English Special 2008

SBU – The Swedish Council on Technology Assessment in Health Care

MEDICAL SCIENCE & PRACTICE

SPECIAL JOINT NEWSLETTER FROM SBU AND FINOHTA

Laertis Art Studios / Getty

Science or Propaganda?

Robust, comparative treatment studies are strikingly absent in scientific publications. Yet, irrelevant or misleading articles on individual treatments – usually drugs – are plentiful. Studies should focus more heavily on patient needs, not on special interests.

Healthcare providers need to know which treatment options offer the best outcomes in mortality, morbidity, and quality of life at the lowest possible risk and cost. But much of the research is not designed to provide such information.

Many drug studies pose questions that are irrelevant in routine clinical practice, or they are designed in ways that fail to provide meaningful answers. Such research serves the interests of the researcher, university, or corporation more than the interests of the patient.

Nick Veasey / Getty

– What we need is an independent sponsor of studies based on patient needs, says Professor Nina Rehnqvist, Chair of the SBU Board.

Scientific quality in drug trials is often too poor to answer key clinical questions. For instance, SBU's project on treating chronic pain found that scientific quality was low in 20% of the relevant studies. In the other 80%, measurement methods differed too greatly to accurately compare findings.

– We must question whether all of this research is ethically and economically defensible – particularly in subject areas where there are wide knowledge gaps, says Rehnqvist.

As an example, she mentions that many studies are too short to capture side effects that appear much later, even though patients treated for chronic pain often take medication for many years.

EFFECT WEAKENS

– Studies need at least one year of followup, and preferably more – otherwise our knowledge about long-term effects will never increase.

Shorter studies do not show how analgesic effects often weaken with time – which of course is particularly important in chronic pain, emphasizes Nina Rehnqvist.

In this debate, Professor Curt Furberg levels some of the strongest criticism at clinical drug researchers for pursuing objectives that differ substantially from those needed to improve health services.

– Entirely too few robust studies directly compare competing treatment options head-to-head, says Furberg.

– Too often, the comparisons that are actually carried out are misleading, he adds.

The self-interests of those who finance research can play a major role in a study's design and hence its results.

For example, a Danish analysis of 370 studies shows that 51% of the drug trials funded by for-profit organizations yield positive results favoring the test drug. The corresponding figure for trials funded by non-profit organizations is only 16%.

– At times, the influence is particularly obvious, explains Furberg, pointing to an analysis of studies on new antipsychotic drugs that the American Journal of Psychiatry published in 2006.

– When different studies compared olanzapine and risperidone head-to-head the outcomes conflicted, often favoring the company that had funded the trial.

This example is exceptionally glaring. But not infrequently, research is clearly skewed in favor of the sponsor, claims Curt Furberg.

– Comparisons of different treatments can be unfair in many ways, he says. Perhaps control groups are given an inferior drug to enhance the contrast against the trial drug. Or perhaps the doses of the trial substance and the control group's drug are not comparable. If the control group receives a dose that is too high, the drug's side effects become unjustly prominent. By contrast, if the dose is too low the drug appears to be ineffective.

Curt Furberg also points to studies that used control substances in a non-approved form, which dampens their effect, or administered medication to the control group directly after a meal, which reduces uptake of the drug in the intestine.

DELETED MEASURES

Another common practice involves revising or deleting certain outcome measures in published scientific reports. For instance, an analysis of Danish randomized trials shows that only 38% had been reported completely as planned.

– Denying funds to initiate studies, or prematurely discontinuing studies that might call into question the superiority of a sponsor's product can also skew the scientific literature, says Furberg.

Many investigations have uncovered examples of unfavorable research outcomes that were never published.

– A very prominent case of publication bias concerns a question addressed by the United States Congress in 2004. It revealed that 12 of 15 studies indicating that SSRI treatment was ineffective in children had not been published. While unfavorable results remain in the dark, we also find the opposite problem – that favorable data are used in multiple publications. A documented example concerns ondansetron, which is used to treat nausea following surgery. A review in the British Medical Journal shows that 17% of published articles contain duplicate data, but do not cite the original study.

– Since different authors submit the articles, duplication is difficult to detect. Consequently, the drug's effect is overestimated by 23%.

HEALTHY SKEPTICISM

Research is a complicated process, and potential sources of error are many. Doing things right is much more difficult than doing things wrong. Misleading findings presented by some studies might be intentional – but need not be.

SBU emphasizes the need for a healthy measure of skepticism and for training in critical review.

The conclusion is not that people should suspect every study of being influenced by special interests. However, substantially greater vigilance is needed by researchers themselves and by those who read scientific reports and apply the results. [Ragnar Levi]

Policy-Makers Urgently Need Evidence

Paradoxically, the success of modern health services and our increased longevity have added to the burden of disease. Meanwhile, new health technologies increase the opportunities to improve the population's health. Needs and opportunities alike are expanding.

As these two trends continue, the task of allocating scarce resources will become increasingly difficult for decision-makers. They urgently need evidence to inform their priority setting – in other words, they have an acute need for health technology assessment.

Examples from Sweden: A cancer patient today lives 6 to 7 years longer than a cancer patient in the 1960s. One-year mortality in patients with heart failure has decreased between 30% and 50% during a 10-year period. More elderly patients survive their first 5 years after acute myocardial infarction. Life expectancy for diabetics has improved substantially. These improvements have led to a rapid increase in the prevalence of heart disease and diabetes among the elderly in Sweden.

Meanwhile, new and promising – but expensive – technologies appear regularly. For instance, SBU has reported that HPV vaccination in girls would require a large investment today to achieve health benefits 30 years down the road. For Sweden, the annual costs exceed 22 million EUR. Decisions are made without knowing the specific long-term effects on cervical cancer.

SBU's assessment of bilateral cochlear implants for hearing loss in children showed that inserting two implants during a simultaneous operation would cost approximately 70 000 EUR, including evaluation, surgery, fitting of the speech processor, and followup visits for the first year. If the two devices were implanted sequentially, with an interval of several months, the cost would be higher (at least 80 000 EUR). SBU noted that no studies had addressed the cost effectiveness of bilateral cochlear implantation in children.

SBU recently assessed another new intervention – ranibizumab for neovascular age-related macular degeneration. This new method could greatly improve vision in many elderly people. Although ranibizumab could benefit 5000 eyes in Sweden annually, the treatment costs are massive – the drug alone would cost around 140 million EUR per year.

Growing needs and expanding opportunities raise important political questions. What can society afford? Who should pay? Can we achieve equity in access to care?

From my point of view, decision-makers have only one viable option to gain control over this situation. They must put greater emphasis on evaluations of health interventions – comprehensive assessments of benefits, risks, costs, and ethical and social issues.

The results must be made public and thoroughly discussed. Otherwise, it will be difficult to gain acceptance for the tough decisions that inevitably lie ahead.

Måns Rosén
Professor, Executive Director of SBU


Annah Wirgén

MEDICAL SCIENCE & PRACTICE

SPECIAL JOINT NEWSLETTER FROM SBU & FINOHTA • CIRCULATION: *12 500* • EXECUTIVE EDITOR (SBU): *Ragnar Levi, levi@sbu.se*
PUBLISHER (SBU): *Måns Rosén* • ISSN *1104-1250* • MAILING ADDRESS: SBU, *P.O. Box 5650, SE-114 86 Stockholm, Sweden*
PHONE: *+46-8-412 32 00* FAX: *+46-8-411 32 60* • *www.sbu.se* • ENGLISH ADAPTATION: *Ron Gustafson* • DESIGN: *Nilla Westin Design*

1 EUR = 1.54 USD
1 EUR = 1.55 CAD
(May 12, 2008)

VISION

Useful but Costly Treatment Puts Focus on Budget

Getty

FACTS MACULAR DEGENERATION

Age-related macular degeneration (AMD) is the most common cause of severe vision loss in people over 60 years of age in industrialized nations.

Several different types of AMD are found. The most common is an early type where visual acuity is often retained, or only mildly impaired. A less prevalent type is atrophic or dry AMD, involving gradual vision loss in the affected eye. Neovascular or wet AMD is the only type that can be treated. An estimated 30 000 people in Sweden have wet AMD, and the disease is detected in about 3500 individuals annually. Often both eyes are affected.

In wet AMD, central vision and reading ability can be lost. Locomotor vision, however, is often retained. New blood vessels form beneath and in the retina or the retinal pigment epithelium. The vessels are brittle and can leak fluid, proteins, and blood. When the vessels heal, scars form and lead to deterioration in visual acuity.

Early signs of disease: straight lines appear crooked and a blind spot appears in the central field of vision.

