INAHTA Briefs

INAHTA

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Technology Assessment

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INAHTA Briefs

The series, *INAHTA Briefs,* is a forum for member agencies to present brief and structured overviews of recently published reports. *INAHTA Briefs* are published regularly and are available free-of-charge at www.inahta.org. Information presented in the INAHTA Briefs is developed and submitted by the member agencies. This publication series would not be possible without the members' ongoing commitment and support.

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INAHTA
c/o SBU
PO Box 5650, Tyrgatan 7
SE-114 86 Stockholm, Sweden

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Susanna Jonas, Claudia Wild, ITA, Austria

Griffin, Leanne Sutherland, Pham CT, Tooher, ASERNIP-S, Australia

Kim Dalziel, Renea Johnston, Alex Raulli, CCE, Australia

Mike McKenzie, Department of Health and Ageing, Australia

Dekker G, Hiller JE, Merlin T, HTA Unit, Mundy L, HTA Unit, Univ of Adelaide, Australia

Lachlan Standfield, M-Tag, Australia

Elizabeth Barr, Kirsten Howard, Sally Wortley, NHMRC CTC, Australia

Laurie Brooks, Samantha Bowker, Bing Guo, Christa Harstall, Patricia Leggett Tait, Maria Ospina, Ann Scott, AHFMR, Canada

Banerjee S, Boucher M, Brady B, Brown A, Doherty TJ, Dubé C, Garces K, Hailey D,

Herrmann N, Ho C, CCOHTA, Husereau D, Jacobs P, Jolicoeur E, Joyce J, KH Pwee, Mayers I, McGahan L, Mensinkai S, Mensinkai S, Noorani HZ, Rostom A, Shukla VK, Skidmore B, Stone J, Stuart GCE, Taylor R, Teasell R, Turnbull J, CCOHTA, Canada

Andersen B, Haaeman P, Hansen NW, Ingerslev HJ, Juhl HH, Kjærsgaard LL, Krogsgaard K, Lange M, Larsen M, Møller JK, Olesen F, Østergaard L, Sigmund H, Svenning AR, Weis N, DACEHTA, Denmark

Caroline Latapy, Anne Isabelle Poullié, ANAES, France

CJ (Hanneke) van de Klippe, GR, The Netherlands

Viveka Alton, Anders Norlund, SBU, Sweden

Alison Round, North & East Devon Health Authority, UK

Joy Townsend, London School Hygiene and Tropical Medicine, UK

Malcolm Law, St Bart's & The Royal London School of Medicine, UK

Nicholas Wald, Barts and the London Queen Mary School of Medicine and Dentistry, UK

Anne-Marie Bagnall, CRD, UK

June Cody, Graham Mowatt, IAHS, UK

Emma Loveman, NCCHTA, UK

Joyce Craig, Susan Quinn, Emma Riches, Karen Ritchie, Jim Slattery, NHS QIS, UK

Jim Chilcott, Daniel Hind, Allen Hutchinson, Jeremy Wight, ScHARR, UK

Peter Sharp, Univ of Aberdeen, UK

Clare Davenport, Fujian Song, Univ of Birmingham, UK

Jenny Donovan, Univ of Bristol, UK

Andrew Kennedy, Univ of Brunel, UK

Ken Stein, Univ of Exeter, UK

Wendy Clark, Univ of Keele, UK

Gillian Parker, Richard Riley, Univ of Leicester, UK

Rumona Dickson, Univ of Liverpool, UK

Rachael Elliott, Anne Kennedy, Univ of Manchester, UK

Margot Gosney, Univ of Reading, UK

John Kanis, Suzy Paisley, Univ of Sheffield, UK

Jacq. Dinnes, Paul Roderick, Univ of Southampton, UK

Heather Gage, Univ of Surrey, UK

J G Williams, Univ of Swansea, UK

Gill Grimshaw, Univ of Warwick, UK

Introduction

The International Network of Agencies for Health Technology Assessment (INAHTA) is a global network linking 42 non-profit, governmental institutions from 21 countries (2004).

INAHTA was established in 1993 with the aim

- To accelerate exchange and collaboration among HTA agencies
- To promote information sharing and comparison
- To prevent unnecessary duplication of activities.

The mission of INAHTA is

"To provide a forum for the identification and pursuit of interests common to health technology assessment agencies."

The INAHTA membership is open to any organization which

- Assesses technology in health care
- Is a non-profit organization
- Relates to a regional or national government
- Receives at least 50% of its funding from public sources.

The Network stretches from the USA, Canada, and Latin America to Europe, Australia, and New Zealand. The Secretariat is located at SBU in Sweden.

Further information on INAHTA is available at www.inahta.org

Title **A Systematic Review of the Costs and Effectiveness of Different Models of Pediatric Home Care**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;6(35). Feb 2003. www.ncchta.org/execsumm/summ635.htm

Aim

To establish: 1) the range and types of pediatric home care (PHC), 2) the effectiveness and costs of PHC, 3) if and how cost-effectiveness differs between different groups of children, 4) the speed of growth of the evidence base, and 5) what recommendations could be made for further research.

Conclusions and results

Almost 15 000 papers were identified. Ten RCTs (24 papers), 16 economic papers, and 14 non-RCT studies (15 papers) were eventually included. Five main types of PHC were evident for the following: very low birth weight or medically fragile babies; asthma or diabetes; technology-dependent children; children with mental health problems; generic models of PHC. Reporting was limited on clinical or developmental outcomes of earlier discharge, accompanied by home care, for very low birth weight babies. Physical and mental development may be enhanced, but sample sizes were too small to be confident about this. PHC may be cheaper than the alternative, but the costing methods used were weak. Impact on family members was rarely reported. Whether PHC for children with diabetes or asthma affects clinical or 'social' outcomes or costs, for children, their families, or the health service remained unsure. It was concluded that early discharge with home care after diagnosis may reduce parents' costs, largely by reducing children's initial length of hospital stay.

For technology-dependent children, controlled studies were rare, as were studies that measured clinical outcomes, impact on families or children's quality of life. PHC for technology-dependent children may be cheaper for the health service, but little else could be concluded about it. For children with mental health problems, few other effects were reported apart from parents' satisfaction with services. For generic pediatric home care, only one study was identified. No major clinical effects were evident at early followup.

The evidence and methods in this area were weak. Common methodological weaknesses included sample sizes, timing of data collection, objectivity, long-term followup, accurate description of PHC models, impact beyond the hospital, and the ages of children researched. Narrow ranges of children and parents in terms of socioeconomic status, ethnicity, and geographic location were included in studies. Children's views were largely absent.

Recommendations

Further research required, see below.

Methods

Guidelines from the NHS Centre for Reviews and Dissemination were followed. Twenty electronic databases, publication lists, and current research registers were searched. Reference lists, handsearching, personal contact with researchers, and forward citation searching were also used. Analysis was predominantly descriptive, given the heterogeneity of focus, outcome reporting, and quality of the studies.

Further research/reviews required

Fourteen detailed and specific areas of research required are described in the full report.

Written by Professor Gillian Parker, Nuffield Community Care Studies Unit, University of Leicester, UK

Title **The Cost Effectiveness of Screening for Helicobacter Pylori to Reduce Mortality and Morbidity from Gastric Cancer and Peptic Ulcer Disease: A Discrete-event Simulation Model**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(6). Mar 2003. www.ncchta.org/execsumm/summ706.htm

Aim

To develop a discrete-event simulation model to evaluate the cost effectiveness of population screening for H. pylori in England and Wales to prevent gastric cancer and peptic ulcer disease.

Conclusions and results

Population screening would screen about 25 million individuals if uptake were 70%, with over 5 million people being treated. The number of deaths prevented falls with increasing age at screening, but so does the present value of costs because of less prevalent screening and deferred costs. In the base case, the cost effectiveness of H. pylori screening improves with age and is under £10 000 per life-year saved (LYS) in all age groups. However, this cost/LYS is over an 80-year followup. Screening once at age 40 with a prevalent round for people aged 40–49 appears to be the most pragmatic policy. The effect of eradication of H. pylori on gastric cancer (GC) risk is uncertain. Extensive H. pylori opportunistic testing of all dyspeptic cases in primary care would reduce the cost effectiveness of H. pylori screening.

Recommendations

Population screening for H. pylori is likely to be cost effective in the long term (a cost/LYS of under £10 000 for the base assumptions). This compares favorably with other such programs, but more research is needed to clarify uncertainties before introducing population screening.

Methods

A discrete-event simulation model was developed using the 'patient-oriented simulation technique'. In this model, without screening most H. pylori-positive cases remained asymptomatic, but some developed dyspepsia and presented to primary care for testing and eradication therapy. H. pylori-positive cases were assigned increased risks of developing peptic ulcer disease and GC. Some cases of peptic ulcer disease were fatal, and most GC cases were incurable. In the screening scenarios, the population was invited to screening; the H. pylori-positive were offered eradication therapy. In those treated, the risk for peptic ulcer fell immediately to that of H. pylori-negative cases. The effect of eradication on GC risk was modeled by assuming a time lag before such risk reverted to H. pylori-negative levels. The decline in GC incidence was taken into account by age cohort modeling. Key parameters for the model are presented in the report. UK data were used where available. Costs were NHS costs (2000 prices, discount rate of 6%). The model covered an 80-year period to allow the impact of screening on GC risk to accrue. Sensitivity analyses addressed different scenarios and the estimated values in the model. Both incident and prevalent screening rounds were modeled.

Further research/reviews required

These include: clarifying the relative risk of H.pylori and complicated peptic ulcer disease, the efficacy of eradication of H.pylori on pre cancerous gastric changes, and the scale of wider opportunistic testing.

Written by Dr Paul Roderick, Health Care Research Unit, University of Southampton, UK

Title **A Multicenter Randomized Controlled Trial Assessing the Costs and Benefits of Using Structured Information and Analysis of Women's Preferences in the Management of Menorrhagia**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(8). Feb 2003. www.ncchta.org/execsumm/summ708.htm

Aim

To develop decision aids to provide evidence-based information and formal preference elicitation for women with menorrhagia; and to evaluate their effects on patient outcomes, patient management, and cost effectiveness.

Conclusions and results

Preference formation: Compared to the control group, women were more likely to hold a treatment preference in both the information (adjusted odds ratio 1.87, 95% CI 1.25 to 2.80) and interview (2.51, 1.66 to 3.79) groups, post-consultation. The interview also influenced preferences toward individual treatments, where they were less likely than controls to want hysterectomy (0.54, 0.35 to 0.85) or drug therapy (0.44, 0.24 to 0.82).

Health status: The interventions had no consistent effect on health status compared to control.

Treatments undergone: After 2 years of followup, women in the interview group were less likely to have undergone hysterectomy than controls (0.60, 0.38 to 0.96) and women who were only given information (0.52, 0.33 to 0.82).

Satisfaction: The results of the satisfaction analyses were mixed. At short-term followup, the information group was significantly more satisfied with the opportunities given to be involved in treatment decision-making compared to control (1.39, 1.04 to 1.86). At long-term followup the interview group rated both these opportunities (1.49, 1.11 to 2.01) and the results of their treatment (1.44, 1.03 to 2.78) higher than women in the control group.

Cost-effectiveness: A high probability that information provided in conjunction with preference elicitation is cost-effective. Even under a range of sensitivity analyses this result does not change. The probability that interview is the most cost-effective form of management, assuming decision-makers are willing to pay at least £30 000 per additional QALY, is 78% and 55% under sensitivity analysis.

Recommendations

Neither intervention had a major impact on health outcomes relative to control. Information plus interview gave major additional benefits compared to the information pack alone. It helped women form preferences, reduced hysterectomy rates, and increased long-term satisfaction. The interview also had the highest probability of being cost effective.

Methods

The interventions were evaluated using a pragmatic, parallel group, multicenter, randomized controlled trial with 2 years of followup. Women were randomized to 1 of 3 arms: Control (usual practice), Information only, Interview plus information.

Further research/reviews required

Recommendations for future research are:

1. Approaches to training clinicians in patient-centered decision making
2. Practical methods of clarifying and eliciting patient's treatment related preferences and communicating them to clinicians
3. Scenarios of clinical decisions under which these methods would prove most effective and cost effective.

Written by Mr Andrew Kennedy, Health Economics Research Group, Brunel University, UK

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Issue 2003/29

Title **The Feasibility of Conducting a Multicenter Randomized Controlled Trial of Treatment for Localized Prostate Cancer: The ProtecT (prostate testing for cancer and Treatment) Study**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(14). Mar 2003. www.ncchta.org/execsumm/summ714.htm

Aim

To evaluate the feasibility of a full-scale multicenter, randomized controlled trial of treatments for localized prostate cancer, including: feasibility of 'case finding' in 3 UK cities, the reliability of PSA testing, and the psychosocial impact of case finding. To determine the most efficient/effective design for full-scale treatment trials, including specifying treatment arms and investigating comparative cost effectiveness of nurses and urologists in recruitment. To understand randomization and treatment decision-making. To pilot outcome measures and procedures for proposed main trial.

Conclusions and results

Case-finding: 8823 men (57% of invited) checked at prostate clinics. 879 (10%) had high PSA. Biopsy found 230 cases of prostate cancer (184 clinically localized). Detection rate was 2.1%. Positive predictive values confirmed that a PSA cut-point of 3ng/ml was suitable.

Randomized trial of recruitment: 90% of eligible cases consented to randomization to nurse or urologist. Effectiveness was similar in both arms, but the urologist arm was more expensive since higher salary costs outweighed their tendency for shorter appointments.

Randomized trial of treatment: The 3-arm trial was the most popular treatment trial option, with 84% opting for this rather than the 2-arm trial ($p<0.001$). Acceptance of treatment allocation was high (71% in 3-arm trial).

Qualitative research: PSA testing viewed as an opportunity to detect an unknown condition. Most men understood that the study involved investigation of treatments. Recruitment rose gradually during the feasibility study, from 30%–40% at outset to 70% by May 31, 2001.

Recommendations

A full-scale randomized trial of treatment for localized prostate cancer, preceded by case finding, is feasible in the UK. Case finding was acceptable and prostate cancer was detected in 2% of clinic attendees. No significant difference in urologist vs nurse ability to recruit men for the treatment trial, but nurses were more cost effective.

Methods

RCT of treatment preceded by community case finding, integrating qualitative research methods at each stage.

Case-finding: Men aged 50–69 years from specific primary care centers in 3 UK cities were invited to a 30-minute prostate check clinic where they were informed about the study and asked to consent to a PSA test. Men with elevated PSA were invited for biopsy.

Randomized trial of recruitment: Men with localized prostate cancer were asked to consent to randomization to a nurse or urologist to discuss recruitment, the need for a treatment trial, and the advantages/disadvantages of each treatment.

Randomized trial of treatment: All subjects were asked to consent to followup, and these formed the pilot for the trial procedures and outcomes.

Further research/reviews required

The NHS HTA Programme has funded a proposed full-scale, 3-arm randomized treatment trial to be undertaken in 9 clinical centers in the UK. It will involve over 100 000 men, and recruitment will take 5 years (commenced September 2001). An MRC Programme grant is being prepared to further investigate the role of qualitative research methods in RCTs.

Written by Professor Jenny Donovan, Dept of Social Sciences, University of Bristol, UK

Title **Treatment of Established Osteoporosis: A Systematic Review and Cost–Utility Analysis**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;6(29). Feb 2003. www.ncchta.org/execsumm/summ629.htm

Aim

To assess the effectiveness of treatments for established osteoporosis.

Conclusions and results

A systematic review indicated that bisphosphonates, calcitonin, calcium, fluoride salts, and raloxifene reduced the incidence of vertebral fracture. The bisphosphonate, alendronate, also decreased non-vertebral fracture, including hip fracture.

For several agents, failure to demonstrate efficacy was due to the lack of RCTs. Epidemiological evidence suggested that treatment with calcium, calcitonin, hormone replacement therapy (HRT), thiazide diuretics, etidronate, and anabolic steroids reduced hip fracture risk. RCT evidence showed that calcium plus vitamin D reduced fracture risk in patients with unknown bone mineral density. It was not cost effective to treat established osteoporosis with raloxifene in the model used. HRT was not cost effective except below the age of 60 years. However, treatment became cost effective from the age of 50 years if the effects on appendicular fractures were included. Calcium alone was cost effective compared with no intervention from age 60 years, assuming an effect only on vertebral fracture risk, but cost effective at all ages if effects on appendicular fractures were included. Calcitonin was not cost effective at any age because of its high costs, whereas alendronate was only cost effective from age 70 years. Fluoride was not cost effective until over 60 years. Compared with no treatment, it was not cost effective to treat osteoporosis with alfacalcidol except over 70 years. The conclusions are conservative, mainly due to insufficient data.

