treatment to the patient.

– The role of health services is to improve the health of sick people. If a patient chooses a treatment that is risky and of questionable value, a conflict arises between the role of health care and the patient's right of self-determination, says Tore Nilstun.

– Patients do not have the right to choose an intervention that is contrary to scientific evidence and standard practice, he says.

But what standards should the county councils and health services actually impose on the interventions that patients demand? This question is raised each time SBU or others identify variations in practice patterns. It has received renewed focus given the recent legislation proposed by the EU Commission.

The proposed legislation would allow patients within EU to receive health services in another member state, so-called cross-border care. Some patients will probably choose to seek care in other countries, for instance, to access a new test or treatment not available at home. But all countries do not impose the same scientific standards on the methods practiced by health services. In which cases should the home country reimburse a diagnosis or treatment?

NETWORK FORMED

The directive presupposes that a European network would be formed to scientifically assess healthcare methods. Network members would include SBU and similar agencies in other countries.

Such a network should develop common methods for assessment and develop an evidence base to enable more effective and equitable health services throughout Europe. Seeds for such a network have already been sown by the EUnetHTA Project, where SBU has been an active partner from the outset.

Another issue is whether it will be only those patients with strong resources that will be aware of and use the option of cross-border care. If so, what are the implications for the cornerstone of the Swedish Health Services Act; to assure good care on equal terms for the entire population? [RL]

Increasing Pressure to Open Doors to Evidence

Free web access to research findings is in increasing demand worldwide.

Open access means that researchers make their articles available on the Internet free of charge instead of publishing the findings only in scientific journals that require expensive subscriptions.

The basic idea is that everyone interested should be able to access the research findings, even institutions with very limited resources, eg, in developing countries. There is no cost for reading, citing, downloading, and printing copies of scientific articles. Hence, the resources now used for subscriptions could be applied instead to research.

OPEN ARCHIVE

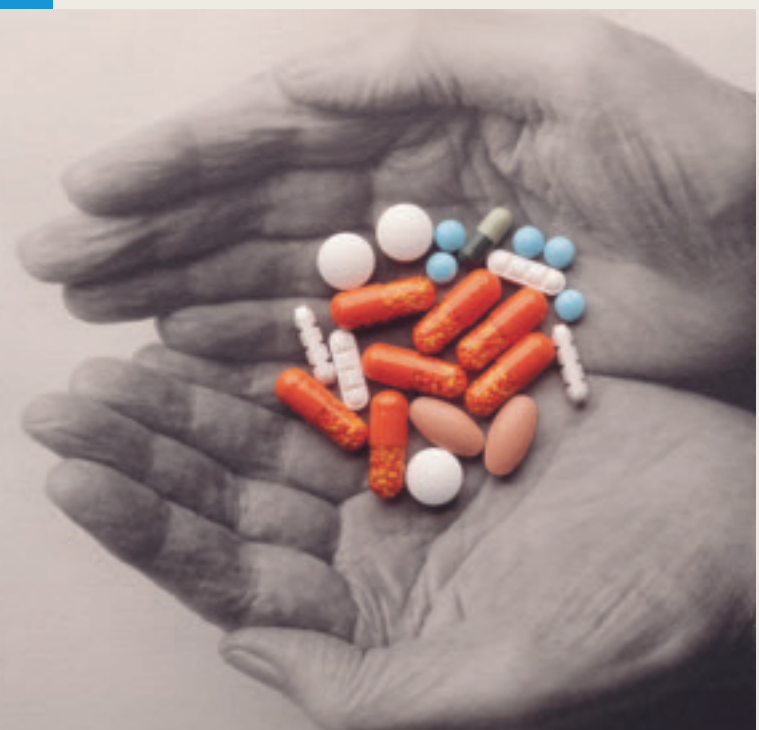
Increasingly more scientific journals are freely accessible on the Internet (see www.doaj.org), eg, via the *Public Library of Science,* www.plos.org. But even when an article is published by a journal without open access, researchers often have the opportunity to publish the article in parallel in their own open archive. However, the author must have retained the right for parallel or open archive publication, which many journals will not accept.

Major sources for research funding, such as the National Institutes of Health in the USA, stipulate that articles based on the research they finance must also be available through open access on www.pubmedcentral.nih.gov Sweden has a similar initiative, OpenAccess.se operated by the National Library of Sweden, the Knowledge Foundation, the Association of Swedish Higher Education, the Royal Swedish Academy of Sciences, and the Swedish Research Council. Among other objectives, this initiative aims to promote publication in open archives and open access journals. [RL]

Drugs for the Elderly Need Systems Thinking

Elderly people with multiple comorbidities need full medical evaluation and active followup as their condition worsens – not simply one more prescription. A comprehensive care plan is key, even in the acute phase. Today, inappropriate medication causes suffering and high costs.