Ranibizumab prevents formation of new vessels by affecting VEGF (vascular endothelial growth factor). Treatment should be initiated as soon as possible after the patient has been diagnosed.

SBU Report: Ranibizumab in treating neovascular age-related macular degeneration (2008). Read SBU's summary and conclusions on www.sbu.se

Strong SBU evidence indicates that a new drug, ranibizumab (Lucentis®), slows the loss of visual acuity in patients with age-related macular degeneration. According to a recent SBU report, the drug can even improve vision in some patients. But the estimated cost is high.

Patients with age-related changes in the macula, ie, wet macular degeneration, lose part or all of their central visual acuity and reading vision. This loss can take less than 6 months and often affects both eyes, although vision in the second eye can deteriorate later.

EYE INJECTION

Ranibizumab injected into the vitreous body of the eye slows degeneration. Patients retain greater visual acuity than with standard treatment (ie, photodynamic therapy), or placebo (simulated injections). Strong evidence supports this.

But treatment is expensive. An ophthalmologist must give each injection in a sterile environment – costing just over 1400 EUR, whereof the drug cost alone is 1100 EUR. If the health services were to give one injection per month to every patient with wet macular degeneration, assuming that treatment could be terminated after 2 years, the annual cost would reach 140 million EUR per year. Offering the drug to everyone who could benefit from it would also require more ophthalmologists and specially trained ophthalmology nurses.

LACKING KNOWLEDGE

The report shows knowledge is lacking on whether patients can terminate treatment once started, or if the injections must continue for a prolonged – even lifelong – period to be effective. It is also unclear whether injections would be effective if given less frequently than once per month. Hence, the method's long-term costeffectiveness cannot be determined.

Several county councils have already introduced the drug. But its use varies across Sweden. Several clinics have already started providing this treatment, although they are uncertain how it should be financed. Some treat patients affected in one eye. Others treat patients only after vision in the second eye has begun to deteriorate. Some clinics have few or no restrictions on treatment.

[Johanna Thorell]

CANCER

HPV Vaccine Promising, but Effect on Cancer Rate Unknown

Today's vaccines target only 2 of at least 13 viruses that cause cervical cancer. General childhood immunization would offer some protection against cell abnormalities. But benefits in terms of cancer rates and years of immunity are not known, shows a new SBU report.

Research has not shown how childhood immunization programs for human papilloma virus (HPV) 16 and 18, if introduced today, would affect future morbidity and mortality from cervical cancer. However, findings show that current vaccines can prevent certain pronounced cell abnormalities in vaccinated subjects, at least within the timeframe studied. In some cases, the cell changes develop into cancer.

SHORT FOLLOWUP

SBU has reviewed the body of scientific research published on the topic, and SBU's assessment forms the base for Sweden's National Board of Health and Welfare in its decision regarding a general HPV immunization program.

Strong scientific evidence shows that current HPV vaccines prevent cell changes from HPV 16 and 18 among young women who have not yet been infected. Studies followed these women for 3 years on average; a relatively short period considering that protection is intended to last for decades.

The SBU report emphasizes that general immunization does not replace organized gynecological checkups for cell changes in vaccinated women. One reason is that vaccines target only 2 of at least 13 HPV types associated with cervical cancer. The prevalence of HPV 16 and 18 in Sweden is not known.

A general immunization program to vaccinate girls against HPV 16 and 18 would cost an estimated 22 million EUR annually. If a booster dose were necessary, the annual cost would reach 28 million EUR. Vaccinating both boys and girls would double the cost.

BENEFITS UNCERTAIN

Since the medical benefits remain somewhat uncertain, estimates of cost effectiveness also remain uncertain.

No followups have been published on the effects or safety of the vaccines beyond 5 years. Hence, the need for booster doses is not known. Introducing a general HPV immunization program would require systematic followup of the effects, safety, and cost effectiveness of all preventive interventions against cervical cancer. [Ragnar Levi]

Getty

SBU Report: General Childhood Vaccination Against HPV 16 and 18 Aimed at Preventing Cervical Cancer (2008). SBU's summary and conclusions on www.sbu.se

DEMENTIA

Find the Person Behind the Disease

SBU's report on dementia clarifies the need to train caregivers to provide the most appropriate care to people with dementia.

SBU also shows that diagnostics can be improved and that Alzheimer's drugs can provide some benefit for people with mild or moderate Alzheimer's disease, but the effects of medication must be monitored and reappraised in each patient.

TRAINED STAFF NEEDED

SBU's review of the entire body of research available in this field also highlights the need for well-trained staff to assure the delivery of appropriate health and social services for people with dementia. In Sweden, the municipalities deliver the greatest share of dementia-related care.

– Care must be based on a strong, ethical approach, says Professor Måns Rosén, SBU's Executive Director. This requires giving municipal caregivers and family members the support and education needed to deal with the disease.

– Caregivers need more training on how to interact with people suffering from severe dementia and who have lost the ability to express themselves. As a caregiver, one must learn to understand and address this.

MAY MISINTERPRET

– Without special training, caregivers might easily misinterpret a grasping reflex as "pinching", or yelling as provocation.

Through education and more open discourse on dementia-related disorders, people's attitudes become less negative.

– Not until people with dementia are treated as capable individuals will their remaining abilities become clear to us, says Måns Rosén.

Lars-Olof Wahlund is Professor of Geriatrics at Karolinska Institutet and one of the experts behind the SBU report.

– Today, we have no methods that are particularly good at detecting dementia early, he says.

– The SBU report shows that current tests often trigger false alarms. This fact, along with the narrow range of treatment options, means that mass screening has no scientific support, says Lars-Olof Wahlund.

Instead, the objective is to help the patients and families that seek care. Anders Wimo, Adjunct Professor at the Alzheimer's Disease Research Center, Karolinska Institutet, also worked on the report.

– Treatment focuses primarily on trying to slow the progression of the disease, says Anders Wimo. There are no curative interventions.

SOME EFFECT

Moderately strong scientific evidence suggests that cholinesterase inhibitors affect Alzheimer's symptoms. Studies lasting up to one year show that this type of drug has some effect on intellectual and general functional capacity in some people with mild to moderately severe Alzheimer's disease. However, many of these patients experience side effects such as nausea and dizziness.

In more severe Alzheimer's disease, there is corresponding evidence that memantine can have some effect.

MONITOR TREATMENTS

– But it is important to monitor all treatment in every patient, says Anders Wimo. It is not possible to predict which individuals will benefit from medication, so treatment should never continue routinely. It must be reappraised.

A somewhat surprising finding is that ginkgo biloba extract, a natural medicine, appears to ameliorate certain symptoms. But its effect beyond 6 months is not established.

The cost effectiveness of medication, ie, how the treatment effects of the various drugs compare to their cost, cannot be assessed, according to SBU. The same applies to the cost effectiveness of various treatment programs.

The report also emphasizes that certain drugs are shown to impair cognitive function and are inappropriate for treating people with dementia. These include benzodiazepines and earlier drugs used to treat psychosis and depression.

INCREASE MORTALITY

Some evidence suggests that certain atypical antipsychotic drugs, ie, newer medications to treat psychosis, which have been tested on behavioral symptoms in dementia, could increase mortality.

The total annual cost of dementia in Sweden is nearly 5400 million EUR. Since the municipalities bear over 80% of the cost, this fact is important to consider in distributing resources for dementia-related services. [Ragnar Levi]

Nick Daly / Tony Stone

FACTS ABOUT DEMENTIA

Around 140 000 people in Sweden have some form of dementia. Two out of three have Alzheimer's disease, 10% have vascular dementia, and 5% have frontal lobe dementia. Common characteristics in all forms of dementia include impaired memory and cognitive function due to nerve cell death. The level of consciousness is unaffected.

Memory impairment is the fundamental defect. But dementia also includes one or more of the following symptoms: impairment in thinking, communicating, and orientation and impaired practical skills, ie, greater difficulty in retaining learned skills or managing daily activities.

Those affected also develop personality changes involving impaired cognition, poor judgment, aggressiveness, lack of inhibition, emotional bluntness, and lack of empathy. Furthermore, anxiety, depression, suspicion, delusions, and obsessive behavior are reactions of the underlying disease.

SBU has not reviewed treatment for mild cognitive impairment (MCI) since current diagnostic methods are poor at differentiating people with MCI from those who are healthy.

SBU Report: Dementia – A Systematic Review (2008). Read SBU's summary and conclusions on www.sbu.se

PREMATURE

Can Health Care give Preterm Infants a Better Start?

NIDCAP is a new method designed to stimulate preterm infants. Limited scientific evidence supports its positive effects on child development. But securing reliable results on the method's benefits would require larger and longer studies with a narrower focus, concludes SBU.