Recommendations

Cost-effectiveness ratios decrease with age. At age 50 years, only HRT and calcium plus vitamin D were cost effective (assuming that the agent would decrease the risk of appendicular fractures at this age). At age 80 years, HRT, calcium with or without vitamin D, alfacalcidol, alendronate and bisphosphonate were all cost effective.

Methods

All relevant RCTs were systematically reviewed. The annual risk of osteoporotic fracture was characterized for women from the UK. Published meta-analyses were used to determine the risk of osteoporotic fractures in women at the threshold for osteoporosis and the risk for such fractures after prior osteoporotic fracture. The consequences of fracture on mortality were assessed for each fracture type. Annual breast cancer, coronary heart disease, and mortality risks were reviewed. Costs and utilities were determined for osteoporosis in the UK by systematic review of the literature. A model was developed to simulate cohorts at fixed ages with osteoporosis..

Further research/reviews required

Health economic assessment based on probability of fracture is an important area for further research. Other areas arise from gaps in empirical knowledge on utilities and side effects that are amenable to primary research. Further secondary research should be undertaken to more closely evaluate the impact of vertebral deformities on cost effectiveness.

Written by Professor John Kanis, Centre for Metabolic Bone Disease, University of Sheffield, UK

Title **Which Anaesthetic Agents are Cost Effective in Day Surgery? Literature Review, National Survey of Practice and Randomized Controlled Trial**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;6(30). Mar 2003. www.ncchta.org/execsumm/summ630.htm

Aim

To identify and value resource use, impact on patients, and relative value for money associated with different anaesthetic agents in day surgery.

Conclusions and results

Many of the RCTs available that investigated clinical outcomes involved the use of various anaesthetic combinations and approaches. There were few good comparative studies of patient-based outcomes and economic evidence. No optimal regimen was identified for adults or children on the basis of clinical outcomes, patient acceptability, or efficiency.

The national survey of anesthetists (response rate 76%) indicated the following in adult urology, adult orthopedic, and pediatric general day-case surgery, respectively:

- Use of premedication, 6%, 12%, and 19%
- Propofol as the preferred induction agent, 78%, 81%, and 51%
- Isoflurane as the preferred maintenance agent, 52%, 54%, and 45%
- Use of prophylactic anti-emetics, 32%, 41%, and 24%
- Use of a laryngeal mask airway, 86%, 83%, and 85%.

Results from the adult RCT and the pediatric study are discussed in detail in the full report.

Recommendations

Sevoflurane/sevoflurane is not a cost-effective regimen for day surgery in adults or children. It is associated with higher rates of PONV than propofol followed by propofol, isoflurane, or sevoflurane. It is more expensive than mixed anesthesia regimens. In the adult study, there were no statistically significant differences in the incidence of PONV between the regimens that used propofol for induction. However, there were statistically significant differences in the variable costs of the regimens. The propofol/isoflurane regimen was associated with the lowest cost per episode of PONV avoided.

Methods

The study consisted of three parts:

1. A literature review of clinical outcomes, patient-based outcomes, and economic data.
2. A national survey of 270 anesthetists (October 2000) to determine anaesthetic practice in adult and pediatric day surgery.
3. A prospective RCT to compare the cost effectiveness of anaesthetic regimens. Prospective patient-based resource-use data were collected up to day 7 post-discharge, from the perspective of the NHS and the patients.

Further research/reviews required

Further research is needed in the following areas:

1. Optimization of perioperative analgesia
2. Routine perioperative PONV prophylaxis should be reviewed
3. Risk factors for PONV
4. Cost of volatile anesthetics
5. Role of patient preferences in anesthesia.

Written by Dr Rachael Elliott, School of Pharmacy & Pharmaceutical Sciences, University of Manchester, UK

Title **A Review of the Clinical Effectiveness and Cost Effectiveness of Routine Anti-D Prophylaxis for Pregnant Women Who Are Rhesus Negative**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(4). Feb 2003. www.ncchta.org/execsumm/summ704.htm

Aim

To evaluate the clinical effectiveness of antenatal anti-D prophylaxis (AADP) for pregnant women who are RhD negative, and the comparative cost effectiveness of: 1) offering routine AADP to all pregnant women who are RhD negative, 2) offering routine AADP only to primigravidae who are RhD negative, and 3) not offering routine AADP.

Conclusions and results

Eleven studies met the inclusion criteria. Two non-randomized, community-based studies suggest that routine AADP may reduce the sensitization rate from 0.95% to 0.35%. This gave an odds ratio for the risk of sensitization of 0.37, and an absolute reduction in risk of sensitization in RhD-negative mothers carrying a RhD-positive child of 0.6%. The number needed to treat (NNT) to avoid one case of sensitization was 278, and to avoid a fetal or neonatal loss in next pregnancy the estimate is 5790. If cost savings from reductions in treating hemolytic disease of the newborn are considered, the total net cost to the NHS in England and Wales would be £5.7–6.4 million per year. If routine AADP is only given to RhD-negative primiparae, the total net cost, including potential savings from reductions in hemolytic disease of the newborn, is estimated at approximately £2.3–2.6 million. Routine AADP for RhD primiparae was economically attractive based on disability prevention alone, irrespective of parental grief and valuation of stillbirths, neonatal and postneonatal deaths. Routine AADP in all pregnant RhD-negative women is economically attractive, using a maximum acceptable cost-effectiveness ratio of £30 000 per QALY, if the lost child, associated parental grief, and high intervention pregnancy are valued above 9 QALYs.

Recommendations

The evidence suggests that routine AADP is effective in reducing the number of RhD-negative pregnant women who are sensitized during pregnancy. Some cases of sensitization in the UK are due to failure to adhere to the existing guidelines. It should be possible to reduce sensitization rates by stricter adherence to current guidelines, and this could be pursued before initiating guidelines to routinely offer AADP to pregnant women who are RhD negative.

Methods

A systematic literature review identified all studies that compared women receiving routine AADP with untreated controls or that evaluated the economic impact of routine AADP. Economic evaluation was based on a model offering routine AADP to all pregnant RhD-negative women, and to RhD-negative primigravidae only, in addition to conventional AADP applicable to the NHS. This evaluation assessed the cost per fetal loss, stillbirth, neonatal, or postneonatal death avoided, the cost per life-year gained (LYG), and the cost per quality-adjusted life-year (QALY) gained from disabilities avoided.

Further research/reviews required

Further research is required to:

1. Identify characteristics which might identify the 10% of RhD-negative women at risk of sensitization, so antenatal prophylaxis may be targeted specifically at these women
2. Confirm or disprove the preliminary findings that protection against sensitization provided by AADP in primigravidae extends beyond the first pregnancy.

Written by Mr Jim Chilcott, ScHARR, University of Sheffield, UK

Title **Intravascular Ultrasound (IVUS), July 2001**

Agency **MSAC, Medical Services Advisory Committee**
Commonwealth Department of Health and Ageing
GPO Box 9848 Canberra ACT 2601 Australia; http://www.msac.gov.au

Reference MSAC Application 1032. Assessment Report ISSN 1443-7120

Aim

To assess the safety and effectiveness of intravascular ultrasound and the circumstances under which public funding should be supported for the service.

Conclusions and results

Safety: IVUS appears to be relatively safe. Adverse events relate primarily to vasospasm (readily treated with intravenous nitrate therapy). The rate of major acute procedural complications associated with IVUS, eg, dissection or vessel closure, is about <0.5%. Major complications are more likely in therapeutic IVUS than in diagnostic IVUS imaging.

Effectiveness: Diagnosis: Information from IVUS appears to complement coronary angiography. It more accurately shows the likely extent of coronary and peripheral vessel lesions; appears to have good sensitivity and specificity for detecting plaque dissections and media rupture, but lower sensitivity for detecting plaque rupture and thrombus formation; has quite high accuracy in predicting the likely functional severity of lesions; and provides information on plaque composition. Some evidence suggests that it can predict clinical events, and alter management of patients with angiographically indeterminate or ambiguous lesions.

Treatment: RCT evidence suggests that stents placed with IVUS guidance reduces the odds (statistically significant) of patients requiring target lesion revascularization (TLR) at 9–12 months in the IVUS vs non-IVUS treatment groups (odds ratio 0.73, 95% CI 0.54–0.99, p=0.04) It is unclear whether the reduction in TLR can be sustained over longer followup or will improve either Q-wave myocardial infarction or survival, as the trials were not powered to detect significant differences in these parameters.

Cost-effectiveness: Using published RCT evidence, the estimated baseline cost per clinically-driven target lesion revascularization (TLR) prevented from IVUS-guided stent deployment is about $26 000. This estimate varies from about $12 000 to $800 000 per TLR prevented over the evidence-based ranges examined in sensitivity analyses.

Recommendations

MSAC recommended against public funding due to insufficient evidence on the effectiveness and cost effectiveness of IVUS as a diagnostic or therapeutic tool.

Method

A systematic literature review by the NHMRC Clinical Trials Centre addressed (a) the diagnostic accuracy of IVUS and (b) its role as an adjunct to coronary interventions. Biomedical databases, existing reviews, the Internet, and international HTA organization websites were searched. For (a) the literature was searched from 1990 to August 2001 and, for (b), from 1999–2000, with pre-1999 papers identified by Berry et al. 2000 ("Intravascular ultrasound-guided interventions in coronary artery disease: a systematic literature review, with decision-analytic modeling, of outcomes and cost effectiveness", Health Technology Assessment (South Hampton, NY), vol. 4, no. 35, pp. 1–117).

Written by Kirsten Howard and Sally Wortley, NHMRC CTC, Australia

Title **Recombinant Human Thyroid Stimulating Hormone (rhTSH) – Diagnostic Agent for Use in Well-differentiated Thyroid Cancer**

Agency **MSAC, Medical Services Advisory Committee**
Commonwealth Department of Health and Ageing
GPO Box 9848 Canberra ACT 2601 Australia; www.msac.gov.au

Reference MSAC Application 1043 Assessment Report First printed: Dec 2002.
ISBN 0-642-82140-2

Aim

To assess the safety, effectiveness, and cost effectiveness of recombinant human thyroid stimulating hormone (rhTSH) in detecting thyroid remnants and well-differentiated thyroid cancer in post-thyroidectomy patients maintained on hormone suppression and at risk of recurrence of thyroid cancer, relative to the comparator method of thyroid hormone therapy (THT) withdrawal.

Conclusions and results

Safety: About 800 patients have received rhTSH in clinical trials. Adverse events associated with rhTSH appear to be mild, the most frequent being headache and nausea. However, some individual case studies report serious adverse events associated with the swelling of metastases after rhTSH administration. To reduce the incidence of serious adverse events, pretreatment with corticosteroids may be considered prior to administering rhTSH in patients with metastatic disease in confined spaces. Adverse events associated with rhTSH should be considered in the context of the hypothyroidism in patients undergoing THT withdrawal.

Effectiveness:

- *Diagnostic accuracy:* The primary efficacy measure was the diagnostic accuracy using rhTSH relative to using the comparator, THT withdrawal. When used with concurrent serum Tg testing and whole body scanning, the unadjusted sensitivity of rhTSH was 87%, specificity 95% and accuracy 89%. Using rhTSH instead of THT withdrawal would reduce diagnostic accuracy, so that 11% of patients' disease status would be misclassified.
- *Quality of life:* This assessment suggests that patients experience a poorer general quality of life during THT withdrawal compared with rhTSH. Although the magnitude of the differences is considerable, the effect is transient and infrequent.
- *Cost-effectiveness:* A decision-analytic cost-utility model was used to determine the cost effectiveness of rhTSH relative to THT withdrawal in the cohort of patients who have already had one negative followup using THT withdrawal. With significantly increased cost and a marginal improvement in average utility, the incremental cost effectiveness in this patient group is AUD 51 344 per quality-adjusted life-year.

Recommendation

MSAC recommended that on the strength of evidence pertaining to the diagnostic use of rhTSH in well-differentiated thyroid cancer, public funding should be supported for this procedure only in patients in whom THT withdrawal is medically contraindicated. Also, based on current evidence, both rhTSH-stimulated whole body scanning and serum Tg testing should be undertaken concurrently. MSAC recommended that public funding for rhTSH should not be supported in patients who are able to tolerate THT withdrawal, on the basis of lower diagnostic accuracy and a high cost-effectiveness ratio. The Minister for Health and Ageing accepted this recommendation on 16 October 2002.

Methods

The medical literature on rhTSH was systematically reviewed. A thorough search of the literature was carried out via electronic databases and HTA websites. Citations that met predefined inclusion criteria were included. The value-for-money of rhTSH relative to the standard THT withdrawal method in detecting well-differentiated thyroid cancer or thyroid remnants in post-thyroidectomy patients maintained on hormone suppression and at risk of recurrence of thyroid cancer, was evaluated using a decision-analytic cost-utility model.

Prepared by Mr Lachlan Standfield, Medical Technology Assessment Group, Australia

Title **Endoluminal Gastroplication – May 2002**

Agency **MSAC, Medical Services Advisory Committee**
Commonwealth Department of Health and Ageing
GPO Box 9848 Canberra ACT 2601 Australia; www.msac.gov.au

Reference MSAC Application 1047, Assessment Report ISBN 0642-82071-6

Aim

To assess the safety, effectiveness, and cost-effectiveness of endoluminal gastroplication (ELGP) for gastroesophageal cancer and under what circumstances such services should be supported with public funding.

Conclusions and results

The evidence for the efficacy and safety of ELGP is based on one small, published study with no control group. Hence, the review is primarily a critical appraisal of the one published study that met the eligibility criteria on ELGP. Below are recommendations on the safety, effectiveness, and cost-effectiveness of the procedure.

Safety: Limited evidence was available to assess the safety of ELGP in patients with gastroesophageal reflux disease (GERD). From the data provided in the one case-series paper, it would appear that a minority of patients suffered adverse events 6 months after the procedure. Some of the adverse events may be explained by the limited experience of surgeons in performing the procedure; however, more data are needed before a decision can be made regarding the safety of the procedure in patients with GERD.

Effectiveness: Data at 6-month followup, from the one case-series paper, indicate that endoluminal gastroplication may reduce some symptoms of GERD. However, the paucity of good-quality data limits the ability to draw any conclusions regarding the efficacy of this procedure. Further research focusing on randomized trials is needed in this area.

Cost effectiveness: There is a paucity of data on the effectiveness of ELGP beyond 6 months of followup. It appears that medication use at 6 months is reduced, but the duration of this effect is unknown due to the limited data available on this procedure. A comprehensive economic evaluation should be conducted on ELGP when sufficient data are available.

Recommendation

Since there is insufficient evidence pertaining to endoluminal gastroplication for gastroesophageal reflux disease, MSAC recommended that public funding should not be supported at this time for the procedure.

Method

The National Health and Medical Research Council (NHMRC) Clinical Trials Centre at the University of Sydney conducted a systematic review of the literature (with eligibility criteria defined a priori) on the role of endoluminal gastroplication. The following sources were searched from commencement to December 2001: MEDLINE, PreMedline, International Pharmaceutical Abstracts, Best Evidence, Current Contents, EMBASE, the Cochrane Library, ISTAHC, and the NHS Databases, DARE, EED, and HTA. Internet and health technology assessment agency sources were also searched.

Written by Sally Wortley and Kirsten Howard, NHMRC CTC, Australia

Title **Multifocal Multichannel Objective Perimetry, November 2002**

Agency **MSAC, Medicare Services Advisory Committee**
Commonwealth Department of Health and Ageing
GPO Box 9848 Canberra ACT 2601 Australia; www.msac.gov.au

Reference MSAC Reference 13 Assessment Report, ISBN 0-642-821437, ISSN 1443-7120,

Aim

To assess the safety, effectiveness and cost effectiveness of multifocal multichannel objective perimetry (MMOP) and under what circumstances public funding should be supported for the service.

Conclusions and results

Safety: There was a lack of safety data, although risks to subjects should be minimal as the test is noninvasive.

Effectiveness: Limitations associated with the evidence preclude evaluation of the clinical effectiveness of MMoP. Two studies with suboptimal design for determining the effectiveness of a diagnostic test were identified. Both reported sensitivities ranging from 95% to 100% and specificities from 93% to 97%. These are likely to be overestimates since the studies were susceptible to bias due to study design constraints resulting in a failure to meet important validity criteria. In particular, the test and the reference were not performed in a consecutive set of patients, but rather in a group known to have the target disorder and a group of control subjects known not to have the disease. As patient management and clinical outcomes were not addressed in any of the studies, it cannot be determined whether the test would improve patient management or whether it could help to slow the progression of glaucoma or any other disease that results in visual field defects.

Cost effectiveness: There is no reliable, high-quality evidence on the costs or outcomes of MMOP in Australia or elsewhere.

Recommendation

Public funding for MMOP should not be supported in Australia at this time.