Elderly people are often prescribed inappropriate drugs or combinations of drugs. Better education and information for physicians are two of many ways to improve prescriptions. But single interventions are not enough – a systems approach is needed.



Romilly Lockyer / Getty

This summarizes SBU's view of the current situation following its assessment of interventions to improve the use of drugs among the elderly.

ADVERSE EFFECTS

Although medications can contribute to a longer life and higher quality of life, the elderly often experience adverse effects from their prescriptions, regardless of care setting. Between 30% and 50% of the negative effects potentially can be avoided.

Common causes include inappropriate prescriptions, insufficient followup (eg, routines or reactions to warning signals), and inappropriate drug combinations.

Research on this topic suggests that intervention is needed at many levels concurrently: more comprehensive medical investigation and more accurate diagnostics, long-term planning starting as early as possible in the acute phase, individually adapted doses, and recurrent reviews of drug prescriptions.

ETHICALLY DEFICIENT

SBU finds health services to be ethically deficient when they lack the routines to regularly, and in each individual case, follow patients' treatment results.

The organization of health services related to pharmacotherapy should also be reviewed and clarified, along with the divisions of responsibility, writes SBU. Changes could be needed in managing information, routines, and supportive technology for prescribing and monitoring treatment, distributing drugs, and providing education.

SBU's review shows that several interventions in combination can help patients comply better with prescribed treatment. The benefits of multi-dose drug dispensing cannot be assessed due to inadequate studies. However, some evidence suggests that patient education with repeated information, and simplified drug lists, more often results in patients taking their medications as prescribed. Special measures for different categories of staff and for patients can reduce the prevalence of medication problems among the elderly.

However, studies have not investigated if such measures also affect mortality, morbidity, quality of life, utilization of health services, or healthcare costs.

MUST COLLABORATE

If the situation for the elderly is to improve, those involved must collaborate, writes SBU. It is essential to quickly produce an action plan based on a systems approach. Regions, county councils, municipalities, executive teams, pharmaceutical advisors, societies

of healthcare professionals, and patient representatives must design the plan collaboratively.

Individual physicians can take important steps already today. The report reiterates that several types of pharmaceuticals may be inappropriate for elderly people with multiple comorbidities. For example, it might be necessary to avoid agents with anticolonergic effects (eg, certain medications for psychosis, depression, and incontinence) NSAIDs (anti-inflammatory and analgesic drugs such as ibuprofen, naproxen, ketprofen, diclofenac, and acetylsalicylic acid) and benzodiazepines (sedatives such as diazepam, nitrazepam, and flunitrazepam).

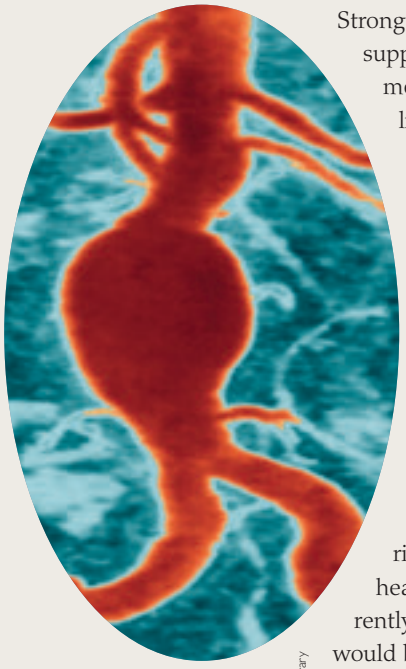
IMPORTANT METHODS

Although inappropriate medications cause harm, it must be remembered that drugs are among the most important treatment methods for providing sick and aging people with better health and higher quality of life.

But pharmacotherapy in the elderly must improve substantially. Many people continue to be harmed for no reason, and society pays out billions annually to treat problems that could have been avoided. [RL]

Aortic Screening Saves Men's Lives

Ultrasound screening for abdominal aortic aneurysm in all 65-year-old men is lifesaving, cost effective, and ethical. But evidence of its value in women is lacking.



Zephyr / Science Photo Library

Strong scientific evidence supports screening as a means to reduce mortality from abdominal aortic aneurysm in men, according to a new report from SBU.