Previously, reflexes and inherited patterns were thought to control most actions in preterm infants. This perspective has changed. Attention now centers on the infant's ability to interact with its environment. Health services have introduced various methods to promote bonding, neurological development, and breast feeding.

SMALL TRIALS

One of these methods is the Neonatal Individualized Developmental Care and Assessment Program (NIDCAP). It aims at stimulating each infant at a level

FACTS NIDCAP

Annually in Sweden, 2600 children are born prior to gestational week 37. Approximately 750 of these infants are born prior to gestational week 33.

Today, more lives can be saved. But during early infancy problems can arise in the central nervous system, eyes, or lungs. In the long term, performance at school and behavior can be affected in some children.

NIDCAP involves observing an infant's behavior every seventh to tenth day, in accordance with a special schedule. Observations take place before, during, and after a caregiving activity, eg, changing a diaper or shifting position. Information on respiration, color, stomach/bowels, muscle movement, face, alertness, and attention are noted. Also noted are the infant's position, the interventions performed, and sensory input in the environment.

A specific care plan is designed, based on an assessment of how the infant reacts and the situations in which it show signs of seeking or avoiding contact.

Interventions in the care plan may involve the environment in the room, incubator, or bed, assistance with self-regulation (positioning, sucking and griping devices, eye protection), timing and coordination of healthcare activities and daily rhythm, and the transition between different activities. The care plan is updated successively.

Corbis

SBU Report: Newborn Individualized Developmental Care and Assessment Program – NIDCAP (2006). Read SBU's summary and conclusions on www.sbu.se

appropriate to the maturity of its nervous system.

A recent SBU assessment has found limited scientific evidence showing that NIDCAP promotes cognitive and motor development in preterm infants. This conclusion is based on 6 randomized controlled trials involving 250 children. Most of the trials are small, and some include many variables. The longest trial followed children for just over 5 years.

In every study showing differences between the treatment and comparison groups, the outcomes are consistently better in the NIDCAP group. This finding applies mainly to cognitive and psychomotor development. The evidence base, which is limited, also suggests a reduced need for respiratory support.

SPECIAL REQUIREMENTS

NIDCAP requires specially trained staff and continual observation of the infant's behavior. The cost to train a certified NIDCAP observer is estimated at approximately 4600 EUR plus the costs for work-leave and travel. For an infant born after gestational week 27, the cost for 10 behavioral observations is estimated at 575 EUR.

To date, no studies have weighed the effects against the costs. [Ragnar Levi]

Young & Old

Beneficial to Reduce Eye Pressure in Glaucoma

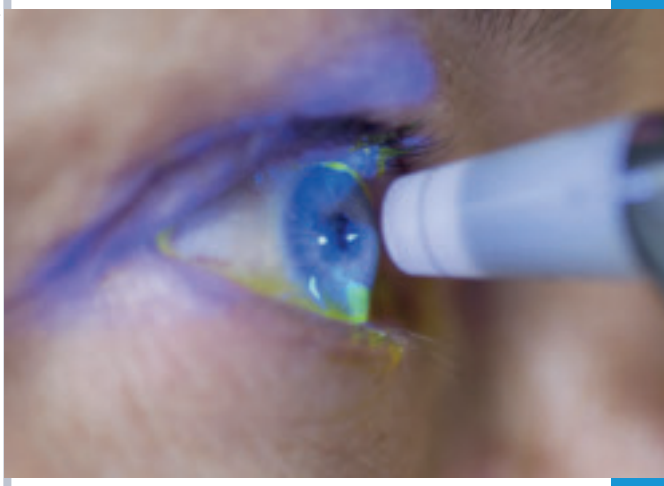
Reducing pressure in the eye slows deterioration in the field of vision in glaucoma patients. Treatment to reduce intraocular pressure also reduces the risk that patients with elevated eye pressure will develop glaucoma, but this requires a reduction of 20%. No effect has been shown at more moderate reductions. In both instances, a new SBU assessment shows that scientific evidence is limited.

However, studies have reached contradictory findings, making it impossible to tell whether one type of treatment to relieve eye pressure – drugs, lasers, or surgery – is more effective than any other type. Questions concerning which method can best treat a particular group of patients are not sufficiently studied, according to the report.

A survey of current health services, conducted by SBU in conjunction with the review, found that pharmaceutical costs, the number of laser treatments, and the number of surgical interventions have increased in recent years. The survey revealed that in 2006, the county council providing the most operations (per 100 000 population >70 years of age) to reduce intraocular pressure provided nearly 40 times more operations than the county council providing the least. Drug and laser use also varies among the county councils. SBU has not analyzed whether this indicates that patients are undertreated or overtreated, but highlights this as an important question for further research. [Johanna Thorell]

See also the article by Finohta in this newsletter, page FI/6

Dr P Marazzi / Science Photo Library



HEARING

Timely SBU Findings on Screening in Newborns

In only 3 years, general hearing screening in newborns has expanded from 5 county councils, plus a few hospitals, to nationwide coverage. Although the time was right to expand coverage, SBU's report from 2004 also played a role. The next step is to monitor these programs to analyze the scope of patient benefits.

Screening of all newborns prior to discharge from the maternity ward helps detect hearing loss early. Habilitation – testing of hearing aids, cochlear implants for deaf children, teaching sign language, and support for families – can also be started early to promote language and communication skills. These were SBU's findings in its assessment.

DRAMATIC CHANGE

At that time, 5 of Sweden's 21 county councils and a few additional hospitals offered general screening. Within 3 years, by 2007, all county councils had decided to introduce screening programs.

SBU's report on hearing screening was used in several formal decision-making processes.

– This represents a dramatic change in the level of coverage, says Leif Hergils, Associate Professor at Linköping University Hospital's ENT department, and scientific contributor to the SBU report.

He observes several reasons behind this change. In part, the timing was right since many county councils were already prepared to introduce screening, but had to arrange financing. In part, the level of coverage was greatly influenced when the metropolitan regions started their screening programs. But Leif Hergils is convinced that SBU's report also played a role.

– The report was used in several formal decision-making processes, eg, in Stockholm County Council and in the regions of Skåne and Västra Götaland. Sweden's association for the hearing impaired also referenced the SBU report to influence the county councils to introduce screening programs.

DETECTED EARLIER

It is still somewhat premature to quantify the patient benefits of screening nationwide in Sweden. Comparable data are available from large British studies. Before screening was introduced early in this decade, half of the permanent hearing impairments were detected when children reached 18 months. By 2007, the corresponding age was 4 months, and those that needed hearing devices generally received them before 5 months of age.

– It would be interesting to follow up on the corresponding figures in Sweden, now when all county councils provide this service. Sweden's registry on child hearing could be used for part of this effort, says Leif Hergils.

– We detect hearing loss earlier nowadays. It remains to be seen whether or not we can lower the age to the level indicated by the English figures. [Johanna Thorell]

Getty

Punchstock

FACTS HEARING SCREENING

The most common method used in Sweden involves measuring otoacoustic emissions (OAE). Newborns are screened by inserting a small earplug that transmits a clicking sound. Healthy hair cells in a child's ear react by transmitting a weak sound that is detected by a microphone and analyzed by computer.

A normal response suggests that the inner and middle ear are healthy. The examination takes 10 to 15 minutes and causes no pain.

The test is performed at the maternity ward and can be conducted by specially trained maternity ward staff or audiometrists.

Congenital permanent hearing loss that requires habilitation is uncommon – just over 1 in 1000 among the 100 000 births annually in Sweden.

Screening costs approximately 30 EUR per child.

FACTS SBU REPORT ON HEARING SCREENING

- The SBU report presents scientific evidence that screening with OAE or aABR (automated auditory brainstem response) leads to early detection of congenital hearing impairment and early intervention.
- Limited scientific evidence also indicates that early detection and habilitation improve a child's language and communication skills. Comparison involves the use of traditional screening and distraction tests, eg, BOEL test.
- When the report was written, data were unavailable to estimate the health gains of a general screening program.

SBU Report: Universal newborn hearing screening (2004). Read SBU's summary and conclusions on www.sbu.se

PREGNANCY

Early Prenatal Diagnosis Raises Ethical Issues

Fetal diagnosis raises difficult and sensitive questions. In 2006, SBU's systematic review concluded that testing a mother's blood plus using ultrasound to scan the neck of the fetus provide the best grounds for deciding to investigate for Down syndrome. Combined, the two tests are superior to relying on maternal age alone, which until now has been the most common indicator used in Sweden.