Method

MSAC conducted a systematic review of medical literature using the Cochrane Library, MEDLINE, PreMedline, EMBASE, CINAHL, Current Contents, and Biological Abstracts databases from 1966 to 2002 to identify the accuracy and precision of MMOP and its usefulness in terms of patient outcomes. This report adopted the criteria for assessing validity of evidence recommended by the Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Tests. This assesses evidence against the ideal study design for assessing the accuracy of diagnostic tests defined as follows: Patients in the study should have undergone both the diagnostic test in question and a reference "gold standard" test that would confirm whether or not they have the target disorder.

Written by Alex Raulli, Kim Dalziel, and Renea Johnston, Centre for Clinical Effectiveness, Australia

Title **Percutaneous Transluminal Coronary Rotational Atherectomy for Lesions of the Coronary Arteries – May 2002**

Agency **MSAC, Medicare Services Advisory Committee**
Commonwealth Department of Health and Aged Care
GPO Box 9848 Canberra ACT 2601 Australia; www.msac.gov.au

Reference MSAC Application 1036. ISBN 0-642-82135 6 February 2003

Aim

To assess the safety, effectiveness and cost effectiveness of adjunctive percutaneous transluminal coronary rotational atherectomy (PTCRA) with particular reference to noncomplex lesions, complex lesions, in-stent restenosis, and lesions refractory to or contraindicated for coronary angioplasty, relative to the comparator methods of coronary artery bypass graft (CABG) surgery and percutaneous transluminal coronary angioplasty (PTCA).

Conclusions and results

Safety: PTCRA with or without PTCA is no more likely to result in Q-wave infarcts or emergency surgery compared to PTCA alone. Patients are also less likely to experience angiographic dissection or proceed to bailout stenting. PTCRA is as safe as PTCA in the first 24 hours of the procedure. However, minor complications, eg, temporary vessel spasm and slow flow are more likely. The data are insufficient to conclude whether PTCRA is as safe as PTCA in revascularizing different types of coronary artery lesions.

Effectiveness: When conventional PTCA with or without stent placement is feasible, PTCRA appears to confer no additional patient benefit. In cases of in-stent restenosis, the evidence is limited but conflicting, and no long-term data support the routine use of rotational atherectomy. Expert clinical opinion indicates that in certain circumstances rotational atherectomy is a useful adjunctive procedure to increase the success of angioplasty in revascularizing complicated or calcified lesions. In cases where conventional angioplasty and stenting cannot be undertaken successfully, or where clinical or angiographic outcome is poor, PTCRA may be an effective adjunctive procedure.

Cost effectiveness: Cost-effectiveness ratios could not be determined due to limited research data on effectiveness and the paucity of robust cost estimates from high-quality studies.

Recommendations

MSAC recommended, on the evidence pertaining to percutaneous transluminal coronary rotational atherectomy, that public funding:

- Is supported for revascularization of complex and heavily calcified coronary artery lesions which cannot be treated by PTCA alone or when previous PTCA attempts have not been successful; and for revascularization of complex and heavily calcified coronary artery stenoses where CABG surgery is contraindicated.
- Is not supported for revascularization of coronary artery stenoses which can be satisfactorily treated by PTCA alone, with or without stent placement; and for revascularization of coronary artery in-stent restenoses as a result of prior coronary artery intravascular interventions (since no long-term data exists and short-term data are conflicting).

The Minister for Health and Ageing accepted this recommendation (17 September 2002).

Methods

The Centre for Clinical Effectiveness systematically reviewed the literature (with eligibility criteria defined *a priori*) on the role of rotational atherectomy. Sources searched from 1966 to March 2001: MEDLINE, PreMedline, National Library of Medicine Health Services Research Databases, Biological Abstracts, Best Evidence, Current Contents, EMBASE, the Cochrane Library, ISTAHC, and the NHS Databases, DARE, EED, and HTA. Internet and HTA agency sources were searched and studies were identified from MSAC applications and members of the Supporting Committee.

Prepared by Mr Mike McKenzie, Department of Health and Ageing, Australia

Title **Intravascular Brachytherapy – November 2001**

Agency **MSAC, Medicare Services Advisory Committee**
Commonwealth Department of Health and Aged Care
GPO Box 9848 Canberra ACT 2601 Australia; www.msac.gov.au

Reference MSAC Application 1041. Assessment Report

Aim

To assess the safety and effectiveness of intravascular brachytherapy (IVB) and under what circumstances such services should be supported with public funding.

Conclusions and results

Safety: The following safety conclusions were made:

- An appropriate multidisciplinary clinical team should conduct IVB.
- Catheter-based IVB exposes staff to radiation that is considered to be at an acceptable level.
- Patients are exposed to very low levels of radiation, as only a small local area of vessel wall is irradiated. Consequently, adverse events are more likely to be associated with vessel wall damage than with the development of malignancy.
- IVB may be associated with late thrombosis, but long-term antiplatelet therapy with new stent avoidance appears to reduce the likelihood of late thrombosis.
- Edge restenosis appears to be more pronounced with the use of beta-based IVB (either radioactive stents or catheter-based IVB).

Effectiveness: The effectiveness conclusions were based on level II and III-3 evidence:

- In the short-term, catheter-based IVB appears to significantly reduce angiographic restenosis and clinical revascularization. It does not significantly reduce the rate of MI or death. Current trials may be insufficiently powered to detect differences in these relatively rare outcomes;
- Long-term followup is limited, and it is unclear whether IVB defers rather than prevents the onset of restenosis following intervention.
- Significant technological and radiological differences between gamma and beta catheter-based IVB systems prevent direct comparison of the evidence on each system.
- The Guidant Intravascular Radiotherapy System and the Novoste® Beta-Cath™ Intracoronary Radiation System show comparable effectiveness, but have not been directly compared in the same group of patients.

Cost effectiveness: Published, randomized controlled evidence suggests that the baseline cost per target lesion revascularization (TLR) prevented by IVB is $31 500 per TLR prevented. Sensitivity analyses suggest that the estimated cost effectiveness of IVB is sensitive to estimates of IVB treatment effect, baseline risk of TLR, and the cost of providing IVB. Based on an annual incidence of 500 to 1000 cases, the total incremental cost will be around $2.2 to 4.4 million.

Recommendations

MSAC recommended, on the strength of evidence, that public funding for IVB should be supported. However, as IVB could be replaced by drug-eluting stents in 3 to 4 years, the supporting committee recommends only interim funding, pending review in 3 years.

Method

The National Health and Medical Research Council (NHMRC) Clinical Trials Centre systematically reviewed the literature (eligibility criteria defined a priori) on the role of IVB. Sources searched to November 2001 were: MEDLINE, PreMedline, National Library of Medicine Health Services Research Databases, Biological Abstracts, Best Evidence, Current Contents, EMBASE, the Cochrane Library, ISTAHC, and the NHS Databases, DARE, EED, and HTA. Internet and HTA agency sources were searched and studies were identified from MSAC applications and members of the Supporting Committee.

Written by Kirsten Howard, Elizabeth Barr, NHMRC CTC, Australia

Title **Antenatal Screening for Heritable Thrombophilia – August 2002**

Agency **MSAC, Medical Services Advisory Committee**
Commonwealth Department of Health and Ageing
GPO Box 9848 Canberra ACT 2601 Australia; www.msac.gov.au

Reference MSAC Reference 9B. ISBN 0642 82105 4. January 2003

Aim

To assess screening for heritable thrombophilia, antenatally, in unselected high-risk women (with history of obstetric complications) for safety, effectiveness, and cost effectiveness.

Conclusions and results

No studies have compared a group of women screened antenatally for heritable thrombophilia with a group of unscreened women.

Prevalence and risks associated with heritable thrombophilia. Heterozygous factor V Leiden (FVL), prothrombin, and homozygous MTHFR C677T mutations are relatively common in unselected women, while protein C, S, or antithrombin deficiencies are rare. Limited evidence suggests that unselected FVL carriers are 8 times more likely to suffer venous thromboembolism during pregnancy than non-carriers (absolute risk increase of 1%). They may have a 5-fold increased risk of fetal loss, but this must be confirmed by higher quality studies. No association was found between either FVL or homozygous MTHFR and intrauterine growth restriction. Good quality data on assessing outcomes in high-risk women were unavailable.

Diagnostic accuracy of the tests: No high-level evidence on test accuracy. Protein S deficiency should not be investigated antenatally due to likelihood of inaccurate diagnosis.

Safety and effectiveness of prophylaxis: No substantive evidence that prophylaxis effectively prevents or reduces maternal adverse events in high-risk pregnant women with thrombophilia. Limited level III-2 evidence suggests that heparinization of these women will reduce fetal loss at clinically significant levels. The data on the impact of prophylaxis on perinatal mortality, gestational age at delivery, and intrauterine growth restriction were inconclusive, but improvements were observed in the prophylaxed groups. Good quality, but limited, evidence showed that low-molecular-weight heparinization was associated with nearly 4 times the risk of increased blood loss (>600 ml) during delivery and of postpartum anemia. Good quality data were unavailable on prophylaxis in unselected women.

Cost effectiveness: Costs and consequences of antenatal screening for heritable thrombophilia could not be analyzed since epidemiological or primary research evidence are lacking.

Recommendations

On the strength of evidence on antenatal screening for heritable thrombophilia, public funding should not be supported for systematic screening of all pregnant women. Since the evidence on high-risk women with obstetric indications is insufficient, selective antenatal screening should not receive public funding at this time. This recommendation will be reviewed in 2 years. The Minister for Health and Ageing accepted the recommendation.

Methods

Systematic literature review based on search of MEDLINE, EMBASE, Current Contents, Cochrane Library, SSCI, ProceedingsFirst, internet databases and sites, and reference lists from 1966–2001. Studies were selected using a protocol. Evidence was assessed and classified using dimensions from the National Health and Medical Research Council. Quality was appraised using standard checklists, and clinical importance and relevance of benefit (or harm) were assessed.

Written by Merlin T, Mundy L, Dekker G, Hiller JE, HTA Unit, University of Adelaide, Australia

Title **Sentinel Node Biopsy (SNB) in Breast Cancer: Progress Report**

Agency **ANAES, French National Agency for Accreditation and Evaluation in Healthcare**
159, rue Nationale, 75013 Paris, France;
Tel: +33 1 42 16 72 72, Fax: +33 1 42 16 73 73, www.anaes.fr

Reference (Internet access to full text, ISBN (if any), publication date)

Aim

To update existing assessments of SNB, focusing on: (1) its feasibility and reliability, (2) study of the technical steps, (3) impact on surgery, and (4) economic analysis.

Conclusions and results

1. SNB was feasible and could be used to diagnose lymph node involvement under certain surgical and analytical conditions. The examination has been incorporated into TNM staging since 2003 (6th edition). A meta-analysis and 5 systematic reviews have reported 66%–100% identification of the SN, with 0%–17% false negatives depending on the study (10 preliminary studies of >100 patients, with SNB followed by axillary clearance (AC)).
2. Only 1 of the 12 studies on choice of tracer was randomized. Case series studying isotope methods, injection site, and learning curve had many design deficiencies. The histopathology methods used varied and were not standardized.
3. No recurrence was noted in patients without SN involvement who had not undergone AC in 1 of 2 prospective (unrandomized) studies and in 2 case series. No comparative trials (with AC) assessed short- and medium-term local and regional complications or long-term followup (disease control and survival). These trials, and a trial of the impact of SNB on management strategies for breast cancer and quality of life, are in progress.
4. It was not possible to produce an economic assessment of SNB compared with AC, as there were no comparative studies.

Methods

We carried out a systematic search on SNBs in the MEDLINE, EMBASE, Pascal, CancerLit, and Cochrane Library databases, useful internet sites, and the grey literature: between 1996 and June 2002 for consensus conferences, guidelines, systematic reviews, and economic studies, and between 2000 and June 2002 for clinical trials. We also searched the contents pages of specialist journals and article reference lists. Studies were selected according to level of evidence and design quality using critical review checklists. We selected: comparative trials and series of >100 cases for the feasibility analysis; series of >50 cases for the study of technical steps; only those studies in which data sources and methods of data analysis were specified. The report was discussed by a group of 13 specialists, then submitted to a multidisciplinary peer review group of 21 specialists nominated by professional societies.

Further research/reviews required

Whilst the results of multicenter trials comparing SNB and AC according to lymph node involvement are impending:

1. Learned societies should draw up protocols to define the conditions under which SNB should be performed (standardization of the various steps, training of multidisciplinary teams, defining the indications for lymph node sampling, and construction of decision trees)
2. Clinical researchers should study unresolved technical aspects and new indications (in relation to previous treatment, tumor characteristics, and non-axillary lymph nodes)
3. Patients undergoing SNB without AC should take part in a follow-up protocol
4. Economic studies should analyze direct and indirect costs within the framework of clinical protocols.

Written by Dr Caroline Latapy, Anne Isabelle Poullié, ANAES, France

INAHTA Briefs

Issue 2003/41

Title **The Effectiveness and Cost-effectiveness of Imatinib in Chronic Myeloid Leukemia: A Systematic Review**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;6(33). Mar 2003. www.ncchta.org/execsumm/summ633.htm

Aim

To systematically review the efficacy and cost effectiveness of imatinib in treating chronic myeloid leukemia (CML) in the chronic, accelerated, and blast phases, and compare it to existing drug regimes.

Conclusions and results

Only 3 unpublished Phase II studies of imatinib, one in each phase of CML, were available for inclusion. Due to limited data, information relating to existing treatments was examined to allow indirect comparison. Eleven RCTs (10 chronic phase CML and 1 accelerated/ blast phase) comparing hydroxyurea, busulphan, interferon-a, and other chemotherapy were included. Also, 40 case series studies of existing treatments (27 chronic phase and 13 accelerated/ blast phases) were included. No economic or quality of life studies were found. The imatinib studies had not been peer reviewed. There were important differences in patient characteristics, treatment, and doses between trials. The RCTs were of moderate quality. The case series studies were often small and quality varied widely. Indirect comparisons between case series (as was necessary in this review) are susceptible to confounding and should be interpreted with caution.

In the chronic phase, imatinib shows similar 1-year survival to other treatments, but higher complete HR and CR rates. No information on survival beyond 1 year with imatinib treatment was available. In the accelerated phase, survival with imatinib appears to be longer than with other drugs, but this relies on indirect comparisons of case series. In the blast phase, imatinib appears to show limited longer survival compared to other reports, and complete CR and HR rates for imatinib are within the range of other studies. Patients enrolled in these other studies are not well described, making conclusions difficult. Few studies are published, and study populations are small. Absence of control groups limits the reliability of analysis.

Recommendations

Based on limited evidence, imatinib appears to offer an alternative treatment for CML in the accelerated and blast phases. Information about imatinib in the chronic phase was insufficient to draw firm conclusions about survival. Cost–utility estimates for imatinib are particularly sensitive to assumptions about long-term survival, and may be extremely high.

Methods

Randomized controlled trials (RCTs), cohort studies, case series of first- and second-line drug treatments (minimum of 20 participants), economic analyses, and quality of life studies were included. Novartis provided pre-publication reports of 3 Phase II studies. The report represents a narrative summary – no formal statistical synthesis of results was undertaken.

Further research/reviews required

More research into imatinib for CML is needed. Key areas include:

1 Efficacy of imatinib in chronic phase CML in the long term

2. RCTs to establish the effectiveness of imatinib in all phases of CML compared to IFN-a, hydroxyurea and other chemotherapy

3. Further elucidation of the relationship between response rates (HR and CR) and long-term survival with different treatments in all phases of CML.

Written by Dr Alison Round, North & East Devon Health Authority, Exeter, UK

Title **A Systematic Review and Evaluation of the Use of Tumor Markers in Pediatric Oncology: Ewing's Sarcoma and Neuroblastoma**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(5). Feb 2003. www.ncchta.org/execsumm/summ705.htm

Aim

1. To perform the first systematic review of studies of tumor markers in the Ewing's sarcoma family of tumors (ESFT) and neuroblastomas to identify measures of potential clinical value for the clinical areas of screening, diagnosis, prognosis, and monitoring; the review focuses particularly on the role of markers for defining prognosis.
2. To facilitate development of future research strategies, including improving scientific reporting and specifying deficiencies in the literature.

Conclusions and results

Many papers were identified. For ESFT, the following were found to be potentially important prognostic tools and associated with a worse outcome: high levels of serum lactate dehydrogenase, lack of S-100 protein expression in the tumor, and lack of expression of the EWS–FLI type 1 fusion transcript in the tumor. For neuroblastomas, the following were found to be potentially important tools and associated with a worse outcome: amplification of the MYC-N gene; expression of diploid cells (a DNA index of 1) in the tumor; high expression of neurone-specific enolase in the tumor at diagnosis; high serum levels of lactate dehydrogenase and/or ferritin; high multidrug resistance gene-product expression in the tumor; gain of chromosome 17q; deletion of chromosome 1p; low tumor expression of CD44 and/or TrkA; and a low urinary VMA:HVA ratio.