The body of scientific evidence on the cost effectiveness of the method is also strong. Screening exams and the greater number of planned surgeries would increase healthcare costs. Concurrently, however, costs would be expected to decrease for the more expensive option, emergency surgery.

STUDIES ON WOMEN

Studies on screening in women are in progress, but SBU is currently unable to draw conclusions since the scientific evidence is insufficient.

Abdominal aortic aneurysm forms a bulge on the aorta caused by weakness in the vessel wall. The bulge can grow, but the rate of growth varies considerably.

Usually an aneurysm expresses no symptoms until it becomes large enough to rupture. Then it becomes life threatening and is fatal in 75% of cases. Approximately 600 men and 200 women in Sweden die annually from abdominal aortic aneurysm.

INCREASES RISK

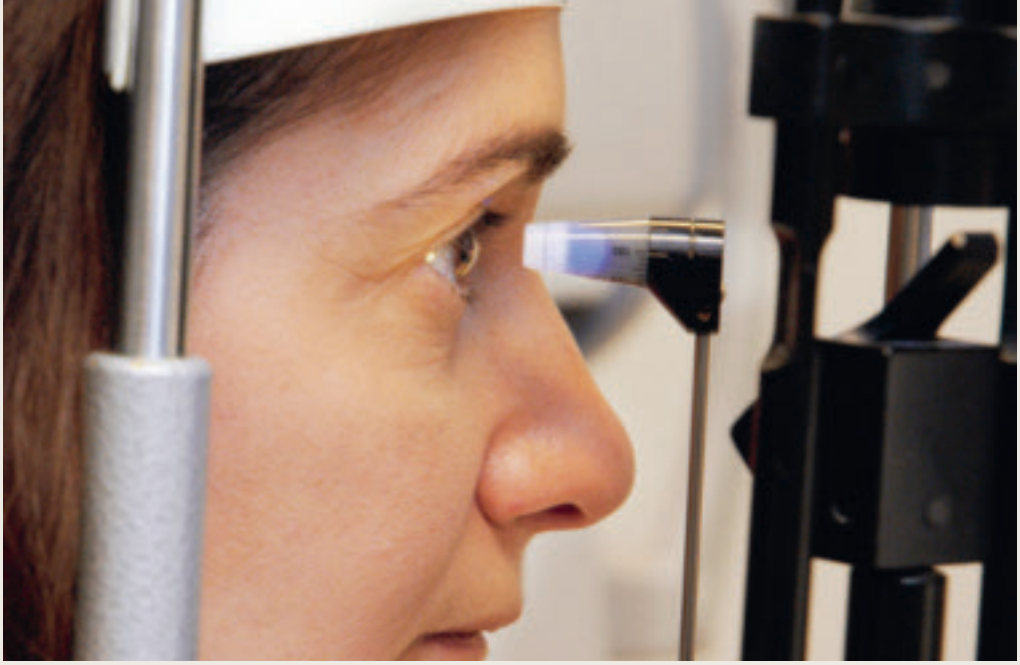
The preventive surgical procedure per se increases the risk of death by less than 3%.

Taxi

For screening to be ethically defensible, everyone called for ultrasound examination must receive balanced, easily understood information about the consequences of examination and treatment. They should also be given an opportunity to consider the different options in consultation with their family and the attending physician.

Many healthcare providers in Sweden currently screen men, and more county councils plan to introduce the method.

This report updates an SBU report published in December 2003. [JT]



AJ Photo / Science Photo Library

Lowering Eye Pressure Key in Glaucoma

Reducing intraocular pressure can delay visual field loss in patients with glaucoma. Also, quick and effective methods can improve diagnosis and follow-up.

A recent SBU review confirms that lowering intraocular pressure delays visual field loss in glaucoma patients. Reducing the pressure also cuts the risk for developing glaucoma in persons with elevated intraocular pressure. In these cases, a pressure reduction of at least 20% is necessary. Research has not shown any treatment effects at reductions below 20%.

Chronic, open angle glaucoma is a disease affecting the optic nerve. The disease develops slowly and causes gradual loss in the visual field, in the worst case leading to blindness. Glaucoma has no early symptoms, and patients can live with the disease for a long period without it having a marked effect on daily life. The key risk factor is elevated intraocular pressure.

REMAIN UNDIAGNOSED

In Sweden, an estimated 100 000 people have a diagnosis of glaucoma. Approximately one fourth of all visits to ophthalmology departments in Sweden are glaucoma-related. Although glaucoma affects 5–6% of the population aged 65–75 years, around half remain undiagnosed.