OFFERED ROUTINELY

Health services in Sweden routinely offer chromosome analysis to mothers over 35 years of age. This, however, presents a problem. Taking samples for chromosome analysis increases the risk for miscarriage – the risk that the fetus will not survive increases around one percentage point. Research shows that couples considering fetal diagnostic tests could benefit from maternal blood testing plus nuchal ultrasound scanning of the fetus.

Ultimately, SBU showed, the combined approach exposes fewer fetuses to the risks of amniocentesis or sampling of placenta cells for chromosome analysis. The combined tests detect the highest number of cases without yielding a high rate of false indications for Down syndrome. Because of its sensitivity and ability to provide specific information about the fetus, the combined approach is superior to other screening methods for Down syndrome, according to SBU's assessment.

CONTROVERSIAL

However, the new combined screening test is controversial. In a few county councils, some local politicians want to stop the test – or at least wait. Their fear is that more women and couples will make erroneous decisions to abort fetuses with Down syndrome.

"Does it make sense to provide this freely and to always let the woman decide for herself?" asks Monica Selin of the Christian Democrats party, Stockholm County Council, in an interview for the Swedish medical weekly, *Dagens Medicin.* "I am prepared to review this legislation, even if it means a step back", she says.

Others want to make the combined diagnostic test available as soon as possible. According to Jonas Andersson of the Liberal Party in Västra Götaland, the combined test should be accessible this year to women older than 35, and later to all pregnant women. "Many unnecessary amniocenteses can be avoided", he says. "And many women want the test. Therefore we think it is right to use the new, modern technology."

ETHICS COUNCIL

Even if policies on fetal diagnosis are generally decided by county councils, ethical issues have also been discussed at the national level. While SBU's task was to assess the technologies per se, the ethical aspects were specifically addressed by the Swedish National Council on Medical Ethics (SMER). In September 2007, SMER concluded "the combined test is preferable to age indication", and "the combined test does not threaten human dignity as long as it is made clear that both the combined test and the genetic prenatal diagnosis is an offer that the woman can accept or decline at her own discretion."

BETTER INFORMATION

The latter reservation is important. SBU's assessment shows that health services must become much better at informing expectant parents wanting to know more about the options for fetal diagno-

Dick Clintsman/Getty

sis. The test results will bring some expectant parents face-to-face with difficult questions and choices – demanding good communication with healthcare providers. Most studies point to deficiencies on this front. Expectant parents are not receiving what they need to make well-informed decisions.

To improve information, SBU has produced a leaflet in Swedish for women and couples who ask for more information on fetal diagnosis. However, the ethical questions raised by the new technologies have no simple answers – so the debate continues.

[Ragnar Levi]

Reading tips

• Methods of Early Prenatal Diagnosis. A systematic review (2006). SBU report no 182. English summary: http://www.sbu.se/upload/Publikationer/Content1/1/Methods_of_Early_Prenatal_Diagnosis.pdf
• Opinion on new method for risk assessment as a basis for decision-making in prenatal diagnosis. Swedish National Council on Medical Ethics, published Sept 2007. http://www.smer.se/Bazment/168.aspx

See also the article by Finohta in this newsletter, page FI/4

EARLY FETAL DIAGNOSIS

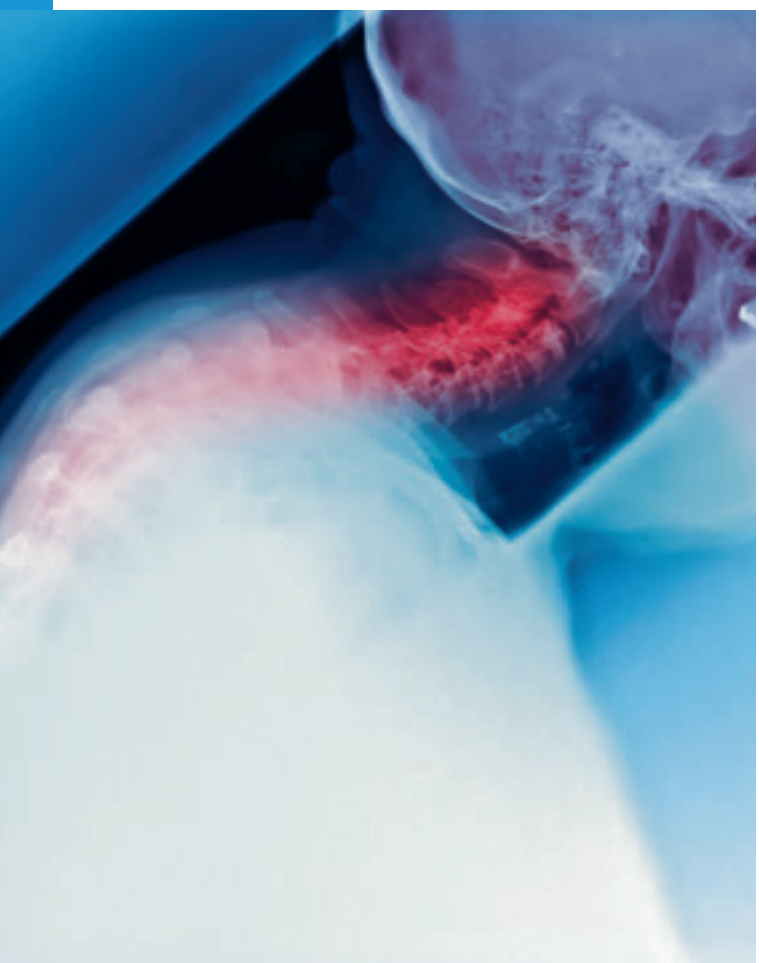
▶ A combined test of ultrasound nuchal translucency measurement and maternal serum biochemistry (biochemical screening) in early pregnancy (10–14 gestational weeks), along with maternal age, is the clinically evaluated method of assessing the probability of fetal Down syndrome that gives the best balance between the percentage of detected cases and false positive results. (1)

▶ All of the methods (nuchal translucency measurement, maternal serum biochemistry in the second trimester, and the combined test) for assessing the probability of fetal Down syndrome examined by the SBU report and evaluated in clinical practice give a better balance between the percentage of detected cases and false-positive results than maternal age alone. Thus, the use of these methods requires fewer amniocenteses and chorionic villus samplings per detected case of Down syndrome than maternal age alone. (1)

The figures in parentheses indicate the evidence grade. See www.sbu.se for definition, full summary, and conclusions.

FRACTURE

Some Evidence for Injecting Bone Cement in Vertebrae



Custom Images / Science Photo Library

Vertebral fractures can be extremely painful. Limited scientific evidence presented by SBU shows that bone cement, when injected into damaged vertebrae of patients with osteoporosis, provides better short-term pain relief and function than analgesic drugs alone.

A new method to treat severe pain caused by vertebral fractures, eg, from osteoporosis, involves injecting bone cement directly into the damaged vertebra. The method is called percutaneous vertebroplasty (PVP).

In reviewing the research on this method, SBU found limited scientific evidence that PVP is superior to conventional treatment as regards short-term pain relief and functional ability in patients with osteoporotic vertebral compression (Evidence Grade 3)*. Compared to analgesic drugs alone, PVP can provide faster pain relief, increase functional capacity, and enhance quality of life. Complications leading to symptoms occur in 3% to 4% of all procedures, but serious complications are uncommon.

RESEARCH GAPS

SBU discovered several gaps in research. The long-term effects and risks of PVP have not been fully investigated. Potentially, PVP could increase the risk for new compression in adjacent vertebrae, but research has not confirmed this. Furthermore, it is unclear whether PVP helps patients with vertebral fractures from causes other than osteoporosis.

Scientific evidence is insufficient to appraise the benefit of PVP in treating patients with vertebral metastases and myeloma, ie, tumors originating in bone marrow. Also, too little is known about the method's long-term effects, risks, and side effects.

HIGH-QUALITY STUDIES

SBU emphasizes the need for randomized and blinded trials to reduce the risk of overestimating the treatment effects. High-quality observational studies with prolonged followup, eg, national quality registries, are necessary to determine long-term effects and risks.

Currently, PVP is considered for severe cases where conventional methods have not provided acceptable pain relief. Without pain relief, these patients find it difficult to remain mobile and manage their daily activities unassisted. [Ragnar Levi]

SBU Report: Percutaneous Vertebroplasty in Severe Back Pain From Vertebral Compression Fractures (2007). Read SBU's summary and conclusions on www.sbu.se

OTITIS

Ear Tubes Can Help Children With Fluid in Middle Ear

A tiny tube through the eardrum can help children whose hearing is impaired by fluid in the middle ear for a prolonged time. But scientific evidence has yet to prove the benefit of ear tubes in children with recurrent, acute ear infections. This type of problem currently accounts for 1 in 5 such operations.