Recommendations

The evidence is insufficient to judge the clinical role of tumor markers in treating the two childhood malignancies studied. Many markers have been studied, but most studies are so poorly designed and reported that strong clinical conclusions cannot be made from this systematic review. However, the authors identified markers that showed possible prognostic importance. Rapid development of genetic epidemiology may soon provide new genetic markers and sequences that supersede many of the markers identified as important.

Methods

MEDLINE, EMBASE, and CancerLit were searched from 1966 to February 2000. Papers had to provide a quantitative result or tabulated individual patient data (IPD) evaluating the use of a tumor marker in ESFT or neuroblastomas, based on primary research data from humans relevant to screening, diagnosis, prognosis, or monitoring. Meta-analysis was performed for tumor markers on which 3 or more papers provided data. For meta-analysis of prognostic data, estimates of the natural log of the hazard ratio and its variance were sought. If direct estimates were not reported, indirect estimates or IPD were used.

Further research/reviews required

Nine key issues for further research are discussed. The review demonstrates the need for better reporting and design of studies. The authors present guidelines on how to report the results of prognostic marker studies. Primary studies of prognostic markers need to make available their individual patient data, as this is the most viable way to facilitate evidence based reviews, and thus would allow evidence based conclusions and policy decisions to be made to improve patient care.

Written by Dr Richard Riley, Dept of Epidemiology and Public Health, University of Leicester, UK

Title **First and Second Trimester Antenatal Screening for Down's Syndrome: The Results of the Serum, Urine and Ultrasound Screening Study (SURUSS)**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(11). April 2003. www.ncchta.org/execsumm/summ711.htm

Aim

To identify the most effective, safe, and cost-effective method of antenatal screening for Down's syndrome using nuchal translucency (NT), maternal serum, and urine markers in the first and second trimesters of pregnancy, maternal age in various combinations.

Conclusions and results

The false-positive rates (FPR) for an 85% detection rate (DR) were as follows: integrated test 1.2%, serum integrated test 2.7%, combined test 6.1%, quadruple test 6.2%, triple test 9.3%, double test 13.1%, NT measurement 20%. With the serum integrated test, 10 weeks is the preferred time in pregnancy for the PAPP-A measurement. For the integrated test and the combined test this timing is less critical. The lower FPR with the integrated test compared with other tests means that at an 85% DR there would be 9 diagnostic procedure-related unaffected fetal losses per 100 000 women screened compared with 44 using the combined test or 45 with the quadruple test. Screening using the integrated test is less costly because savings in the cost of diagnosis due to low FPR may offset extra screening costs. To achieve an 85% DR, the estimated cost to the UK NHS would be £15 300 per Down's syndrome pregnancy detected. The corresponding cost using the second trimester quadruple test would be £16 800, and using the first trimester combined test it would be £19 000.

Recommendations

Screening performance in the first trimester of pregnancy was similar to that in the second trimester, and in either it was much less effective than integrating screening measurements from both trimesters into a single test. The evidence in this report does not support retaining the double test, the triple test, or NT measurement on its own (with or without maternal age) – each would lead to many more women having invasive diagnostic tests, without increasing the proportion of Down's syndrome pregnancies detected.

Methods

A prospective study of women booked for antenatal care at about 9–13 weeks of gestation, with followup to identify pregnancies with Down's syndrome ascertained through second trimester screening or at birth. NT measurements were included if obtained between 9 and 13 weeks of pregnancy. A pair of serum and urine samples was collected in the second trimester and included if obtained between 14 and 20 weeks. Urine and serum samples from each affected pregnancy and five matched controls were tested. The matching criteria were gestation, duration of storage, and center. Screening performance of individual markers and combinations of markers together with maternal age was assessed by standard methods. Serum samples from 600 controls collected between 9 and 22 weeks' gestation were tested to secure a larger set to determine screening performance using distribution parameters based on dates.

Further research/reviews required

Described in the main report.

Written by Prof Nicholas Wald, Barts and the London Queen Mary School of Medicine and Dentistry, London, UK

Title **Novel Antipsychotics for Agitation in Dementia: A Systematic Review**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada;
Tel: +1 613 226 2553, Fax: +1 613 226 5392

Reference CCOHTA Technology Report, Issue 36, March 2003. ISBN 1-894620-78-X (print); ISBN 1-894620-79-8 (electronic): www.ccohta.ca

Aim

To assess the efficacy and safety of the eight novel antipsychotic drugs (amisulpride, clozapine, olanzapine, quetiapine, risperidone, sertindole, ziprasidone, and zotepine) used to manage dementia-associated agitation (DAA).

Conclusions and results

Seven randomized controlled trials (RCTs) met the criteria for inclusion: two of low quality and five of moderate to high quality. No trials comparing different novel antipsychotics to each other were found. Of the eight novel antipsychotics developed, only RCTs involving olanzapine and risperidone were identified. For institutionalized elderly patients, the efficacy of intramuscular olanzapine was comparable to that of lorazepam (a benzodiazepine) and better than that of placebo. Adverse events at 24 hours were the same for all three patient groups studied. Of the longer-term trials (6 to 12 weeks) identified, the results of the newer trials supported the efficacy (measured using behavioral scales in elderly patients) of olanzapine and risperidone compared to placebo, whereas the results of the older trials did not. Both drugs increased some types of side effects. When risperidone was compared to the conventional antipsychotic agent haloperidol, efficacy was the same for both drugs. However, haloperidol significantly increased the incidence of extrapyramidal symptoms.

Recommendations

Not applicable.

Methods

Databases were searched for studies published from 1985 onwards that compared a novel antipsychotic prospectively with placebo, with a traditional antipsychotic, or with another novel antipsychotic. Results were augmented by searching relevant websites, hand searching bibliographies and abstracts, and contacting appropriate experts and agencies. Information regarding unpublished studies was requested from the drug manufacturers. Two reviewers independently reviewed the citations and abstracts.

Further research/reviews required

As DAA is a long-term condition, trials longer than the currently identified 6- to 12-week studies are needed. Also, cost-effectiveness analyses are needed to help clarify relative costs and benefits of these expensive drugs.

Written by KH Pwee, VK Shukla, N Herrmann, B Skidmore, CCOHTA, Canada

Title **Exercise-Based Cardiac Rehabilitation Programs for Coronary Artery Disease: A Systematic Clinical and Economic Review**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada;
Tel: +1 613 226 2553, Fax: +1 613 226 5392

Reference CCOHTA Technology Report, Issue 34, March 2003. ISBN 1-894620-20-8 (print); ISBN 1-894620-19-4 (electronic): www.ccohta.ca

Aim

- To assess the clinical effectiveness and cost effectiveness of exercise-based cardiac rehabilitation (CR) for secondary prevention of coronary artery disease (CAD)
- To discuss the impact of the evidence on the direction and development of CR services for secondary prevention of CAD in the Canadian healthcare system.

Conclusions and results

Clinical Effectiveness: Forty-six clinical trials met the criteria for meta-analysis, including 10 randomized controlled trials (RCTs) not included in the 2001 Cochrane Collaboration review. CR programs with an exercise component – both exercise-only (EX CR) and comprehensive cardiac rehabilitation (CCR) programs – have beneficial effects on cardiac mortality. In total mortality, EX CR programs show a statistically significant reduction, whereas CCR programs show a trend in that direction.

Cost-Effectiveness: Three full economic evaluations were analyzed. The results suggest that CR with exercise is cost effective. Analysis of three cost studies suggests that CR with an exercise component may lower costs through reduced rehospitalization and drug use. The literature reports maximum cost effectiveness when patients maintain the required exercise level over the long term.

Health Sector Impact: Although the cost studies suggest that switching to CR from standard care would save cost over time, short-run annual expenditures could increase by $225 million if supervised CR became standard practice in Canada.

Recommendations

Not applicable.

Methods

Updating a Cochrane Collaboration review (2001), RCTs of CR programs with an exercise component were systematically reviewed in two groups: CCR vs. usual care or CR EX vs. usual care. The study included both genders of all ages, in hospital and community-based settings, who had documented CAD. Main outcome measures were all-cause mortality and cardiac mortality. Economic studies (RCT and non-RCT) using the same population and interventions were also systemically reviewed. To assess the potential impact of CR programs on health policy, comprehensive literature searches and consultations with clinical experts were carried out.

Further research/reviews required

Patients should be tracked to better assess the long-term impact of CR. A prospective RCT in a Canadian setting with a concurrent economic evaluation is needed. Other areas to be explored further include compliance, alternative care settings and delivery approaches, and under-represented populations (females, the elderly, ethnic groups, and higher risk patients).

Written by Brown A, Taylor R, Noorani H, Stone J, Skidmore B, CCOHTA, Canada

Title	**Stroke Rehabilitation Services: Systematic Reviews of the Clinical and Economic Evidence**
Agency	**CCOHTA, Canadian Coordinating Office for Health Technology Assessment** 865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada; Tel: +1 613 226 2553, Fax: +1 613 226 5392
Reference	CCOHTA Technology Report, Issue 35, March 2003. ISBN 1-894620-76-3 (print); ISBN 1-894620-77-1 (electronic): www.ccohta.ca

Aim

To examine the clinical effectiveness and cost effectiveness of stroke rehabilitation interventions through four comparisons:

- Stroke unit (SU) care vs. care on a general medical ward or geriatric ward
- The impact of different intensities of rehabilitation therapies
- Early supported discharge (ESD) services vs. usual care
- Rehabilitation in the community vs. usual care.

Conclusions and results

No primary studies of different therapy intensities were identified.

Clinical Effectiveness: Twenty-two randomized controlled trials (RCTs) met the inclusion criteria, but none was carried out in Canada or the US. Methodological quality averaged moderate to good. Results show that stroke patients who receive organized inpatient care in a SU are more likely to be alive, independent, and living at home. Patients receiving ESD show significant reductions in the length of hospital stay. No significant differences were observed in primary outcomes between home-based rehabilitation and usual care.

Cost-Effectiveness: Fourteen primary economic studies, mostly of moderate quality, met the inclusion criteria: 3 of SU care, 8 of ESD services, and 3 of community rehabilitation. There is some evidence that the total cost of SU care is comparable to general ward care. Some studies suggest a trend toward lower cost for ESD services compared to usual care. No firm conclusions can be drawn about the relative cost of home-based care vs. usual care.

Recommendations

Not applicable.

Methods

A clinical trial filter and an economics filter were used to search databases and bibliographic systems to identify literature from January 1995 to July 2002. RCTs with a followup of 6 months or longer postrandomization were included in the effectiveness review. The study population included men and women of all ages, in hospital-based and community-based settings, who met a clinical definition of stroke. Outcome measures included death, physical dependency, residence at the end of scheduled followup, health-related quality of life, and length of hospital stay. Studies eligible for the economic review included either economic evaluations or comparative cost analyses.

Further research/reviews required

For stronger conclusions regarding clinical effectiveness, quality of life, and cost effectiveness of interventions after stroke, further research is needed, particularly in a Canadian setting.

Written by Noorani HZ, Brady B, McGahan L, Teasell R, Skidmore B, Doherty TJ, CCOHTA, Canada

Title **Treatment of Drug-Addicted Detainees**

Agency **GR, Health Council of the Netherlands (Gezondheidsraad)**
PO Box 16052, 2500 BB The Hague, The Netherlands; Tel: +31 70 3407520
Fax: +31 70 3407523

Reference Health Council of the Netherlands, 2002; publication no. 2002/08. Full text available at www.healthcouncil.nl (in Dutch, with Executive Summary in English)

Aim

To advise the Minister of Health, Welfare and Sport and the Minister of Justice on the scientific state of the art concerning treatment options for detainees addicted to drugs.

Conclusions and results

Approximately 33% to 50% of detainees in the Netherlands have a serious addiction. About 15,000 people, mostly male, with severe addiction are placed in penal institutions each year. Many addicted detainees are polydrug users, mainly heroin and cocaine. At least half of addicted detainees have had previous addiction-related contacts with help providers. Addicted detainees have the same rights to health care as addicts in the community, but continuity of care is not currently guaranteed. Treatment of patients also varies widely among Dutch penal institutions. Some physicians, without the detainee's consent, replace methadone treatment with abstinence-based treatment. The Health Council finds this to be undesirable. The Penal Care Facility for Addicts (Dutch acronym: SOV) is a new sanction in the Dutch Penal Code implying involuntarily admission to a drug addiction treatment center for a maximum of 2 years. The SOV is the most draconian measure within the range of pressure and compulsion that the State can apply to delinquent addicts. Pressure will be exerted on detainees to cooperate with treatment. Whether this will produce the desired result remains an open question.

Recommendations

The Health Council recommends that the professional group should reach consensus on treatment standards, and that a person's methadone treatment should not be interrupted during brief detentions. The Council recommends that it should be possible to continue methadone treatment in addicts detained on remand. Convicted persons imprisoned beyond 6 months may undergo abstinence treatment, but only with their consent. Although compulsion is inappropriate, the detention period should be used to encourage drug addicts to work on their addiction. Abstinence is generally seen as the goal. Harm reduction is also an important objective. Addicted ex-detainees should receive followup care to help reduce the consequences of addiction or maintain abstinence. Followup care is a major factor in the success of treatment programs, but followup care is often absent. The Health Council recommends broadening the legal option to impose followup care. This could be achieved by, eg, combining a sentence with mandatory probation contact or by reintroducing conditional release.

Methods

Systematic review of published scientific literature. Expert committee. Peer review of draft report.

Further research/reviews required

The Health Council feels that the SOV measure should be evaluated. Rather than focusing solely on reducing criminal behavior, such evaluation must address the issue of long-term reduction of addiction. The Health Council also feels that the effects of methadone treatment for addicts for whom SOV makes up part of their sentence should be investigated.

Written by Mrs CJ (Hanneke) van de Klippe, LL.D., GR, The Netherlands

Title	**Acupuncture: Evidence from Systematic Reviews and Meta-Analyses**
Agency	**AHFMR, Alberta Health Technology Assessment Unit** Alberta Heritage Foundation for Medical Research Suit 1500, 10104-103 Avenue NW, Edmonton, Alberta T5J 4A7, Canada
Reference	ISBN 1-896956-56-4HTA 27: Series A (English), May 2002, full text downloadable www.ahfmr.ca

Aim

To systematically review the scientific evidence and analyze the evidence from systematic reviews on the effectiveness of acupuncture for any condition.

Conclusions and results

The included reviews (n=23) covered dental/temperomandibular dysfunction pain, headache, tinnitus, asthma, stroke rehabilitation, antiemesis, neck/back pain, chronic pain, fibromyalgia, induction of labor, addiction, smoking cessation, and weight reduction. There were wide variations in methods, eg, manual or electrical stimulation, number of needles per treatment, needle insertion technique, and treatment frequency. All of these factors may influence the outcome.

Acupuncture is relatively safe, but may have minor (eg, fainting) and serious (eg, hepatitis) adverse effects. Techniques differ across cultures and practitioner groups, and these variations are associated with different risks. The rate of adverse events varies by the condition being treated and body part involved. Overall, the rate of reported, serious adverse events was low.

The evidence supports acupuncture as an effective treatment for dental pain and postoperative nausea and vomiting. Evidence for other conditions, eg, idiopathic headache, chronic pain, smoking, and fibromyalgia, was inconclusive. Most reviews with a good quality rating found acupuncture to be as effective, in the short-term, as conventional or no treatment for these conditions. However, better quality research is needed. There was no indication as to the specific acupuncture method that is most appropriate for treating dental pain. For treating postoperative nausea and vomiting, acupuncture was shown to be effective in adults, except when administered under anesthesia.

Recommendations

Many issues in acupuncture research require further study. Based on the limited evidence, it would appear premature for regional health authorities to implement an acupuncture program, other than for postoperative nausea and vomiting for selected indications and patients. For all other conditions the effect of acupuncture is unclear, and its clinical value is questionable. Due to the lack of detail on service providers, it was not possible to associate treatment effect, or lack of effect, with the expertise/training of the provider.

Methods

A systematic review of the literature published from 1990 to July 2001, and an appraisal of the quality was conducted. The search included MEDLINE (Ovid) and PreMEDLINE, HealthSTAR (Ovid), Best Evidence (Ovid), CINAHL (Ovid), EMBASE (Ovid), AMED (Ovid), Cochrane Database of Systematic Reviews, CMA practice guidelines- CPG infobase, National Guideline Clearinghouse, DARE, HTA, EED; www: ECRI, Bandolier, and other HTA agency websites. This report was externally reviewed by 5 methodological or field experts.

Written by Patricia Leggett Tait, Laurie Brooks, Christa Harstall, AHFMR, Canada

Title **Prevention of Relapse in Alcohol Dependence**

Agency **NHS QIS, NHS Quality Improvement Scotland (formerly HTBS)**
Delta House, 50 West Nile Street, Glasgow G1 2NP, Scotland

Reference Slattery et al., 2003. Health Technology Assessment Report 3, Glasgow: Health Technology Board for Scotland. ISBN 1-903961-38-6

Aim

To determine which intervention(s) yield the maximum maintenance of recovery among those with alcohol dependence who have undergone detoxification.