SBU's review also shows that new methods used to assess the patient's visual field are highly accurate. Furthermore, they can be conducted in about half the time as previous tests.

NATIONAL SURVEY

A national practice survey presented in the report shows that the average Swedish glaucoma patient undergoes a visual field exam every second year.

– We know now that we have effective treatment methods and good instruments to diagnose and monitor glaucoma. And suitable equipment is accessible at all ophthalmology services in Sweden, says Anders Heijl, Professor of Ophthalmology at Malmö University Hospital and Chair of the SBU project.

– Nevertheless, he says, there is potential for improvement – vision function exams are a prerequisite for optimum treatment, and here access must improve substantially. [JT]

Childhood Vaccine Safe and Lifesaving

The benefits of Sweden's child immunization program far outweigh its risk for adverse effects. International data confirms that diseases are much riskier than vaccines.

Thanks to modern vaccines very few people fall ill or die from infectious diseases that once were common and caused serious harm in children and adults. This is reinforced by a critical review of several vaccines used in Sweden's current child immunization program.

SBU's systematic literature review is among the first of its kind, and covers vaccines against measles, mumps (epidemic parotitis), rubella, whooping cough (pertussis), Haemophilus influenzae type b, hepatitis B, and tuberculosis.

PARENTS REFUSE

Some parents refuse to accept the vaccines offered to their children through the public immunization program. But the international body of empirical evidence on these vaccines leads to the following conclusions.

Combined vaccination against measles, mumps, and rubella (MMR) protects against these diseases and their potentially serious consequences. Fever is a common side effect, and the risk for febrile convulsions increases in the first 2 weeks after immunization. But vaccination does not increase the risk for autism, epilepsy, type 1 diabetes, or serious infections requiring hospitalization.

LESS HOSPITALIZATION

Public immunization against whooping cough (pertussis) – a highly contagious infection that can be lengthy and have severe consequences – protects children from contracting the disease and reduces the need for hospitalization. Protection lasts at least 5 years after three or four doses. The body of research does not suggest that the vaccine would cause serious adverse reactions.

SEVERE INFECTION

Vaccination against the Haemophilus influenzae type b (Hib) bacteria provides effective protection and is supported by strong scientific evidence. Protection lasts at least 3 to 5 years. Hib infections can be severe, and no data suggests that Hib vaccine would cause serious adverse reactions.

Vaccination against hepatitis B (in select children only) protects effectively against infection, which can harm the liver. In rare cases the vaccine can result in a serious allergic reaction. The scientific evidence is insufficient to either rule out or confirm that hepatitis B vaccine would lead to multiple sclerosis (MS), but the body of data currently available weighs against a causal association. Nothing would suggest that the vaccine has other serious adverse effects.

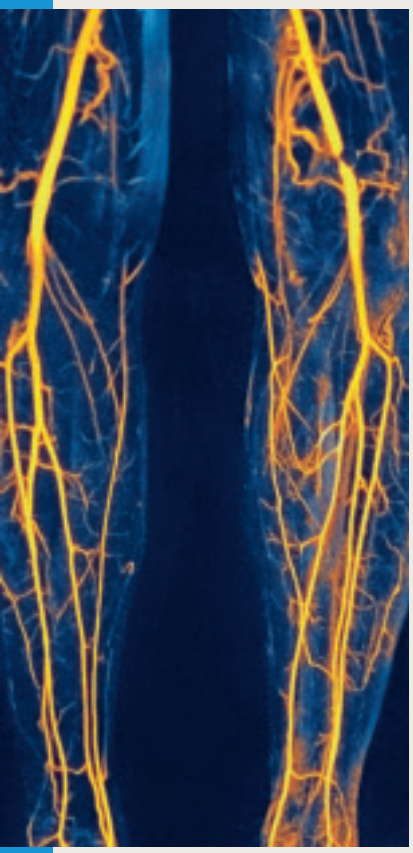
RARE ADVERSE EFFECT

Vaccination against tuberculosis (in select children only) shortly after the perinatal period protects 3 in 4 children against different types of tuberculosis, at least during the first 5 years. Tuberculosis infection is a life threatening, but rare, adverse effect of vaccination. It affects about 1 in 100 000 children vaccinated, mainly children with a rare genetic immune deficiency that can also increase the risk for other diseases. To allow time to detect this immune deficiency, the recommendation in Sweden is not to vaccinate for tuberculosis before 6 months of age and not to vaccinate newborns.