The benefit of inserting ear tubes in children with recurrent, acute ear infection (acute otitis media) is not scientifically confirmed. Studies show conflicting findings, and further research is needed to determine whether or not to continue using the method.

RECEIVE SURGERY

SBU reports this finding in a review of the research on ear tubes in treating middle ear infections. Annually, around 10 000 children receive surgery in Sweden, whereof about 2000 have procedures to treat recurrent, acute ear inflammation.

SBU's report shows that ear tubes improve hearing and quality of life for at least 9 months in children who have had fluid in the middle ear (serous otitis media) for 3 months or longer.

Surgically removing the adenoid tissue behind the nose (adenoidectomy) improves hearing equally as much as inserting ear tubes, measured after 6 months. Studies do not show any additional improvement in hearing by combining the two treatment methods.

Suctioning the fluid from the ear during surgery does not affect ear tube function. Research has not shown any benefits from routine surgical removal of ear tubes that do not fall out spontaneously. Furthermore, it is unclear whether pneumococcal vaccination reduces the risk for new ear infections.

WATER PLAY

Several studies have investigated whether normal swimming and water play increase the number of new infections or discharge through the tube. These studies do not show any effects from protective measures such as earplugs, bathing caps, or eardrops.

[Johanna Thorell]

SBU'S CONCLUSIONS
TUBES FOR EAR INFLAMMATION

- Scientific evidence is insufficient as regards the use of ear tubes in treating recurrent, acute ear inflammation. Given that over 2000 children annually have tubes inserted for this indication, it is important to conduct adequate studies in the immediate future.
- Using ear tubes in treating long-term problems of fluid in the middle ear improves hearing (1) and quality of life (2) for at least 9 months. Inserting an ear tube through the eardrum of a child having fluid in the middle ear is motivated if impaired hearing and a subsequent reduction in quality of life have been objectively verified. Questionnaires designed and tested for children with ear disorders can be used to estimate quality of life.
- Surgically removing the adenoid tissue behind the nose, improves hearing equally as much as inserting ear tubes, measured after 6 months. (3). Hearing, measured from 3 months, is not shown to improve further by combining ear tube treatment and adenoid tissue removal (2).
- The review could not show that protecting the ears in water had a clinically meaningful effect on the number of displaced tubes. Using a bathing cap or earplugs during swimming and water play did not reduce the number of tube displacements (2).
- Scientific evidence is insufficient to determine whether ear tubes are cost effective in treating ear inflammation involving fluid in the middle ear, or recurrent, acute ear infections.

Science Faction / Getty

Explore the Global Health Evidence Community

Finding reliable evidence on what works in health care and health promotion is easier today than ever before. Users of health evidence now benefit from several international initiatives to share the results of health technology assessments and systematic reviews. Here are a few examples of such collaboration.

Focus on HTA DATABASE

The HTA database provides free access to details of completed and ongoing health technology assessments from around the world.

Thousands of abstracts of quality assessed systematic reviews and economic evaluations, as well as summaries of ongoing and completed technology assessments are available in the HTA database. Many of these are conducted by the 47 member agencies of INAHTA.

The HTA database is hosted by the Centre for Reviews and Dissemination (CRD) and is produced in collaboration with the INAHTA Secretariat, based at SBU, Sweden. CRD is a department of the University of York and is part of the National Institute for Health Research.

The HTA database is located at: **www.york.ac.uk/inst/crd**

Focus on EUNETHTA

Connecting organizations involved in HTA, the European network for Health Technology Assessment, EUnetHTA, facilitates cross-border collaboration by focusing on development of practical tools to avoid duplication of effort in HTA. For example, the network is producing a Web-based handbook on a core model for HTA, scheduled for release during the fall of 2008. It has also developed a newsletter – On the Horizon – targeting new and emerging health technologies.

The EUnetHTA project started in 2006, supported by a grant from the European Commission. EUnetHTA involves 63 organizations from 31 countries, with the secretariat hosted by Denmark's National Board of Health.

On **www.eunethta.net**, you can find the Stakeholder Open Forum and learn more about "HTA's Future in Europe", a conference to be held in Paris on November 20, 2008.

Focus on INAHTA

The International Network of Agencies for Health Technology Assessment, INAHTA, is a global network aimed at supporting the delivery of effective health care. The network promotes information sharing, comparison, and collaboration among health technology agencies on national and regional levels worldwide.

INAHTA was established in 1993 and currently has 47 members in 24 countries. The Swedish Council on Technology Assessment in Health Care hosts the secretariat.

You can read INAHTA briefs – summaries of recent reports from member agencies – on INAHTA's website, **www.inahta.org**. The website also presents an English glossary of health technology terms and a toolbox of supportive materials from several organizations.

Focus on EUROSCAN

EuroScan is an international information network on new and changing health technologies. Its members identify, exchange information on, and evaluate important emerging new drugs, devices, procedures, processes, and settings in health care.

The members of EuroScan share methods for early assessment and information about early identification and assessment activities. The network supports both member and non-member agencies who are establishing early warning systems to identify technologies that are visible on the horizon and soon coming into use.

The 15 EuroScan members are non-profit HTA agencies that have an officially recognized role in relation to a regional or national government. Each member agency has its own program to identify and assess new health technologies.

For more information on EuroScan, please visit: **www.euroscan.bham.ac.uk**

Focus on HEN

The Health Evidence Network (HEN) is an information service primarily for healthcare policy-makers in the European region. It is hosted by the World Health Organization's Regional Office for Europe.

HEN has adopted a broad definition of evidence that includes research findings and other knowledge. Information is retrieved from websites, databases, documents, and national and international organizations and institutions.

HEN replies to specific questions that policy-makers may have and operates a mailbox function to facilitate this.

After HEN receives a request, a decision is taken on the most appropriate way to answer: a short answer by e-mail, a one-page summary based on existing reviews, or a HEN synthesis report or joint policy brief.

Currently 37 reports are available in English. Summaries are available in English, French, German, and Russian. See **www.euro.who.int/HEN**

Focus on COCHRANE COLLABORATION

The Cochrane Collaboration is an international not-for-profit organization that produces and disseminates up-to-date systematic reviews about the effects of healt hcare, making them available worldwide. Those who prepare the reviews are mostly healthcare professionals who volunteer to work in Cochrane Review Groups.

The major product of the Collaboration is the Cochrane Database of Systematic Reviews which is published quarterly as part of The Cochrane Library. Currently there are 3500 Cochrane reviews. The abstracts are available free of charge at **www.cochrane.org**. Some countries provide their residents free access to the full texts of Cochrane reviews online.

Cochrane reviews have become known internationally as a source of high-quality, reliable health information. Guideline makers and HTA units increasingly make use of Cochrane reviews.

Nordic Photos

high-quality research is needed to compare different alternatives.

Active use is often considered to indicate user benefits. However, benefits cannot necessarily be measured by how much a device is used, since the use is situational; even if a device is seldom used, it may efficiently meet the user's functional needs. The principal purpose of mobility devices is to promote an individual's activity and participation. Effects on activity and participation are therefore the most important outcome indicators of mobility devices.

Design important

Other important mobility device characteristics include durability, the impact of seat cushions on pressure sores, wheelchairs' maneuvering and their turning angle. Outcomes research is particularly challenging, since the use of a mobility device is an ongoing process influenced by the user, the mobility device, the environment and services received.

A wheelchair, for example, is not of much help if the user cannot move through doorways with it or is unable to use it alone. Another issue is whether the device breaks easily or there are long servicing times. A good outcomes study considers such factors during planning, implementation and analysis.

Future research on the effectiveness of mobility devices should focus on new devices and those where eligibility criteria and costs need to be considered with particular care.

Anna-Liisa Salminen
Outi Töytäri
Åse Brandt
Kersti Samuelsson
Antti Malmivaara

Review Methods:

Seventeen Different Outcome Instruments

Original studies and systematic reviews of mobility device interventions were searched for in seven electronic databases. Controlled studies and all types of follow-up studies that used both baseline and follow-up data were accepted.

The studies were included if the participants were over 18 years of age and needed sticks, crutches, walking frames, rollators, manual wheelchairs or powered wheelchairs (including scooters). Activity and participation were regarded as primary outcomes, and frequency of use, mobility, the need for assistance, user satisfaction, quality of life and adverse effects as secondary outcomes.

The seven studies used 17 different instruments and scales to measure mobility device outcomes. EuroQol 5D (EQ-5D) and Individually Prioritised Problems Assessment (IPPA) were the only ones used in several studies.