Conclusions and Results

The meta-analysis suggested similar, statistically significant, beneficial effect sizes for four psychosocial interventions, ie, behavioral self-control training, motivational enhancement therapy, marital/family therapy, and coping/social skills training. A similar, statistically significant, beneficial effect was found for two pharmacological interventions, ie, acamprosate and naltrexone. No benefit was demonstrated for disulfiram, however only unsupervised disulfiram could be included in the analysis. One well-conducted randomized study of supervised oral disulfiram found a benefit likely to contribute to prevention of relapse. The economic analysis shows that four psychosocial therapies, and acamprosate and naltrexone (when combined with effective psychosocial therapies) are cost effective. Furthermore, all yield savings to NHSScotland by avoiding costs of alcohol-related disease.

Recommendations

- Psychosocial interventions that should be available to those with alcohol dependence who have undergone detoxification and are newly abstinent are: coping/social skills training, behavioral self-control training, motivational enhancement therapy, and marital/family therapy. Other psychosocial treatments are not recommended.
- Acamprosate and supervised oral disulfiram are recommended as treatment options in conjunction with psychosocial interventions. Naltrexone does not have authorization for treatment of alcohol dependence in the UK and is not recommended for routine use in NHSScotland.
- The recommended psychosocial interventions should be administered by appropriately trained and competent professionals using standardized protocols.
- Health professionals should carefully consider the choice of treatments following discussion with patients about their individual needs, preferences, and circumstances.
- NHS specialist services should contact people who drop out of treatment to offer another appointment and make provision for continuing care. They should be aware of mutual help and nonstatutory agencies operating in their area. Introduction to such agencies should be part of the overall strategy.
- NHS Boards should ensure that their core services are uniformly acceptable and accessible to all, considering the special service needs of subgroups.
- Long-term audit data should be collected for all interventions to evaluate patient outcomes and resource consequences of using the therapies in various Scottish settings.

Methods

Systematic literature searching was used to identify evidence published in scientific literature. Evidence was submitted from professional and patient groups, manufacturers, other interested parties, and experts. Clinical effectiveness, organizational issues, and patient issues were appraised and an economic evaluation performed. A meta-analysis of success rates following 4 psychosocial and 3 pharmacological interventions provided input to the cost-effectiveness analysis. A qualitative study was commissioned to elicit the views of service users.

Written by Jim Slattery and Susan Quinn, NHS QIS, UK

Title **A Systematic Review of Holmium Laser Prostatectomy for the Treatment of Benign Prostatic Hyperplasia**

Agency **ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical**
PO Box 688, North Adelaide, South Australia 5006, Australia; Tel +61 8 8239 1144, Fax +61 8 8239 1244

Reference ASERNIP-S Report Number 23, ISBN 0909844577; Full text available: www.surgeons.org/asernip-s/publications.htm

Aim

To compare the safety and efficacy of holmium laser resection of the prostate (HoLRP) and/or holmium laser enucleation of the prostate (HoLEP) and transurethral resection of the prostate (TURP).

Conclusion and results

Three randomized controlled trials (RCTs) comparing HoLRP and TURP and two comparing HoLEP and TURP were identified, as was one uncontrolled comparative study comparing each of the holmium techniques with TURP. There were 13 HoLRP case series and 10 HoLEP case series. The quality of the evidence was average. Both of the holmium laser procedures were found to be superior to TURP in several key indicators of blood loss (transfusion rates, postoperative bladder irrigation, duration of catheterization, and length of hospital stay), although blood loss itself was not often reported. For other safety outcomes, eg, mortality and rates of perforation, it was difficult to draw firm conclusions due to a lack of high quality data. The holmium laser procedures appear to be equivalent to TURP for symptom relief, but TURP was superior to the holmium laser procedures in terms of operative times and retrieved tissue. Adding the mechanical morcellator to HoLEP appeared to result in more tissue retrieval than in TURP. The lack of long-term followup in most holmium laser studies meant that no conclusion could be drawn about the long-term durability of the procedures compared to TURP.

Recommendations

The ASERNIP-S review group classified the evidence base as average. Holmium laser procedures were at least as safe as TURP in terms of blood loss, rates of stricture, and urinary tract infection. For other safety indicators, ie, mortality, perforation rates, and other complications, the relative safety of the holmium laser procedures could not be determined. The holmium laser procedures appear to be at least as efficacious as TURP in the short term, but long-term efficacy could not be determined. At this stage, research priorities should focus on providing long-term followup and addressing problems with losses to followup that threatened the validity of many of the studies.

Methods

OVID PreMEDLINE, OVID MEDLINE, Current Contents, Cochrane Library, EMBASE, UK National Research Register, NIH Clinical Trials.Gov, PubMed, Science Citation Index, SIGLE, and the HTA Database were searched through August 2002. Studies were included, without language restriction, if they dealt with benign prostatic hyperplasia and contained data on at least one of the specified outcomes. Studies that utilized combination laser therapy were excluded. TURP case series derived from RCTs of more than 50 patients were also retrieved as benchmark information.

Written by Tooher et al, ASERNIP-S, Australia

Title **Systematic Review of Laparoscopic Live-Donor Nephrectomy. Second Update and Reappraisal**

Agency **ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical**
PO Box 688, North Adelaide, South Australia 5006, Australia; Tel +61 8 8239 1144, Fax +61 8 8239 1244

Reference ASERNIP-S Report Number 35, ISBN 0909844585, Full text available: www.surgeons.org/asernip-s/publications.htm

Aim

To compare the safety and efficacy of laparoscopic live-donor nephrectomy (LLDN) and open live-donor nephrectomy (OLDN).

Conclusions and results

Included were 72 studies, whereof 44 were comparative and 28 were case series or case reports. The quality of the evidence was average. Regarding safety for donors, a distinct difference was not found between laparoscopic and open approaches. Donor mortality was not reported for either procedure. Complication rates were similar although types differed between the two procedures. Conversion rates for LLDN to an open procedure ranged from 0% to 13%. Regarding efficacy, LLDN appears to be a slower operation with longer warm ischemia times than OLDN, but this did not increase the rate of delayed graft function for recipients. Donor postoperative recovery and convalescence (parenteral narcotic use, time to oral intake, time to ambulation, length of hospital stay, and return to work) was superior for LLDN, making it potentially more attractive for living donors. Short-term graft function and survival did not appear to differ between the two techniques, but long-term complication rates and allograft function remain unclear, and further long-term followup is required.

Recommendations

The ASERNIP-S review group rated the evidence-base as average. LLDN was rated at least as safe as OLDN for donors in the short-term, although long-term complication rates have not been fully established. LLDN was rated at least as efficacious as OLDN for donors, with advantages in convalescence. Graft function and survival were similar for recipients in the short term, but long-term efficacy could not be determined. Well-conducted, concurrently controlled comparative studies and the publication of long-term followup data would assist in resolving some the remaining questions on the safety and efficacy of LLDN. Given the remaining issues, particularly long-term efficacy for recipients, an update and reappraisal of this review should occur within 2 to 5 years.

Methods

OVID PreMEDLINE, OVID MEDLINE, Current Contents, Cochrane Library, EMBASE, UK National Research Register, NIH Clinical Trials.Gov, PubMed, Science Citation Index, SIGLE, and the HTA Database were searched through March 2003. Studies were included if they dealt with laparoscopic live-donor nephrectomy and contained data on at least one of the specified outcomes. Studies that utilized hybrid open-laparoscopic approaches were excluded, as were studies where indications were mixed unless the results of live-donor nephrectomy could be separated. The comparator procedure was open live-donor nephrectomy. The specified outcomes were perioperative, short- and long-term donor morbidity and mortality rates, donor convalescence, and recipient graft function and survival.

Written by Tooher et al, ASERNIP-S, Australia

Title **Systematic Review and Economic Evaluation of the Effectiveness of Infliximab for the Treatment of Crohn's Disease**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(3). April 2003. www.ncchta.org/execsumm/summ703.htm

Aim

1) How effective is infliximab as second- or third-line treatment for severe active Crohn's disease in adults not responding to usual treatment? 2) How effective is infliximab at reducing the number of draining fistulae in adult patients with fistulizing Crohn's disease not responding to usual treatment? 3) What is the rate and severity of adverse effects with infliximab? 4) What adverse events are associated with repeated treatment with infliximab? 5) How cost-effective is infliximab for the above indications compared to standard practice?

Conclusions and results

Infliximab in chronic active Crohn's disease, resistant to usual treatment, was evaluated in 3 trials involving 754 patients. A single dose of infliximab showed significant benefit at week 4, with approximately 30% of patients achieving remission of symptoms. Benefit was short-lived with most patients relapsing beyond week 12. Data on repeated treatment were less clear. One trial evaluated infliximab in fistulizing Crohn's disease. A 3-dose treatment resulted in complete healing of perianal/ abdominal fistulae for more than 21 days in 46% of patients treated with infliximab vs. 13% treated with placebo. Again, benefit was short-lived, with a median duration of 3 months. For a 70 kg patient, the cost of one dose of infliximab, 5 mg/kg, is about £1800, and a 3-dose course costs about £5400. In the Schering-Plough Ltd model, the cost/QALY in treating chronic active Crohn's disease was £6700 with a single-dose treatment, £10,400 with episodic re-treatment, and £84,400 with maintenance treatment. The benefits may be overestimated due to assumptions that the drug influences the natural history of the disease. In fistulizing Crohn's disease, the cost/QALY values were high. The chronic active model was sensitive to rate of 'flare' for episodic treatment. The flare rate chosen was 10%. If more frequent flare was seen, then costs increased substantially. The fistulizing model was relatively insensitive to costs offset, even when assuming 100% offset.

Recommendations

Infliximab is a specialized treatment requiring intravenous administration. Patients considered for infliximab treatment must be fully assessed by specialists experienced in managing severe Crohn's disease. These patients will have disease that is not amenable to conventional medical and surgical management. Use of infliximab is likely to be limited to a small group of patients, in whom benefits over existing treatment can be expected.

Methods

RCTs addressing the above issues were systematically reviewed. The economic evaluation submitted by Schering-Plough Ltd was critiqued and the cost/quality-adjusted life-year (QALY) re-estimated by adjusting the assumptions.

Further research/reviews required

Further research is needed in this rapidly developing field. Research needs to clarify optimal dosage and dosage frequency for infliximab, the characteristics of poorly responding patients, and its optimal place in therapy among the other treatment options, including surgery.

Written by Mrs Wendy Clark, Department of Medicines Management, Keele University, UK

Title **Clinical Effectiveness and Cost Effectiveness of Routine Dental Checks: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(7). May 2003. www.ncchta.org/execsumm/summ707.htm

Aim

1) How effective and cost effective are routine dental checks in improving quality of life and reducing morbidity of dental caries and periodontal disease in children and adults? 2) How effective and cost effective is it to reduce morbidity and mortality from oral cancer in adults?

Conclusions and results

The information included 29 studies in 25 articles. The studies were poorly reported, heterogeneous, and largely not generalizable to the UK. The effects of different dental check frequencies on outcome measures in deciduous, mixed, or permanent dentition were not consistent. Many studies reported an increase in decay, a decrease in teeth, and a decrease in fillings with less frequent dental checks in permanent dentition. In periodontal disease, one study associated decreased attachment with less frequent dental checks (uncertain statistical significance). The effect of dental check frequencies was inconsistent for all other periodontal outcomes. In oral cancer, a study suggests that dental check intervals less than 12 months do not affect tumor size at diagnosis. One study reports that dental check intervals exceeding 12 months may significantly increase the stage and size of tumors at diagnosis. One study showed significant association between increasing dental check frequency and the perception that oral health affects quality of life. Cost-effectiveness analyses were inconclusive. No cost-effectiveness studies were based on UK data and practice. Five resource impact studies appeared to be consistent; less frequent dental checks (7 to 24 months) were associated with reduced assessment and treatment, with little evidence of adverse effects on dental health. The full report presents decision analysis modeling of the cost effectiveness of dental checks of differing frequency on dental caries.

Recommendations

Little evidence supports or refutes the practice of encouraging 6-month dental checks in adults and children. Decision analysis modeling suggests that longer (more than 6-month) dental check intervals, rather than shortening the current interval, would be more cost effective regarding dental caries. The model demonstrates that cost effectiveness varies according to caries risk. Hence, consideration should be given to whether a population recall policy or a recall policy based on an individual's risk of caries would be more appropriate.

Methods

The search strategy for primary studies was designed to identify controlled trials and observational studies (no language restrictions) in electronic bibliographic databases, internet sites, contact with experts, citation checks, and a search of the Cochrane Oral Health Group's specialized register of controlled trials. A Markov decision analysis modeling exercise based on UK data was undertaken for the outcome dental caries.

Further research/reviews required

Further primary research is needed on the role of the dental check and its effectiveness in different oral diseases.

Written by Dr Clare Davenport, Department of Public Health & Epidemiology, University of Birmingham, UK

Title **Effectiveness and Cost Effectiveness of Ultrasound Locating Devices for Central Venous Access: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(12). Mar 2003. www.ncchta.org/execsumm/summ712.htm

Aim

To investigate the clinical effectiveness and cost effectiveness of ultrasound locating devices (ULD).

Conclusions and results

Twenty RCTs of variable methodological quality were identified. Trial evidence suggests that 2-D US is significantly better than landmark for all 5 outcome variables measured for insertions into the internal jugular vein (IJV) in adults. The results also favor 2-D US for insertions into the subclavian vein (SV) and femoral vein (FV) in adults (based on only 1 RCT each). Results of the 3 infant studies on insertion into the IJV suggest that 2-D US has a statistically significant beneficial effect. For Doppler US, only insertions into the IJV in adults (4 RCTs) indicated improved failure and complication rates over landmark. The other 3 Doppler US RCTs for SV insertions in adults and IJV insertions in children offer little support for Doppler over landmark methods. For operators proficient with the landmark method, Doppler US increased the number of failed catheter placements in attempts to catheterize the SV. A spreadsheet decision-analytic model was used to assess cost effectiveness. Because Doppler US is less common than 2-D US, and the effectiveness evidence suggests Doppler is less effective compared with 2-D US, 2-D US compared with landmark was the focus. Costing analysis indicates that the marginal cost of using US for CVA is less than £10 per procedure. Economic modeling indicates that 2-D US in CVA is likely to save NHS resources and improve failure and complication rates. A saving of £2000 per 1000 procedures has been estimated. Sensitivity analysis suggests that the resource saving holds for the three main insertion sites in adults and children.

Recommendations

Evidence suggests that 2-D US-guided CVA particularly via the IJV in adults and children is effective and cost effective. Implications of wider use of 2-D US for CVA are identifiable. Training implications are significant if the US-guided procedure is to be advocated. In emergencies, landmark insertions may still be appropriate. Training in US-guided access should allow operators to remain skilled in the landmark methods.

Methods

Major bibliographic databases were searched up to October 2001 for references on ULDs and central venous lines. Randomized controlled trials (RCTs) were targeted. Only studies with the following features were included: 2-D US or Doppler US compared with the landmark method or a surgical cut-down procedure; study populations requiring placement of central venous lines; and measuring the outcomes listed below. A systematic review of economic analyses was also undertaken.

Further research/reviews required

No RCT evidence was found for the effectiveness of using US for peripherally inserted central catheters or for US versus surgical cut-down. Possible economic and clinical implications of CVA by nurse operators in the NHS may be another area for further research since feasibility has already been demonstrated.

Written by Dr Daniel Hind, Department of Health Policy & Management, ScHARR, University of Sheffield, UK

Title **Can Randomized Trials Rely on Existing Electronic Data? A Feasibility Study to Explore the Value of Routine Data in Health Technology Assessment**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(26). Sept 2003. www.ncchta.org/execsumm/summ726.htm

Aim

To estimate the feasibility, utility, and resource implications of electronically captured routine data for health technology assessment (HTA) by randomized controlled trials (RCTs), and to recommend how routinely collected data could become more effective for this purpose.

Conclusions and results

The study shows that routinely collected data can answer some research questions posed by HTA through RCTs. Data to analyze NHS resource use can usually be identified. Clinical effectiveness can be judged using proxy measures for quality of life (QoL) if clinical data are sufficiently detailed. Patient and professional preferences cannot be identified from routine data, but could be collected by adapting existing instruments. Routine data can facilitate recruitment and may be cheaper to extract and analyze than designed data. Also, they can potentially identify patient outcomes that may be missed in designed data. Despite the potential benefits, the study confirmed that the validity of routinely collected data is suspect, particularly in systems not under clinical and professional control. Other problems include identifying, accessing, and extracting data, and the lack of uniformity in data structures, coding systems, and definitions. If data validity remains suspect, researchers are likely to resist using routine data for HTA by RCTs.