SBU's review does not include childhood vaccines against diphtheria, tetanus, polio, and pneumococcal infection, which are also part of the Swedish childhood immunization program, nor does it include influenza vaccine, which is given only to select children. [RL]

Matton

Atherosclerosis in Legs Often Overlooked



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Magnetic resonance angiography (MRA) scan of the legs of a male with stenosis in both femoral arteries.

Health services need to improve at detecting and helping people with atherosclerosis in the legs, shows SBU's systematic literature review and survey of primary care routines.

At least every tenth person over 65 years of age suffers from atherosclerosis of the lower extremities and experiences leg pain while walking. Peripheral arterial disease caused by atherosclerosis affects the entire cardiovascular system and can have serious consequences. The most important long-term interventions are smoking cessation and treatment for overweight, hypertension, and high lipids. Smoking cessation reduces the risk for continued symptoms, amputation, and premature death. Walking training or other supervised physical activity reduces leg pain.

SIMPLE EXAMINATIONS

According to the SBU report, peripheral arterial disease has not received sufficient attention. Simple examinations that establish the diagnosis can be conducted at all primary care centers and hospitals. In addition to a patient's record containing information about walking distance and pulse readings, simple examinations involving a stethoscope, sphygmomanometer, and Doppler probe are needed to compare blood pressure in the arms and legs.

The most urgent intervention is to help those with vascular disease to stop smoking. In treating atherosclerosis it is also important to actively address overweight, hypertension, high lipids, and high blood sugar. Longer walking distances can be achieved with regular physical exercise, or supervised walking training.

STUDIES LACKING

Many drugs and physical or alternative therapies have been tested on peripheral arterial disease. But SBU's review shows that the benefits and risks of the methods cannot be assessed since the research results are insufficient or contradictory. Reliable, well-executed studies are lacking. This applies, for example, to anticoagulant therapy, estrogen and testosterone therapy, hyperbaric oxygen therapy, spinal cord stimulation, electromagnetic therapy, ultraviolet light therapy, and intermittent pneumatic compression of the lower extremities.

Vascular diseases in the legs are common among the elderly. At least 10% of people over 65 years of age are affected. In the worst-case scenario, occluded blood vessels lead to long-term suffering, amputation, and premature death. Advanced cases with severe pain or the risk for ulcers and gangrene require immediate surgery, endovascular thrombolysis, or percutaneous transluminal angioplasty – interventions that per se involve some risk.

GO UNDETECTED

Reasons why the disease can go undetected for so long point not only to the health services. Some patients experience no problems and do not seek care. Many patients with vascular disease have multiple comorbidities and might not tell their physician about having leg pain that appears while walking and subsides while standing and resting.

Although smoking cessation is one of the most important interventions for this patient group, SBU notes that everyone has the right to the same level of care whether or not they follow the advice given about lifestyle factors. [RL]

Cooling of Newborns Needs Watching

Severe birth asphyxia is an uncommon but serious problem. A new SBU review shows moderately strong evidence that therapeutic hypothermia reduces the risk of disability and death, but adverse effects, complications, and best practice need further investigation.

Ten or more hospitals in Sweden use therapeutic hypothermia to complement standard practice, which includes, eg, intensive care. The target group consists of newborns with symptoms of brain damage (hypoxic ischemic encephalopathy, HIE) resulting from a combination of oxygen deficiency and reduced blood supply, ie, birth asphyxia.

CAREFUL MONITORING

Up to 60% of children with severe asphyxia die. Annually in Sweden, between 50 and 200 children affected by moderate to severe HIE are potential candidates for therapeutic hypothermia. Within 6 hours of birth, the child's body temperature is lowered under careful monitoring to 33–35 degrees Celsius by using a cooling mattress or cap. Treatment requires specially trained staff and special equipment. Later, the child's body temperature is gradually raised to normal. The method does not replace standard treatment in intensive care.

REDUCES RISK

SBU's review shows that there is moderately strong evidence to suggest that therapeutic hypothermia reduces the risk of death and severe functional disability in the target group. The children were followed up to the age of 18 months. In the studies reviewed by SBU, there is nothing to indicate serious adverse effects or complications in relation to treatment. But since the studies were not designed to investigate this question, SBU cannot draw any solid conclusions regarding potential side effects or complications..

LOW EXTRA COST

Likewise, based on the available research, it is not possible to say whether or not therapeutic hypothermia is cost effective. The relatively low extra cost – 5000 to 10 000 Swedish kronor (SEK) per child plus followup and transportation costs – and the outcomes of current research would speak in favor of it.

SBU also emphasizes that we must continue to monitor the method, eg, through a national quality register. [RL]

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