Only one of the studies was of a high methodological quality. The descriptive information on interventions and mobility devices was inadequate in every study. Numerous shortcomings limited the usability of the results while interventions and outcome indicators also varied among the studies. No general conclusions can be drawn as to the impact of mobility device interventions on user activity and participation. Conclusions can only be based on individual studies.

Wheelchairs Increase Participation

A Finnish–Danish–Swedish co-operative HTA project, "Systematic Review of Mobility Devices Outcomes", is the first systematic review on the effects of mobility devices on individuals' activities and participation. The final reports of the project will be published in several languages.

The literature search found more than one thousand articles, of which eight were accepted for inclusion in the review, representing seven studies. Three of these were controlled studies and four were follow-up studies with both baseline and follow-up data. No randomised studies were found.

Two studies examined electric powered wheelchair interventions, one rollators, one walking frames, one focused on individually adjusted wheelchairs and one on a special powered wheelchair. In one study, three different types of mobility devices were examined. All studies were relatively new, starting from 2003. Three of them had been carried out in Sweden.

Self-evident outcomes?

The outcomes of mobility devices were clinically significant in all studies. In two studies, the mobility device helped in reaching individually set activity and participation goals, and one study showed an improved ability to participate in social activities. Two studies found that the mobility device improved the quality of life. The study with the highest quality showed that an outdoor wheelchair has a significant effect on the activities, participation and quality of life of stroke patients.

Increasing need

Mobility devices are generally regarded as important. Both the UN and WHO underline their importance in increasing equal opportunities for people with disabilities. In the Nordic countries, access to mobility devices is guaranteed free of charge if the devices are expected to improve individuals' daily lives. Sizable public funding is currently spent on such devices, and with an ageing population the need will increase. Although the outcomes of mobility devices are often self-evident, more

More Reviews of Assistive Devices Underway

The Nordic research group continues to assess research on assistive device outcomes. Content experts Anna-Liisa Salminen and Outi Töytäri from STAKES, Åse Brandt from the Danish Centre for Assistive Technology and Kersti Samuelsson from Linköping University Hospital receive methodological support from Antti Malmivaara of Finohta. The projects are funded by the Nordic Development Centre for Rehabilitation Technology (NUH) and Finohta. The new literature reviews will evaluate the effectiveness of lower-limb prostheses, environment control systems and smart-home technology. The results are expected in 2009.

Universal or Selective Screening for PKU in Finland?

Phenylketonuria (PKU) is a rare metabolic disorder which can lead to irreversible brain damage. Early diagnosis and a lifelong diet can prevent this disability. The estimated incidence of PKU in Finland is only 1:100 000–1:200 000. PKU is five to ten times more common in other populations.

Due to the rarity of PKU, Finland has no national program for PKU screening. The Screening Committee at the Ministry of Health requested a comparison of screening options. Specifically, the cost-effectiveness of targeted PKU screening of infants born to genetically non-Finnish parents was to be considered. The assessment is based on a previous HTA report, which has been updated with the addition of a systematic literature review, register research, and a hospital survey.

The number of infants born to immigrant parents is increasing. According to the National Birth Register and Population Information System, the percentage of infants born to immigrant parents increased from 2.3 to 3.4% in 2000–2006. Of the 58 000 babies born every year in Finland, some 2000 have both parents who are of non-Finnish origin.

It is often problematic to identify a person's genetic background. This dilemma was tackled by identifying the first language of parents. Infants whose both parents spoke a first language other than Finnish, Swedish, or Sami were classified to have a non-Finnish genetic background.

Screening methods compared

PKU can be screened for with several methods. The Guthrie method and fluorometry are considered cost-effective in many countries, while the newer tandem mass spectrometry (MS/MS) has been found to be cost-effective only when combined with screening of at least one other metabolic disease.

The annual cost of screening PKU in infants born to genetically non-Finnish parents would add up to 96 000 EUR every year. Screening all newborns for PKU would cost 2.7 million EUR and would be more cost-effective if screening for other metabolic disorders would be included.

A survey of maternity hospitals revealed that several already screen for PKU in newborns with immigrant parents. These hospitals care for 80% of all deliveries, so most families with a higher risk of PKU are already offered screening. This spontaneous screening did find the only new case of PKU to emerge in the last 7 years, so PKU still remains very rare in Finland.

Ethical questions

The cost-effectiveness of both universal and selective PKU screening in Finland is dubious. Ethical questions also arise: How is it possible to define and identify ethnic origin? Could targeted screening of a minority group be a justifiable public health strategy? The Screening Board will consider these issues before deciding on a national screening program.

Ella Kuula

Reference: Leipälä JA, Saalasti-Koskinen U, Blom M. et al. Screening for PKU in Finland (in Finnish). Helsinki: Stakes, Finohta, 2008. Finohta publications, Rapid report 1/2008.

In alternative 2, a bacterial culture is taken from the birth canal a month before the due date. The results are sent to the maternity hospital, where all GBS positive mothers are offered chemoprophylaxis at the onset of labor.

Under alternative 3, a midwife takes a sample when the mother arrives in labor, and a rapid test gives the result in 1–2 hours.

Costs estimated

To evaluate the cost-effectiveness of the screening programs, a decision tree has been constructed. The costs per prevented disease and per birth, and the annual health care costs for each screening program, were estimated based on the best information available and estimates provided by an expert group. The costs of suspected and identified cases of perinatal GBS disease were included in the screening models, but costs generated later by disabilities were not included.

Without screening and preventive measures, 87 perinatal GBS diseases would be diagnosed annually. Of these, 74 would recover, but 10 would be disabled and 3 would die. The 20 EUR cost per newborn arises from the diagnosis and treatment of infected newborns.

Screening reduces infections

All screening strategies would reduce the number of infections, disabilities and deaths (see table underneath). Rapid tests would be the most expensive. Screening late in the gestation period would have the lowest cost per disease prevented.

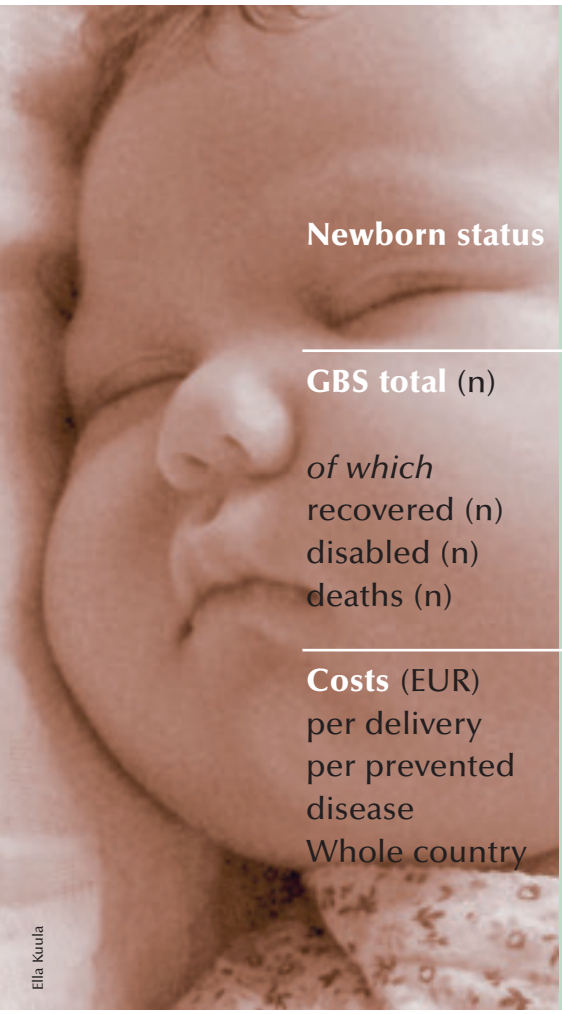
Ethical issues

As with all screening programs, participation in GBS screening is voluntary. Thus, mothers need sufficient information in order to decide whether to participate. It is also important to ensure that screening is equally available to everyone. The possible effects of chemoprophylaxis on the mothers and the newborns must be considered, too.

The Screening Committee of the Ministry of Health will discuss the HTA report in late 2008.