Recommendations

Routine data can potentially support HTA by RCTs. Although the cost of data collection and analysis is likely to fall, the validity of routine data needs to improve. Better knowledge of the capability of local systems, and access to the data, is essential. Routinely captured clinical data, if detailed and precise, could potentially measure patient outcomes.

Methods

The original 4 RCTs were taken as designed, and the trial population as randomized. The research process was modeled from data definition to final writing, substituting routine for designed data activities throughout. The project simulated a novel form of HTA by RCTs, using existing electronic data. The 4 examples addressed different interventions. For each, two analyses were undertaken (one using designed data and the other routine data). The analyses were done independently before discussion and reconciliation of the findings.

Further research/reviews required

Further research is needed to: test prospectively the feasibility of HTA by RCTs through routine data; classify research data needed for HTA and map the data to potential routine sources; assess feasibility, cost, and effects of greater clinical responsibility for hospital episode statistics; explore the feasibility and cost of local information labs maximizing access to, and utility of, routine data; understand and change clinician/researcher attitudes to routine data, particularly as validity and availability improve; define standards to ensure uniformity and validity of data; explore surrogate clinical data for measuring patient-focused outcomes; explore the feasibility and cost of routine completion of health-related QoL questionnaires in clinical practice; and explore the feasibility and cost of routinely capturing patient preference data.

Written by Professor J G Williams, Centre for Post Graduate Studies, University of Swansea, UK

Title **Early Thrombolysis for the Treatment of Acute Myocardial Infarction: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003; 7(15). Apr 2003. www.ncchta.org/execsumm/summ715.htm

Aim

To examine the clinical effectiveness and cost effectiveness of drugs for early thrombolysis in treating acute myocardial infarction (AMI) in hospital and prehospital settings.

Conclusions and results

Hospital: 20 studies met the inclusion criteria (total study population = 142 907 patients). Definitive conclusions on efficacy are that: streptokinase is as effective as nonaccelerated alteplase, tenecteplase is as effective as accelerated alteplase, and reteplase is at least as effective as streptokinase. Some conclusions require interpretation of data, ie, whether streptokinase is as effective as, or inferior to accelerated alteplase, and whether or not reteplase is as effective as accelerated alteplase. Depending on these, two further conclusions on indirect comparisons arise: whether or not tenecteplase is superior to streptokinase, and whether or not reteplase is as effective as tenecteplase. Significant differences exist between drugs in incidence of stroke (streptokinase has the lowest rate). Streptokinase causes more allergic reactions than other drugs.

Prehospital: The search failed to identify prehospital studies that compared the effectiveness of different drugs. Nothing suggests that the effectiveness of a drug will be altered by administration in a prehospital setting. Nine RCTs that examined the efficacy and safety of prehospital thrombolysis are discussed. The required use of heparin with either of the bolus products does not present a practical barrier to their widespread use.

Cost effectiveness and modeling: Eight studies met the inclusion criteria, but were of poor quality and focused on cost effectiveness outside the NHS. Variations in quality-adjusted life-years (QALYs) gained between the individual drugs were small. Streptokinase was the most cost effective.

Recommendations

Decisions on which agent to use must balance risks and benefits relate to mortality and stroke. Statistical comparisons do not offer a basis for conclusions. Given the similarity in outcome, cost effectiveness becomes largely determined by drug acquisition costs. This conclusion was robust to variations in assumptions. Streptokinase was most cost effective.

Methods

A search of the main databases (1980 to 2001) involved several strategies for clinical effectiveness and economic evaluation. Reference lists of included studies, and pharmaceutical company submissions to the National Institute for Clinical Excellence (NICE) were searched to identify other relevant studies. RCTs that compared the specified drugs in the early stages of AMI, in a prehospital or hospital setting, were included. The methodological quality of studies for clinical effectiveness and cost effectiveness was assessed using standard criteria and checklists. Economic evaluation included studies reporting efficacy data primarily based on drug versus drug randomized controlled clinical evidence, explicit synthesis of costs and outcomes in a cost-effectiveness ratio, and full economic evaluation. The economic models in the industry submissions to NICE were critiqued and re-analyzed.

Further research/reviews required

None described.

Written by Ms Rumona Dickson, Department of Nursing, University of Liverpool, UK

INAHTA Briefs

Issue 2003/57

Title **Evaluation of Molecular Tests for Prenatal Diagnosis of Chromosome Abnormalities**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(10). May 2003. www.ncchta.org/execsumm/summ710.htm

Aim

To measure the technical performance of the molecular tests fluorescence in situ hybridization (FISH) and quantitative polymerase chain reaction (Q-PCR) vs. karyotyping, to estimate the relative costs of molecular tests under various conditions, to establish the value to women, clinicians, and others of more rapid molecular test results, to assess the cost effectiveness of molecular tests, and to consider changes in testing protocols.

Conclusions and results

FISH and Q-PCR are not configured to test for rarer abnormalities and do not directly replace karyotyping. Using them to replace karyotyping will leave some abnormalities undisclosed by screening. FISH and Q-PCR are as reliable and precise as karyotyping for the 5 most common chromosome abnormalities. Although 57% of obstetricians prefer molecular tests for most patients and karyotyping for a minority, only 15% would combine both tests. Midwives expressed similar views. Most women and partners expressed a pretest preference for molecular tests. Quality and anxiety measures linked faster test results to a significant increase in health status. Molecular tests cost less than karyotyping. As a replacement in larger laboratories (>1100 specimens per annum), Q-PCR is preferred; for smaller laboratories (<450), FISH is preferred.

Five testing regimes were assessed for cost effectiveness:

1. Molecular test and karyotyping for all women.
2. Molecular test as a replacement for karyotyping.
3. Molecular test for all plus karyotyping for high-risk women.
4. Karyotyping for all plus molecular test for high-risk women.
5. Parental choice plus karyotyping for high-risk women.

Cost-effectiveness analysis found regimes 2, 3, and 5 to be more cost effective than karyotyping. Cost-utility analysis showed a cost per QALY gained of £23 542 to £41 939 for 1 (2–5 could not be assessed by this technique). Regimes 2, 3, and 5 do not detect some rare chromosome abnormalities. Regime 1 could increase annual UK test costs by up to £2.8 million, regimes 2 and 3 save up to £1.76 million per annum, and regime 5 two-thirds of this saving. Regime 4 is cost neutral. Prenatal testing is determined by clinicians, laboratories, and hospitals. Inequities exist, as do regional and local variations in selecting women for screening. Molecular testing without appropriate implementation protocols will result in wide variations. Inattention to patient information will create ethical problems.

Methods

Two-stage trial; assessed in a blinded comparison of molecular tests against karyotyping in a laboratory (stage 1); effectiveness and cost effectiveness measured in a service setting (stage 2). Measurement of anxiety and health status of women; willingness to pay (WTP) for 4 stakeholder groups; and survey of UK obstetricians and midwives.

Further research/reviews required

It was not possible to assess the impact on quality of life and anxiety of replacing karyotyping with molecular tests for all women or selected groups of women within this study. This could be addressed ethically as tests are introduced into service, and should form part of the implementation. Alternative mechanisms to deliver test results should be explored to optimize the advantage of faster results. There is little evidence of the potential impact of false-negative results on parents and on the healthcare system. Further research is needed if molecular tests are to replace some karyotyping tests.

Written by Dr Gill Grimshaw, Warwick Business School, University of Warwick, UK

Title **The Clinical and Cost Effectiveness of Pulsatile Machine Perfusion Versus Cold Storage of Kidneys for Transplantation Retrieved From Heart-beating and Non-heart-beating Donors**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(25). Sept 2003. www.ncchta.org/execsumm/summ725.htm

Aim

To evaluate the clinical effectiveness and cost effectiveness of machine perfusion (MP) vs. cold storage (CS) in preserving kidneys to be transplanted. It addresses MP for kidneys from heart-beating donors (HBDs) and non-heart-beating donors (NHBDs), and the impact on graft function immediately post-transplantation and in the longer term. It also examines whether or not the use of MP can allow valid testing of kidney viability prior to transplantation.

Conclusions and results

Meta-analysis suggested that the use of MP, as compared with CS, is associated with a relative risk of delayed graft function (DGF) of 0.804 (95% confidence limits 0.672 to 0.961). No evidence suggests that this effect is different in kidneys taken from HBDs vs. NHBDs. Meta-analysis of 1-year graft survival data showed no significant effect, but the studies, even when aggregated, were severely underpowered with respect to the likely impact on graft survival. The size of effects demonstrated were in line with those predicted by an indirect model of graft survival based on the association of DGF with graft loss. Economic assessment indicated that in the UK it is unlikely that all costs will be recovered from reducing the incidence of DGF. The probability that MP is cheaper and more effective than CS in the long term was estimated at around 80% for NHBD recipients and 50% to 60% for HBD recipients. Flow characteristics of the perfusate of kidneys undergoing MP may be an indicator of kidney viability, but data were inadequate to calculate the sensitivity and specificity of a test based on this. The concentration of a-glutathione-S-transferase (a marker of cell damage) in the perfusate may be the basis of a valid test. A threshold of 2800 mg/100 g gave a sensitivity of 93% and specificity of 33% (and hence a likelihood ratio of 1.41).

Recommendations

Baseline analysis indicated that in the long term, MP would be expected to be cheaper and more effective than CS for both HBD and NHBD recipients. A definitive study of the clinical benefit of MP to establish its effect on DGF and longer-term graft survival would be valuable, along with an economic evaluation of the benefits. While direct evidence relating to improvements in graft survival would be preferable, the small predicted improvement indicates that a very large sample size would be required.

Methods

A literature search was undertaken to identify relevant studies, and a meta-analysis was performed on the studies that had appropriate comparator groups and reported sufficient data. A structured review examined tests of viability of kidneys on MP. Economic modeling was used to determine the cost effectiveness and cost utility of MP.

Further research/reviews required

In addition to seeking direct evidence of the impact on DGF, research quantifying the impact of DGF on graft survival in this technology is required. Research is also needed to establish whether a valid test (or combination of tests) of kidney viability can be developed.

Written by Dr Jeremy Wight, ScHARR, University of Sheffield, UK

Title **Systematic Review of the Effectiveness and Cost-effectiveness, and Economic Evaluation, of Home versus Hospital or Satellite Unit Haemodialysis for People with End-stage Renal Failure**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(2). May 2003. www.ncchta.org/execsumm/summ702.htm

Aim

To assess the effectiveness and cost effectiveness of home hemodialysis, compared with hemodialysis in a hospital or satellite unit, for people with end-stage renal failure.

Conclusions and results

Twenty-seven studies met the inclusion criteria for effectiveness. Generally, the evidence from the studies suggests that home hemodialysis (HD) is more effective than hospital HD, and modestly more effective than satellite HD. People dialyzed at home generally experienced a better quality of life. However, their partners tended to be less satisfied. Compared with hospital HD, patients on home HD were hospitalized less, tended to live longer, were more likely to be employed full-time, and experienced fewer adverse events during hemodialysis. People on home HD are a highly select group (younger and fewer comorbidities). The evidence indicates lower total costs for home HD compared with hospital HD (payback period about 14 months). Satellite units may vary in cost, depending on staffing intensity and use of the HD machines. In low-risk adults, home HD is less costly than satellite HD, which is less costly than hospital HD. The results of the economic model generally reflected those from the literature for younger, fitter patients without serious comorbidities who received HD for 4–5 hours 3 times per week. The main difference was that, over a 5-year period, the model indicated that home HD was more effective but more costly than satellite HD. Sensitivity analysis was conducted on the cost of home HD, the staffing requirements for satellite HD, the level of benefits each modality of hemodialysis might provide, travel costs, and cost of allowances. The two costs that most influenced the estimates of cost per quality-adjusted life-year (QALY) were travel and allowances for carers of patients on home HD. Generally, the data in the model were limited and came from nonrandomized studies. A new generation of home HD machines is under development, but could not be analyzed in this review.

Recommendations

Home HD has tended to be used on a highly select group of relatively young patients with low comorbidity. This review shows that it is generally more effective than hospital HD on a range of outcomes, and modestly more effective than satellite HD. It is unclear to what extent these findings are influenced by selection bias.

Methods

Electronic searches were used to identify published and unpublished studies. Two reviewers independently extracted data and assessed study quality. A Markov model comparing home with hospital and satellite HD was constructed and used to estimate costs and QALYs for patients starting renal replacement therapy (RRT) on home, satellite, or hospital HD.

Further research/reviews required

Further prospective comparative studies are needed on the effectiveness and cost effectiveness of home versus satellite HD. Further qualitative research is also needed on the acceptability to patients and their carers/families of home HD as a form of treatment.

Written by Graham Mowatt, Health Services Research Unit, University of Aberdeen, UK

Title **A Systematic Review of Atypical Antipsychotic Drugs in Schizophrenia**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(13). June 2003. www.ncchta.org/execsumm/summ713.htm

Aim

To compare clinical effectiveness, safety, and cost effectiveness of 'atypical' antipsychotic drugs in schizophrenia with conventional antipsychotic drugs, placebo, and other atypical antipsychotic drugs.

Conclusions and results

The review included 171 RCTs, of which 28 included commercial-in-confidencedatafromdrugmanufacturers. Additional safety data were found in 52 nonrandomized studies, of which 7 were commercial-in-confidence. In addition to 31 published economic evaluations, 6 were commercial-in-confidence evaluations. Evidence on the effectiveness of new atypical antipsychotic drugs, compared to older drugs, was generally of poor quality. Evidence on the effectiveness of new atypical antipsychotic drugs compared to each other was limited, as was evidence on their cost effectiveness in the UK compared to each other and to older drugs. Risperidone, amisulpride, zotepine, olanzapine, and clozapine were more effective than typical comparators in relieving overall schizophrenia symptoms. Quetiapine and sertindole were no more or less effective than typical antipsychotic drugs in alleviating overall psychosis symptoms. Fewer subjects from atypical drug groups left trials early than from typical drug groups (exceptions were ziprasidone and zotepine). Atypical drugs showed different side-effect profiles. Differences among atypical antipsychotic drugs were observed:

1 More people taking amisulpride, compared to risperidone, reported 'agitation'

2 Fewer people treated with clozapine, compared to risperidone, reported movement disorders, impotence, dry mouth, or insomnia

3 Fewer people treated with olanzapine, compared to clozapine, reported nausea and vomiting, orthostatic dizziness, hypersalivation, and constipation

4 Compared with olanzapine or risperidone, clozapine caused more fatigue, nausea and vomiting excess salivation, tachycardia, orthostatic dizziness, constipation, and leucocytosis

5 Olanzapine caused more weight gain and dry mouth than risperidone, but fewer movement disorders

6 Quetiapine seemed more likely to improve depression than risperidone

7 Zotepine seemed more likely to cause movement disorders than clozapine or risperidone

8 Amisulpride may be more effective than risperidone in terms of 'response'. Clozapine was more effective than typical antipsychotic drugs in treating those with treatment-resistant illness. Clozapine was more effective than typical antipsychotic drugs in improving negative symptoms when illnesses resisted conventional treatment. Zotepine seemed to be more effective on negative symptoms.

Recommendations

Evidence on the effectiveness of new atypical antipsychotic drugs was generally of poor quality, based on short-term trials, and difficult to generalize to the schizophrenia population.

Methods

Cochrane reviews were updated with relevant randomized controlled trials (RCTs) from comprehensive literature searches. Search strategies aimed to retrieve RCTs on effectiveness of atypical antipsychotic drugs and nonrandomized studies of rare or long-term adverse events. Ongoing trial registers were also searched and the reference lists of retrieved papers scanned. A systematic review of cost effectiveness was based on the same sources. An economic model was constructed on data from the systematic review of clinical effectiveness.

Further research/reviews required

Discussed in detail in the report.

Written by Dr Anne-Marie Bagnall, CRD, UK

Title **Towards Efficient Guidelines – How to Monitor Guideline use in Primary Care Agency: NCCHTA (United Kingdom)**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(18). Sept 2003. www.ncchta.org/execsumm/summ718.htm

Aim

To develop a model for using routine data monitoring in evaluating clinical guideline usage in primary healthcare settings.

Conclusions and results

Interviewees recognized some value in guideline-use monitoring, however they were concerned about the practicalities from two perspectives. First, although primary care computing systems were to be found in most general practices, the technology for monitoring was absent in many practices. Training in these skills would be required before monitoring of guideline use could be a practical reality. Second, there were clear signals of a more general lack of interest or awareness in the subject of continuous review of care. This, together with a feeling of being overloaded with new initiatives, meant that implementation of a monitoring framework could be problematic and might need considerable support to make progress.

Recommendations

Effective methods can be developed to monitor guideline use in primary care. However there is a need to address the degree of understanding that many primary healthcare professionals have of the concepts and practical issues in the area of guideline-use monitoring, and of expectations of this within the NHS. In addition, several technical issues are associated with efficient capture of clinical information and its evaluation.