Sirpa-Liisa Hovi

Reference: Hovi S-L, Lyytikäinen O, Autti-Rämö I. et al. Prevention of perinatal group B streptococcal disease: Comparison of operational models (in Finnish). Finohta Report 31/2007. STAKES. Helsinki 2007. finohta.stakes.fi/FI/julkaisut/raportit/index.htm



Ella Kuula

Effects of screening for GBS in Finland

(based on 58 000 births/year)

Newborn status	Alternative strategy **0.** No screening	**1.** Risk factor based	**2.** Late pregnancy sample	**3.** Intrapartum rapid test
GBS total (n)	**87**	**67**	**27**	**28**
of which				
recovered (n)	74	57	23	24
disabled (n)	10	8	3	3
deaths (n)	3	2	1	1
Costs (EUR)				
per delivery	19,80	20,40	27,80	53,10
per prevented disease	–	59 160	26 873	52 200
Whole country	1 148 400	1 183 200	1 612 400	3 079 800

How to Prevent GBS in Newborns

Group B streptococcal (GBS) infection is a relatively rare perinatal disease. The GBS bacterium rarely causes symptoms in pregnant women, but their babies can become infected during birth and develop a severe disease.

Perinatal GBS infection affects infants under seven days old. In Finland, the annual number of early-onset GBS disease cases was between 32 and 38 in 1995–2000, increasing to 58 in 2005. Most infected newborns recover fully, but some are disabled and 1–2 babies die every year.

Varying practices in Finland

Approximately 58 000 babies are born every year in Finland, and it is estimated that every fifth mother is a GBS carrier. Administering chemoprophylaxis to the mother intravenously during labor prevents the transmission of GBS to the newborn.

Since no consistent screening instructions have been issued and practices vary by hospital, the Ministry of Health (MOH) commissioned a study on the cost-effectiveness of potential screening models in Finland. The adoption of a consistent prevention strategy has reduced the number of perinatal GBS infection cases in several industrialized countries.

Mothers can be screened for GBS in several ways. The cost-effectiveness of three alternative screening programs has been assessed. The current strategy, in which no preventive action is taken (alternative 0), was compared with identifying high-risk births (alternative 1), taking bacterial cultures late in the gestation period (alternative 2), and taking a rapid test at the onset of labor (alternative 3).

Three alternatives

Based on alternative 1, chemoprophylaxis is offered during labor to mothers if they have a fever, experience an early labor (before week 38), or a lengthened labor. Treatment is also recommended for mothers whose previous baby was infected by GBS or who have had a GBS urinary tract infection during pregnancy.

Pekka Punkari

Rehabilitation aims to promote functioning, independent living, well-being and employability. Compared with treatment, rehabilitation can be seen as a process that involves and affects patients and their immediate circle to a greater degree. However, the boundary between treatment and rehabilitation is often blurred. Therefore, concepts and classifications need to be clarified. High-quality rehabilitation is individualised, community-oriented, and respects people's privacy.

All HTA reports published by the International Network of Agencies for Health Technology Assessment (INAHTA) from January 2005 to January 2006 were gathered up for a Finohta review from the HTA Database of the University of York. Studies were included in the review if they met the following criteria:

- The intervention aimed to enhance the individual's life management, resources and functioning.
- The outcome variables were linked with the individual's activities and participation as specified in the WHO International Classification of Functioning (www.who.int/classifications/icf/en)

18 reports

Reports were excluded where the intervention consisted of drug treatment, surgery or individual therapy with somatic outcome variables only.

A search in the HTA database found 467 studies. According to the titles 52 possible rehabilitation studies were identified. The final review material included 18 reports assessing rehabilitation. The National Coordinating Centre for Health Technology Assessment (NCCHTA) was the INAHTA member unit with the greatest number of rehabilitation assessment reports. Four of the 18 reports were from NCCHTA.

Little on assistive technology

Several reports assessed the outcomes of psychological interventions by multi-professional teams or interventions affecting health behaviour. The effectiveness of stroke units had also been assessed. Only a few reports dealt with the impact of physical rehabilitation and assistive technology.

International HTA units publish surprisingly few assessment reports on the impact and cost-efficiency of rehabilitation. Many reports described the multi-professional aspects of rehabilitation quite sparsely.

The HTA on cognitive training illustrates the difficulty of summarising study results.

Hannu Alaranta
Antti Malmivaara

The Challenge of Assessing Rehabilitation: Cognitive Training in Dementia

The German Agency for Health Technology Assessment, DAHTA, examined the effectiveness of cognitive training for dementia and other cognitive disorders in 2005. The literature search from 27 databases resulted in selecting 33 publications.

A study on cognitive group training for dementia used eight tests to assess memory, depression, functioning and behavioural symptoms. Group training participants achieved better results in the memory tests, but the differences were not statistically significant. Computer training failed to improve Alzheimer patients' performance in another RCT.

Although Alzheimer patients may improve their performance in memory tests, the severity of the dementia does not change. A Cochrane review of six RCTs dealt with the light form of Alzheimer and vascular dementia. Cognitive training improved performance, but the results were not statistically significant.

A randomised controlled trial on mild cognitive impairment showed that the intervention group had better results in the recall of word lists, but no other differences were observed. In another study, of healthy older people, cognitive training seemed to maintain mental flexibility and performance. By contrast, little evidence exists on training in the early and severe forms of dementia.

In summary, every third study reported improvement in cognitive performance, but it remains unclear why some studies showed a clear positive response while others did not. Training methods were extremely varied, making it difficult to assess what factors contributed to the positive responses.

Reference: http://gripsdb.dimdi.de/de/hta/hta_berichte/hta123_summary_en.pdf

Marjukka Mäkelä

Few HTAs on Rehabilitation

Rehabilitation is a priority area for Finohta in health technology assessment (HTA). An obvious lack of such knowledge was found in an analysis of the prevalence and content of HTA studies concerning the impact and cost-efficiency of rehabilitation.

firm their diagnoses. The visual ability and quality of life of the screen-positives were compared with patients whose glaucoma had been detected opportunistically.

Diagnosing is difficult

Glaucoma is often detected only when patients' visual ability has decayed so much that they seek medical care. On the other hand, less than half of the people currently treated for glaucoma really do have the disease. The number of suspected glaucoma cases is six times higher than that for manifest glaucoma, and treatment is administered for many suspected cases of glaucoma.

Poor targeting of treatment indicates that diagnosing glaucoma is difficult. The sensitivity, specificity and reproducibility of diagnostic tests are low. A reliable diagnosis requires several tests and retesting; this practice is currently not implemented in Finland.

New glaucoma drugs increase the costs of treatment significantly. In spite of this, few economic studies and no cost-utility analyses have been conducted. Previous cost-effectiveness studies have produced inconsistent results.

Simulation for optimal care

The researchers used a Markov model, covering the entire glaucoma care pathway and including various clinical outcomes. The screening involved the measurement of intraocular pressure, autorefraction, fundus imaging and automatic visual field examination. In screen-positive cases, the same tests were repeated on a later occasion. In the follow-up of diagnosed glaucoma patients, tonometry was performed twice a year and the other tests once every two years.

The treatment was targeted at patients with diagnosed glaucoma only. The main outcome measures were: number of cases, years of severe disability avoided, quality-adjusted life years (QALYs) gained and direct healthcare as well as non-healthcare costs.

The screening arm was compared to the current opportunistic case-finding in Finland. Clearly, this system has not ensured equality for glaucoma patients. Two thirds of ophthalmologist consultations are in the private sector, so little is known about their content. Data on reimbursements for glaucoma medication and eye examinations were gathered from the registers of the Social Insurance Institution.

Screening the old is effective

The incremental cost of one year of avoided visual disability was 32 600 EUR compared with current glaucoma treatment practices. One QALY gained cost 9 023 EUR, using a 5% discount rate. Screening one million people every five years during a 20-year period would generate incremental expenses of 30 million EUR, lead to 3 360 incremental QALYs and result in 930 years of avoided visual disability for 701 persons.

The modeling suggests that glaucoma screening could be a cost-effective strategy in Finland, especially in the older age groups. The cases currently undiagnosed could be provided with treatment and expensive medication could be discontinued for the numerous people with ocular hypertension but no risk of developing glaucoma. For people aged 75 to 79 screening would be both more effective and less costly than the current opportunistic identification of glaucoma in 80% of simulated cases.

Iris Pasternack

Klaus Witt

Cost-Utility Analysis

Cost-utility analyses examine effectiveness in terms of quality-adjusted life years (QALYs). The length of life in years is multiplied by a coefficient reflecting the quality of life. The coefficient is 1 for a perfectly healthy life, while the weakening of visual or physical ability or any other factor affecting the quality of life generates a reduced coefficient closer to zero.

Reference: Vaahtoranta-Lehtonen H, Tuulonen A, Aronen P. et al. Cost effectiveness and cost utility of an organized screening programme for glaucoma. Acta Ophthalmol Scand. 2007 Aug;85(5):508-18.

See also the article by SBU in this newsletter, page SE/9.

MODELING STUDY:

The Cost Effectiveness of Glaucoma Screening

The prevalence of glaucoma increases with age, affecting 1.5% of those aged 50+. More than half of people with glaucoma are unaware of their disease, which can rapidly lead to a serious visual disability and full blindness at its worst.

Glaucoma is a chronic progressive optic neuropathy with a highly variable course. In most patients, the disease progresses slowly and can be further delayed using medication and surgery. Visual disturbances appear on average 30 to 40 years after the onset of glaucoma in patients under treatment.

Glaucoma treatments decrease intraocular pressure. However, only half of patients display ocular hypertension. The effectiveness of treatment for glaucoma patients with normal tension remains unclear.

Finohta conducted a modeling of glaucoma screening at five-year intervals for Finnish people aged 50–79. Persons receiving glaucoma medication were included in order to con-

material was prepared in support of professionals in maternity care. Materials are available through the web in Finnish, Swedish, and English; the hospital districts will train their own regions.

Most importantly, expectant parents must be well informed of the screening program, and they must know that participation is completely voluntary. Parents need to understand which types of abnormalities may be identified. Facing such a finding, they need support in taking the difficult decision to continue or terminate the pregnancy.

Law as a by-product

Neither the national Screening Committee nor the Ministry had originally planned for a statute on screening. However, the broad acceptance of the prenatal screening program and a strong need to monitor its results eventually led to the conclusion that a statute is the only possibility for ensuring a unified and justified screening program.

Ella Kuula

Contents of the Prenatal Screening Program in Brief

(i) general ultrasound during weeks 10 to 14 of gestation: length of gestation, plurality, size of fetus.

(ii) screening for chromosomal abnormalities: (a) OR (b):

(a) maternal serum markers (PAPP-A and β-HCG) during weeks 8–11 AND nuchal translucency measurement during weeks 10–12 in connection with the general ultrasound.

(b) maternal serum markers (AFP, estriol and β-HCG) during weeks 14–15.
In addition: women over 40 can be offered placental biopsy or amniocentesis.

(iii) screening for structural abnormalities during weeks 18–21 via ultrasound if parents consider termination of pregnancy due to identified severe fetal malformation as an option. If termination is not an option, the structural ultrasound will not be performed before week 24.

Reference: Autti-Rämö I, Mäkelä M. Screening for fetal abnormalities: From a health technology assessment report to a national statute. Int J Technol Assess Health Care. 2007;23:436-442.

Materials on the web in English: <finohta.stakes.fi/FI/sikioseulonnat/perheille/index2.htm> Click "in English" in the table.

See also the SBU article in this newsletter, page SE/12.

HTA Can Change the Law

Previously, health centers in Finland offered variable fetal screening methods to expectant parents. An HTA assessment on fetal screening reached beyond its original mandate, resulting in new legislation and a comprehensive national training program.

Marjukka Mäkelä

According to a survey in 2002, more than a dozen different fetal screening procedures were used in Finland. Each municipality could independently decide on its own screening program. Most offered a nuchal translucency measurement for chromosomal screening, but only a few municipalities combined this with serum markers. In addition, most hospitals offered invasive diagnostic procedures to "older" mothers, where "old" varied from 35 to 40 years of age.

Due to this wide variation, the Finnish organization for gynaecologists and local health decision makers requested a health technology assessment. The Ministry of Health also needed a thorough assessment to be used as a basis for policy decisions.

Ethical issues essential

During the assessment, possible screening models for Finland were constructed with clinical experts, using evidence culled from the literature. The aim was to identify optimal methods and time frames for detecting chromosomal and structural abnormalities. Ethical issues and the costs of the various screening methods were also considered.

Although the expert group identified and evaluated several effective screening methods, some critical questions still required consideration before a national decision on fetal screening could be made. Equitable access and the quality of screening had to be ensured. Most importantly, a comprehensive public discussion on the justification of screening and its consequences was needed.

The Screening Committee at the Ministry of Health emphasized that the goal of prenatal screening was to allow parents to take informed decisions about the pregnancy. These decisions range from achieving optimal care during pregnancy and following birth, to the termination of a pregnancy due to fetal abnormalities.

It was considered important to involve all stakeholders in an open seminar in 2005. A lively public discussion also spread to the printed media, and after a year the Screening Committee was able to suggest a unified screening program with three options for all parents.

The Ministry of Health sent the draft program for comments to health decision makers, professionals, ethicists and patient organizations. The screening program could have been implemented through a recommendation or code of practice, but after weighing up the alternatives, the Ministry decided to regulate the screening program for fetal abnormalities through a statute in 2006. All municipalities must adopt the program by 2010.

Training under way

In the face of this wide variation in practice, the Ministry wanted to ensure the adoption of joint fetal screening through comprehensive training. Finohta was mandated to inform hospital regions about the new statute and prepare educational materials. To help parents, two brochures were produced: one for all in early pregnancy, and another one to be given out if an abnormality is suspected.

Two seminars were held for regional trainers and training

Atypical Human Beings?

The typical homo sapiens would appear to be a healthy man – at least, when it comes to studying the effects of health technologies. For decades, clinical trials recruited mostly adult Caucasian males, randomizing them to courses of real or fake pills or different types of operations. Benevolently, the men agreed to return for dozens of blood tests, exercise tests, or whatever was needed to advance our understanding of the effects of these technologies on health.

Women have been excluded from such studies for many good reasons. The cyclical hormone production of adult females interferes with many other physiological functions, causing awkward variations in measurements. Similarly, elderly persons and people with chronic diseases have been excluded from studies due to variations in metabolism.

Studies that looked at the effects of drugs on people with asthma, hypertension and other diseases used to reject persons with other chronic health problems. Children have rarely been recruited in trials for obvious reasons. So thank you, healthy white males, for providing all the data!

The difficulty begins when we look at actual patients. Few of them are healthy males; children, women, and the elderly also become ill and need medicines, operations, and other interventions. Can we safely apply technologies to these atypical human beings, too? How should we translate results from middle-aged men to infants, or to frail senior citizens, who may already be using three prescription drugs a day?

In the Health Technology Assessment database at the University of York (www.crd.york.ac.uk), a search for the words "elderly or old" resulted in only 158 hits among 7500 HTA reports. Often these featured dementia, osteoporosis, or geriatric care. "Child or children" returned links to 461 technology assessments on, for example, infections, vaccinations, and sleep disorders.

For these important population groups, we see surprisingly few reports: less than 10% of all HTAs are interested in age groups other than adults. It is difficult, of course, to assess technologies without primary research data. But even without the data, decisions still have to be made.

The national HTA units in Sweden and Finland have conducted a number of health technology assessments on children and the elderly; examples of these provide some reasons why there are so few studies. The international HTA community would be wise to focus more on issues relevant to the young and the old.

Above all, we of working age should call for good research on the effect of technologies on those that are close to us and vulnerable: the generations before and after us.

Marjukka Mäkelä
Professor, Director of Finohta

Tanja Mikkola

CONTENTS

IMPAKTI

Information on health technology assessment

Impakti newsletter is published six times annually – of which one issue is in English. This special joint newsletter with SBU has a circulation of 12 500, whereas the usual circulation of Impakti is 7 500. It is available free of charge. It is also available online at finohta.stakes.fi. If not stated otherwise, the material published in the newsletter does not represent the official views of Finohta or STAKES. The material can be quoted, provided that the source is acknowledged. Articles should not be quoted in their entirety without the author's permission.
ISSN 1455-7940 Volume 11

PUBLISHER
The Finnish Office for Health Technology Assessment

EDITORIAL OFFICE (Finohta)
Editor-in-chief Marjukka Mäkelä, tel. +358 9 3967 2290
Subeditor Ella Kuula, tel. +358 9 3967 2285
Medical Officer Kristian Lampe, tel. +358 9 3967 2180
Medical Officer Iris Pasternack, tel. +358 9 3967 2100
Secretary Terhi Ilonen, tel. +358 9 3967 2297

Postal address P.O. Box 220, FIN-00531 Helsinki, Finland
Street address Lintulahdenkuja 4
Telephone +358 9 39 671 (switchboard), Telefax +358 9 3967 2278
E-mail firstname.lastname@stakes.fi
Website http://finohta.stakes.fi/EN
Design International issue 2008 Nilla Westin Design
Translation Leena Saarela/Stakes, Mark Phillips/Stakes, Done Information OY
Printing Elanders, Falköping, Sweden, 2008

Finohta

IMPAKTI

Newsletter of the Finnish Office for Health Technology Assessment

3/08

HTA CAN CHANGE THE LAW
» p. 4

Jean-Francois Schmutz/Matton

SPECIAL JOINT NEWSLETTER FROM FINOHTA AND SBU

STAKES