Methods

A monitoring framework was developed following several semistructured interviews with potential users. These data informed a postal survey among a random sample of primary healthcare professionals. Then to test the framework, a further semistructured interview study was used to explore the practical issues related to monitoring guideline use. Case studies were then undertaken to investigate the use of evidence-based review criteria and patient-centered outcome measures as methods to provide monitoring information. A case study in one general practice used interviews to examine the possible costs associated with guideline-use monitoring.

Further research/reviews required

- To what extent should patient concordance with the guideline recommendations be taken into account in assessing clinician conformance with guideline recommendations?
- What are the costs and benefits to patient care of guideline-use monitoring?
- What are the most efficient methods of developing valid and reliable review criteria that are policy and evidence (guidelines) based?
- Are review criteria more useful than guidelines in improving quality of care?
- What additional benefits to patient care can be offered by monitoring patient-centered health outcomes in addition to process of care, and at what cost?

Written by Professor Allen Hutchinson, ScHARR, University of Sheffield, UK

Title **Prioritization of Health Technology Assessment. The PATHS Model: Methods and Case Studies**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(20). Sept 2003. www.ncchta.org/execsumm/summ720.htm

Aim

To develop a method of decision analysis for economic evaluation and triage for prioritizing health research funding.

Conclusions and results

Three case studies to test the model indicated net clinical benefit or no clinical loss of benefit, in addition to health service cost savings above the cost of the trials. For two, values of the proposed trials, as evaluated in the (ex ante) predictions, were consistent with the (ex post) evaluations following publication of the trial results, providing positive tests of the value of the model. In the third case, meaningful ex post analysis was not possible as poor compliance with the trial protocol (indicated in the ex ante evaluation) seriously undermined its conclusions. During the study, at the request of the UK HTA program, the model was also used to evaluate a funding request for a large randomized trial of ß-interferon for multiple sclerosis treatment.

Recommendations

The PATHS model plays a valuable part in the research prioritization process. The method emphasizes the impact of research results on policy and practice (the keystone for NHS research) and the net effects on health benefits and costs. It assesses the cost effectiveness of one piece, or area of research relative to others and may identify ways to enhance the research design, endpoints relevant to implementation, analytical methods, and dissemination.

Methods

Papers of primary relevance that included a proposed model were reviewed in detail, and their models appraised using predetermined criteria and previous experience. From this, the Preliminary Assessment of Technology for Health Services (PATHS) model was developed. It assumes 3 or more possible alternative outcomes or scenarios in research results: 'favorable' to the technology being assessed, 'unfavorable' or 'inconclusive'. An associated net flow of benefits or disbenefits, costs or savings, is identified for each potential research outcome depending on the likely implementation of each 'result scenario' as judged by experts. These net benefits and costs are weighted and discounted in the model to give an expected incremental cost-effectiveness ratio (EICER). EICERs can be estimated for any number of research areas or proposals to inform funding prioritization. The model was tested and evaluated on 3 case studies identified in liaison with the NHS R&D HTA program and the UK Medical Research Council. These were funded research projects where full evaluation was underway and results expected to be published during the PATHS project. They were selected to include trials of surgery, other invasive procedures, and non-invasive health services projects.

Further research/reviews required

- Investigate the scope for synthesizing the strengths of the PATHS model with other approaches such as value of information.
- Compare ex ante and immediate ex post assessments of implementation with long-term followup of actual implementation.
- Assess the robustness of such approaches to the choice and number of experts used.

Written by Professor Joy Townsend, London School Hygiene and Tropical Medicine, London, UK

Title **Riluzole for the Treatment of Amyotrophic Lateral Sclerosis: an Assessment of Clinical Efficacy and Safety**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada;
Tel: +1 613 226 2553, Fax: +1 613 226 5392

Reference CCOHTA Technology Report, Issue 37, August 2003. ISBN 1-894620-99-2 (print); ISBN 1-894978-00-5 (online): www.ccohta.ca

Aim

To assess the potential benefits and harms of riluzole in treating patients with amyotrophic lateral sclerois (ALS), also known as Lou Gehrig's disease.

Results and conclusions

Riluzole has the potential to reduce serious morbidity in some patients at the cost of causing some drug intolerance (withdrawals due to adverse events). There is no information to describe the impact of riluzole on quality of life or time to tracheostomy alone.

Recommendations

Not applicable.

Methods

CCOHTA performed a systematic review of published and unpublished literature on the efficacy of treating ALS patients with riluzole. The outcomes examined were all-cause mortality and tracheostomy-free survival, all-cause morbidity, patient withdrawals due to adverse events, number of patients experiencing adverse events, quality of life, and time to tracheostomy. Two independent reviewers selected four randomized controlled trials comparing riluzole to placebo, abstracted the data, and assessed the quality of each trial.

Further research/reviews required

More adequate reporting of adverse events is needed to complete the clinical picture.

Written by Garces K, Husereau D, Skidmore B, Turnbull J, CCOHTA, Canada

Title **The Measurement of Satisfaction with Healthcare: Implications for Practice From a Systematic Review of the Literature**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(32). Feb 2003. www.ncchta.org/execsumm/summ732.htm

Aims

To address the definition and measurement of satisfaction with healthcare; assess the impact of survey methods on reported satisfaction; identify determinants of satisfaction; explore knowledge gaps; and consider implications for the NHS.

Conclusions and results

Satisfaction is a multidimensional concept and can be measured indirectly by asking users to rate service quality. Asking NHS consumers about satisfaction is essential to assure quality. The review identified 37 empirical studies on methods. These showed that: interviews generate more responses than mail surveys (but cost more); responses to mail and other impersonal methods show greater variability; and low response rates introduce bias. Nonrespondents are often minorities, less educated, and uninsured. Questionnaire design can affect responses. Qualitative approaches use more resources, but access more information. The review of the determinants of satisfaction was guided by a structural framework that identified personal and health service delivery factors as potential influences. The search identified 139 articles (127 data sets) with evidence on these factors. Analysis revealed that reported satisfaction is linked to prior satisfaction with healthcare, respondents' predispositions, service utilization patterns, and granting patients' requests. Sicker patients and people with psychological distress tend to record lower satisfaction except for some chronic disease groups. Older respondents generally record higher satisfaction, but evidence on the effects of gender, ethnicity, and socioeconomic status is equivocal. The most important health service factor affecting satisfaction is the patient-practitioner relationship, including information giving. Choice is associated with higher satisfaction.

Recommendations

Accurate feedback requires robust survey methodologies. Researchers need to promote high response rates, include disadvantaged groups, consider the effect of mode of data collection on users' evaluations, and allow for respondents' expectations when interpreting findings. More use should be made of methods that elicit consumers' relative preferences since this information is important for cost-effective decision making. To promote satisfaction, staff training should address interpersonal issues, and financial/regulatory arrangements should encourage practitioners to foster supportive and interactive relationships with patients.

Methods

Electronic search of 7 major bases. Nonelectronic search involved outreach to a wide range of organizations and personal contacts with leading academics. Over 3000 abstracts were screened for relevance. Articles were excluded if evidence was not generalizable. Quality assessment was undertaken independently by 2 readers.

Further research/reviews required

To investigate:

1. How satisfaction affects health behaviors and outcomes
2. How expectations affect reported satisfaction
3. The effect of health status and recovery on satisfaction and the importance of survey timing
4. The impact of systemic incentive structures on provider behavior and satisfaction;
5. Cross-cultural variations in preferences
6. Incorporating feedback into decision making.

Written by Heather Gage, University of Surrey, Guildford, UK

Title **Systematic Review of Endoscopic Sinus Surgery for Nasal Polyps**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(17). Sept 2003. www.ncchta.org/execsumm/summ717.htm

Aim

To systematically review the clinical effectiveness of endoscopic sinus surgery in removing nasal polyps.

Conclusions and results

Of the 33 studies included, the randomized controlled trials and controlled trials reported symptomatic improvement ranging from 78% to 88% for FESS compared with 43% to 84% for similar techniques (including polypectomy, Caldwell–Luc, and intranasal ethmoidectomy). Disease recurrence was 8% for FESS compared with 14% for Caldwell–Luc, and polyp recurrence was 28% for endoscopic ethmoidectomy compared with 35% for polypectomy. Revision surgery was reported in one study and was the same for FESS and Caldwell–Luc procedures. Percentage of overall complications was reported in one comparative study and was 1.4% for FESS compared with 0.8% for conventional procedures. The case series studies reported symptomatic improvement for patients with nasal polyps ranging from 37% to 99% (median 89%). For the mixed patient groups (with and without polypoid disease) symptomatic improvement ranged from 40% to 98% (median 88%). Total complications in the case series studies ranged from 22.4% to 0.3% (median 6%).

Recommendations

Most studies report that symptoms improve after FESS, with relatively few complications, but little of the evidence is comparative. Results from noncomparative studies do not inform the decisions by ear, nose, and throat (ENT) surgeons and commissioners. Health economics data are also lacking and therefore cannot inform these decisions. FESS may offer some advantages in effectiveness over comparative techniques, but the results vary enormously, and methodological limitations are severe.

Methods

An extensive search aimed to identify all articles where FESS is used to excise nasal polyps. Two reviewers independently screened articles for inclusion according to predefined criteria. Comparative studies were included if they were primary research, focused on FESS to remove nasal polyps, reported patient-relevant outcomes, and were published in English. Case series studies were included if they met the above criteria and enrolled more than 50 patients with polyps. Data were then extracted by one reviewer and checked by a second. A structured form was used to assess internal and external validity of included studies. Comparative data were reported where available. Excluded case series and case reports were grouped and described. A group of 9 ENT experts used the literature and their own experience to list priority research questions. Economic evaluations were sought and described.

Further research/reviews required

Outcomes should be measured to draw conclusions on the risk of relapse and revision after surgery. Cost effectiveness should be addressed in future research on FESS. Patient groups should include people with sinus disease, but be powered to demonstrate differences according to whether the predominant picture is polyps or chronic rhinosinusitis. Outcomes should include symptomatic improvement, complications, and quality of life.

Written by Dr Ken Stein, Peninsula TA Group, University of Exeter, UK

Title **Effectiveness and Cost-effectiveness of Acute Hospital-based Spinal Cord Injuries Services: Systematic Review**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(19). Sept 2003. www.ncchta.org/execsumm/summ719.htm

Aim

To examine: (1) the effectiveness and cost effectiveness of spinal fixation surgery, (2) the consequences of immediate vs delayed referral to a spinal injuries unit (SIU), (3) the number of people with a new spinal cord injury (SCI) who are discharged from hospital without being transferred to an SIU, and (4) the effectiveness and cost effectiveness of steroids for people with SCI.

Conclusions and results

For spinal fixation vs no fixation, 68 retrospective observational studies were found. The results suggested some benefits of fixation surgery. Only 4 studies were found on fixation surgery in SIUs compared with non-SIU hospitals, and no significant differences were seen. All 28 studies on delayed referral to an SIU were retrospective observational studies. In most, study details were poorly reported, and comparability of groups at baseline and on confounding factors was in doubt. Referral and transfer times were not reported separately. Evidence suggested an effect favoring the SIU group for neurological improvement. No relevant published studies were found regarding how many people with a new SCI are discharged from hospital without being transferred to an SIU. Two systematic reviews assessed the effectiveness of steroids. No studies were found that considered both costs and the impact on patient outcomes of a given intervention.

Recommendations

The evidence suggested some benefits of fixation surgery and immediate referral to SIUs compared with delayed or no referral, but data were limited. The data were insufficient to assess whether surgery is more beneficial in SIUs. Further research is required. High-dose methylprednisolone steroid therapy within 8 hours of injury may promote some neurological recovery, but the magnitude of this benefit is unclear. No studies showed how many people with acute SCI are discharged from hospital without being transferred to an SIU.

Methods

Three separate search strategies were used in the 4 key areas. Two reviewers independently screened all study citations. The references in retrieved studies were scanned for additional studies. Study quality was assessed and data were extracted by one reviewer, then checked by the second. Data were summarized within each key area. Searches were carried out to identify economic evaluations. Details of these and a critical appraisal of quality are presented in structured tables. Quality was assessed using a checklist supplemented with additional comments on the adequacy of methodology where appropriate.

Further research/reviews required

Well-designed, prospective observational studies with matched controls are needed to assess spinal fixation surgery and consequences of delayed referral to an SIU. Randomized controlled trials (RCTs) are needed of pharmacotherapy for acute SCI. Primary research involving audits of selected hospital records should ascertain the number of SCI patients not acutely admitted to an SIU. Future research should include full economic evaluations, possibly with a large RCT that considers the costs and consequences of interventions.

Written by Dr Anne-Marie Bagnall, CRD, UK

Title **The Clinical and Cost-effectiveness of Patient Education Models for Diabetes: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(22). Sept 2003. www.ncchta.org/execsumm/summ722.htm

Aim

To assess the clinical effectiveness and cost effectiveness of educational interventions for patients with diabetes compared with usual care or other educational interventions.

Conclusions and results

Twenty-four studies (18 RCTs and 6 CCTs) that compared education with either a control group or with another educational intervention were included. The quality of reporting and methodology was generally found to be poor by today's standards. As part of treatment intensification, education in type 1 diabetes (4 studies) resulted in significant and long-lasting improvements in metabolic control and reductions in complications. In type 2 diabetes (16 studies) a diversity of educational programs did not yield consistent results on measures of metabolic control. Inconsistent results on metabolic control were also found in studies of diabetes of either type (4 studies), with studies of lower quality producing significant effects. Few studies evaluated quality of life. Economic evaluations comparing education with usual care or other educational interventions were not identified.

Recommendations

Education as part of intensifying treatment improves diabetic control in type 1 diabetes. Mixed results in type 2 diabetes mean that no clear characterization is possible as to what features of education may be beneficial. Cost analysis and information from sponsor submissions indicated that where costs associated with patient education were in the region of £500–600 per patient, the benefits over time would have to be very modest to offer an attractive cost-effectiveness profile.

Methods

Electronic databases were searched, references of all retrieved articles were checked for relevant studies, and experts were contacted for advice, peer review, and identification of additional references. Randomized clinical trials (RCTs) and controlled clinical trials (CCTs) were included if they fulfilled pre-specified criteria, eg, followup from inception for 12 months or longer. Data were synthesized through a narrative review because the diversity of studies prevented meta-analysis.

Further research/reviews required

Further research should focus on RCTs with clear designs based on explicit hypotheses and with a range of outcomes evaluated after long followup intervals.

Written by Dr Emma Loveman, NCCHTA/Wessex Institute for Health Research and Development, UK

Title **The Role of Modelling in Prioritising and Planning Clinical Trials**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(23). Sept 2003. www.ncchta.org/execsumm/summ723.htm

Aim

To identify the role of modeling in planning and prioritizing trials. Focuses on modeling methods used to construct disease models and on methods for analysis and interpretation.

Conclusions and results

The review found that modeling can extend the validity of trials by: generalizing from trial populations to specific target groups; generalizing to other settings and countries; extrapolating trial outcomes to the longer term; linking intermediate outcome measures to final outcomes; extending analysis to the relevant comparators; adjusting for prognostic factors in trials; and synthesizing research results. The review suggested that modeling may offer greatest benefits where the impact of a technology occurs over a long duration, where disease/technology characteristics are not observable, where there are long lead times in research, or for rapidly changing technologies. It was also found that modeling can inform the key parameters for research: sample size, trial duration, and population characteristics. One-way, multi-way, and threshold sensitivity analysis have been used in informing these aspects but are flawed. The payback approach has been piloted and may have potential. Expected value of information analysis has been the only existing methodology applied in practice that can address all these issues. Its potential benefit is that the value of research is directly related to its impact on technology commissioning decisions, and is demonstrated in real and absolute rather than relative terms; it assesses technical efficiency in different types of research. Modeling is not a substitute for data collection, but it can identify trial designs of low priority in informing health technology commissioning decisions.

Recommendations

Good practice in undertaking and reporting economic modeling studies requires further dissemination and support, specifically in sensitivity analyses, model validation, and in reporting assumptions. Case studies of the payback approach using stochastic sensitivity analyses should be developed. Use of overall expected value of perfect information should be encouraged in modeling studies seeking to inform prioritization and planning of health technology assessments.

Methods

Systematic reviews of the methodological and case study literature were undertaken. Search strategies focused on the intersection between three domains: modeling, health technology assessment, and prioritization.

Further research/reviews required

Research is required: to assess if the potential benefits of value from information analysis can be realized in practice; on the definition of an adequate objective function; on methods for analyzing computationally expensive models; and on methods for updating prior probability distributions.

Written by Mr Jim Chilcott, ScHARR, University of Sheffield, UK

Title **Cost-benefit Evaluation of Routine Influenza Immunization in People 65–74 Years of Age**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(24). Sept 2003. www.ncchta.org/execsumm/summ724.htm

Aim

To determine the cost effectiveness of influenza vaccination in people aged 65–74 years in the absence of comorbidity.

Conclusions and results

In England and Wales, weekly consultations for influenza and ILI (influenza like illness) remained at baseline levels (less than 50 per 100 000 population) until week 50/1999 and then increased rapidly, peaking during week 2/2000 with a rate of 231/100 000. This rate fell within the range of 'higher than expected seasonal activity' of 200–400/100 000. Rates then quickly declined, returning to baseline levels by week 5/2000. The predominant circulating strain during this period was influenza A (H3N2). Five (0.9%) people in the vaccine group were diagnosed by their GP with an ILI compared to two (1.1%) in the placebo group. No participants were diagnosed with pneumonia by their GP, and there were no hospitalizations for respiratory illness in either group. Significantly fewer vaccinated individuals self-reported a single ILI. There was no significant difference in any of the QoL measurements over time between the two groups. Reported systemic side effects showed no significant differences between groups. Local side effects occurred with a significantly increased incidence in the vaccine group (11.3% vs 5.1%, p = 0.02). Each GP consultation avoided by vaccination was estimated from trial data to generate a net NHS cost of £174.

Recommendations

No difference was found between groups for the primary outcome measure, although the trial was too underpowered to demonstrate a true difference. Vaccination had no significant effect on any of the QoL measures used, although vaccinated individuals were less likely to self-report ILI. The analysis did not suggest that influenza vaccination in healthy people aged 65–74 years would lead to lower NHS costs.

Methods

Participants were randomized to receive either influenza vaccine or placebo (ratio 3:1), with all individuals receiving pneumococcal vaccine unless administered in the previous 10 years. Of the 729 people randomized, 552 received vaccine and 177 received placebo; 726 individuals were administered pneumococcal vaccine.

Further research/reviews required

Future research should look at:

- Ways to maximize vaccine uptake in people at greatest risk from influenza
- The level of vaccine protection afforded to people from different age and socioeconomic populations.

Written by Professor Margot Gosney, School of Food Biosciences, University of Reading, UK

Title	**Osteoporosis – Prevention, Diagnosis, and Treatment**
Agency	**SBU, The Swedish Council on Technology Assessment in Health Care** PO Box 5650, SE-114 86 Stockholm, Sweden; Tel: +46 8 412 32 00, Fax: +46 8 411 32 60, info@sbu.se
Reference	SBU Report 165/1, 165/2, 2003, ISBN 91-87890-86-0, 91-87890-90-9. Full text in Swedish and English summary at http://www.sbu.se

Aim

To systematically and critically assess the scientific evidence on the prevention, diagnosis, and treatment of osteoporosis, focusing mainly on prevention of osteoporosis-related fractures, including economic and ethical aspects of the interventions.

Conclusions and results

There is no scientific evidence to support the use of bone density measurement as a screening method in healthy, middle-aged individuals. Patients with osteoporosis-related fractures are an undertreated group as regards pharmacotherapy and other interventions to prevent new fractures. There is some evidence that physical exercise (to reduce falls) and the use of hip protectors can prevent fractures in the elderly. Combination therapy of calcium and vitamin D is shown to reduce the risk for hip fractures and other fractures except vertebral fractures in elderly women.

Bisphosphonates are shown to reduce the number of fractures, mainly vertebral fractures. SERM is shown to reduce the risk for vertebral fractures in postmenopausal women with osteoporosis.

Important and treatable risk factors for osteoporosis-related fractures are physical inactivity, low weight, tobacco smoking, high alcohol consumption, tendency to fall, impaired vision, low exposure to sunlight, and use of corticosteroids. No particular diagnostic method or measurement site is optimal for determining the risk for fracture in all parts of the skeleton. The various measurement methods – dual energy x-ray absorbtiometry (DXA), ultrasound (QUS), and computed tomography (QCT) – are not directly comparable.

Methods

Literature searches were conducted using MEDLINE, the Cochrane Library, reference lists, Swedish dissertations, and personal communications. Studies were selected based on relevance and predetermined inclusion criteria. The selected studies were reviewed and their quality assessed. The strength of the summarized evidence has been rated on a 3-grade scale.

Further research/reviews required

- Studies in men to investigate pharmacotherapy, fracture prediction by bone density measurement, and assessment of post-fracture rehabilitation interventions.
- Economic assessments are lacking, mainly due to insufficient knowledge about the effects that various osteoporosis interventions have on risks, mortality, quality of life, and costs in different age groups and risk groups.

Written by Viveka Alton, SBU, Sweden

Title **Auto-titrating Nasal Continuous Positive Airway Pressure Systems in the Management of Obstructive Sleep Apnea**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada;
Tel: +1 613 226 2553, Fax: +1 613 226 5392

Reference CCOHTA Technology Report, Issue 39, September 2003. ISBN 1-894978-01-3 (print); ISBN 1-894978-02-1 (electronic): http://www.ccohta.ca

Aim

To review the evidence for the efficacy, effectiveness, and costs of auto-titrating nasal continuous positive airway pressure (APAP) devices in their use for:

- Diagnosis of obstructive sleep apnea (OSA)
- Titration to determine pressure values for treatment with continuous positive airway pressure (CPAP)
- Treatment of OSA using variable-pressure mode.

Conclusions and results

On the basis of the available literature, APAP shows promise, but should be used with caution until further studies establish its effectiveness and cost-effectiveness. Observational studies show a potential use for APAP in diagnosing OSA, although its efficacy in auto-titration (unattended adjustment of pressure) has not been established. Further validation is needed from studies with stronger methodology.

For the treatment of OSA, studies show that APAP uses a lower treatment pressure than CPAP. However, clinical outcomes with APAP are no better than those with CPAP, and it is uncertain whether there is better compliance with APAP. Potential safety issues for patients suffering from cardiac, pulmonary, and other medical conditions arise if APAP is used in settings without prompt access to technical support.

Methods

Two reviewers independently extracted data from 39 relevant studies obtained through a comprehensive search of literature from 1994 and onward. Inclusion criteria specified comparative studies with APAP for persons diagnosed with severe OSA who may require treatment using CPAP. Outcomes for the diagnosis of OSA and for titration using APAP to determine final pressure settings for CPAP included accuracy of diagnosis, costs, and identification of adverse conditions – all in comparison with sleep lab studies using polysomnography. For the therapeutic use of APAP in variable-pressure mode, the outcomes considered included compliance with treatment, effects on sleep patterns, other relevant physiological measures, quality of life, and costs – all in comparison with treatment using conventional fixed CPAP.

Further research/reviews required

Preliminary estimates show that APAP may provide cost savings over CPAP under certain conditions, but further cost studies are required.

Written by Hailey D, Jacobs P, Mayers I, Mensinkai S, CCOHTA, Canada

Title **Gastro-duodenal Ulcers Associated with the Use of Non-steroidal Anti-inflammatory Drugs: A Systematic Review of Preventive Pharmacological Interventions**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada; Tel: +1 613 2262553, Fax: +1 613 2265392;

Reference CCOHTA Technology Report, Issue 38, Sept 2003. ISBN 1-894620-92-5 (print); ISBN 1-894620-93-3 (electronic): www.ccohta.ca

Aim

- To assess the effectiveness of common pharmacological interventions used to prevent upper gastrointestinal (GI) toxicity associated with non-selective non-steroidal anti-inflammatory drugs (NSAIDs)
- To compare the upper GI toxicity of cyclooxygenase-isoform type 2 (COX-2) selective NSAIDs with that of non-selective NSAIDs, with or without concomitant use of gastroprotective agents
- To compare with placebo the upper GI toxicity of the COX-2 selective NSAIDs available in Canada

Conclusions and results

Misoprostol, proton pump inhibitors, and double doses of histamine type-2 receptor antagonists (H_2RAs) were shown to effectively reduce the risk of endoscopically identified NSAID-induced gastric and duodenal ulcers. Standard doses of H_2RAs, however, are ineffective. While misoprostol reduces the risk of NSAID-related ulcer complications, its use is associated with significant adverse effects, particularly at higher doses.

Compared with most non-selective NSAIDs, COX-2 selective NSAIDs have a safer G I profile than other NSAIDs and are better tolerated. An exception is with the comparator diclofenac: no statistically significant differences are observed with this agent. The reduced GI complication rate due to celecoxib may be lost when it is administered with acetylsalicyclic acid; this effect has not been tested with rofecoxib. The benefit of the growing clinical use of COX-2 selective NSAIDs with added gastroprotective agents remains unclear.

Methods

A systematic review of randomized controlled trialswas conducted. The literature was searched to identify trials of prophylactic agents used to prevent upper GI toxicity and trials that assessed the GI safety of the newer COX-2 selective NSAIDs celecoxib (Celebrex™), meloxicam (Mobicox™), and rofecoxib (Vioxx®). Two independent reviewers selected studies, rated the quality of each included trial, and extracted data.

Further research/reviews required

Testing of the clinical use of COX-2 selective NSAIDs with added prophylaxis is needed.

Written by Rostom A, Dubé C, Jolicoeur E, Boucher M, Joyce J, CCOHTA, Canada

Title **Non-ionic Contrast Media: Clinical Relevance of Different CM-products**

Agency **ITA/ Institute of Technology Assessment, HTA-Unit**
Strohgasse 24, 1030 Vienna, Austria; Tel: +43 1 515 81 6589,
Fax: +43 1 710 98 83, cwild@oeaw.ac.at

Reference ITA/ HTA report 1/03: available only in German, 66 pages www.oeaw.ac.at/ita/hta/

Aim

To analyze the many different non-ionic (monomer) contrast media (CM) products in regard to the actual clinical relevance of their differences in order to give advice for more concerted purchasing of CM.

Conclusions and results

Central purchasing of pharmaceuticals is a consideration that arises from the increasing economic pressure on hospital budgets. An assessment was conducted, and funded, by the largest Austrian hospital cooperation (25% of hospital market). Seven different NI-CM are used in routine care. The findings show:

- Osmolality, nephrotoxicity, viscosity, hydrophilicity, and electric charge are the criteria along which the CM can be differentiated.
- The analyzed NI-CM show similar pharmacokinetic and dynamic attributes.
- All analyzed NI-CM are safe in their application. Incompatibility and adverse reactions are minimal, and diagnostic accuracy is at a comparably high level.
- If the iodine concentration and the (intravasal) application protocol are similar, there are only minimal, or not reproducible, differences in safety and diagnostic quality.
- There are no clinically relevant differences between the 7 (analyzed) different non-ionic monomer CM-products.
- Along valid definitions, the products are "me-too" agents – under patent protection.
- In reaction to the many me-too pharmaceuticals, and the enormous price-differences between EU countries, purchasing units of hospitals have started to react: interesting models evolve.

A decision to concentrate on 2–3 products would reduce expenses for CM by 30%. A decision between three modes of (re-)action for hospital purchasers were identified and are proposed as options:

1. Tightening the product range on the basis of best clinical performance (e.g. vigilance register), best offers, or cumulated radiologists' preferences.
2. Inquiry on industry's financial support for technical material, education and training, congresses etc., followed by own price calculation without add-ons (but creating an independent fund) and tender by price instead of by product.
3. Linking commissioning with conditions (comparative research from users' perspective, education and training on purchasers' topics, inpayment in independently administered fund).

Methods

Extensive literature search in MEDLINE searching for substance and labeled product, self-limited by actual availability of older citations, systematic review on 7 non-ionic monomer CM. Additional search for literature (mainly gray) on me-too agents, patent law, and market forces.

Written by Dr Claudia Wild, ITA, Austria

Title **Liquid-Based Cytology and Human Papillomavirus Testing in Cervical Cancer Screening**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada;
Tel: +1 613 226 2553, Fax: +1 613 226 5392

Reference CCOHTA Technology Report, Issue 40, November 2003. ISBN 1-894978-07-2 (print); ISBN 1-894978-08-0 (electronic): http://www.ccohta.ca

Aim

- To compare the diagnostic accuracy of liquid-based cytology (LBC) and human papillomavirus (HPV) testing with that of Papanicolaou (Pap) smears indetecting precancerous or malignant cervical lesions
- To evaluate the comparative cost and cost effectiveness of LBC and HPV testing.

Conclusions and results

Diagnostic Accuracy: 17 reports on 13 unique trials undertaken in 9 countries met the selection criteria for comparing LBC and Pap smears; 23 unique trials met the criteria for comparing HPV testing and Pap smears. Evidence (based primarily on results from split-sample trials) suggests that compared with Pap smears, the use of LBC reduces the proportion of unsatisfactory specimens and generates fewer false negatives for ordinary populations, but not for high-risk populations. HPV testing, alone or with cytology, is more sensitive but less specific than Pap smears.

Economic Review: 7 studies on LBC and 6 on HPV met the selection criteria. Results suggest that LBC screening every 3 years or longer may be cost effective relative to Pap smear screening. Economic modelling based on the use of LBC in a Canadian context is needed before the cost effectiveness of HPV testing can be determined.

Methods

Diagnostic Accuracy: To update a previous CCOHTA review, databases were searched for literature published between January 1997 and July 2003. Comparative trials that examined the diagnostic accuracy of LBC and HPV testing and Pap smears were included. Estimates of test sensitivity and specificity were the primary outcomes. Two reviewers independently extracted data from studies that met the inclusion criteria. Report quality was assessed in terms of recruitment method, verification bias, reference standard, blinding of outcome assessment, and level of industry funding for research.

Economic Review: Economic evaluations or cost studies pertaining to LBC and HPV testing were identified through a literature search. Information on study characteristics, average costs per patient, life days saved, and incremental cost per life year saved relative to Pap smears was summarized.

Further research/reviews required

- High-quality trials that control for verification bias are needed to form a valid and reliable judgment about the diagnostic accuracy of LBC and HPV.
- Economic modelling based on the use of LBC in a Canadian context is needed to assess the cost effectiveness of HPV.

Written by Noorani HZ, Brown A, Skidmore B, Stuart GCE, CCOHTA, Canada

Title **Molecular Diagnosis for Hereditary Cancer Predisposing Syndromes: Genetic Testing and Clinical Impact**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, Ontario K1S 5S8 Canada;
Tel: +1 613 226 2553, Fax: +1 613 226 5392

Reference CCOHTA Technology Report, Issue 41, November 2003. ISBN 1-894978-09-9 (print); ISBN 1-894978-10-2 (electronic): http://www.ccohta.ca

Aim

- To assess the evidence regarding the availability, cost, and analytical and clinical validity of genetic tests for screening and diagnosis of hereditary cancer predisposing syndromes
- To document the impact of genetic testing (GT) on the clinical management of patients with specific hereditary cancer predisposing syndromes.

Conclusions and results

The cost, availability, and analytical and clinical sensitivity of 20 hereditary cancer predisposing syndromes were listed in chart form in three distinct groupings:

- Where GT is generally part of clinical management of affected families
- Where the benefit of GT has been demonstrated, but GT is not part of standard management
- Where the clinical benefit of GT is unclear.

A list of GT services and laboratories in Canada according to province and city was also compiled.

Although new molecular techniques are being developed rapidly, the implementation of GT for many disorders into standard clinical management has not been justified. High cost, variable analytical and clinical validity, limited availability, and legal/social/ethical issues affect integration of GT into the healthcare system.

Methods

To obtain published and unpublished literature, investigators searched electronic databases, contacted genetic test laboratories, and hand searched bibliographies of selected papers. Two reviewers independently selected 457 relevant articles that met the predetermined selection criteria.

Further research/reviews required

Additional data about cost and the impact of GT on health outcomes are needed to help determine appropriate integration and funding of these tests.

Written by Ho C, Banerjee S, Mensinkai S, CCOHTA, Canada

Title	**Prescribed Sick Leave – Causes, Consequences, and Practices**
Agency	**SBU, The Swedish Council on Technology Assessment in Health Care** PO Box 5650, SE-114 86 Stockholm, Sweden; Tel: +46 8 412 32 00, Fax: +46 8 411 32 60, info@sbu.se
Reference	SBU Report 167, 2003, ISBN 91-87890-89-5. Full text in Swedish, English summary at http://www.sbu.se. Translation to English of the full report to be published as a Supplement in 2004.

Aim

The *aim* of the report was to:

- Assess the scientific evidence about positive and negative consequences of being sickness absent
- Review the research on sick leave, current knowledge of its causes, and physician sickness-certification practices
- Identify areas where further research is needed.

Conclusions and results (some examples)

In general

- That individuals having the opportunity to influence their working situation have a lower risk for sick leave
- That the design of the sickness insurance system influences the level of sickness absence
- That members of lower socioeconomic groups have a higher risk for disability pension.

Back and neck diagnoses

- That poor work satisfaction increases the risk for sick leave due to acute back problems

Physicians´ sickness-certification practices

- That physicians view the task of sickness certification as being problematic
- That sickness certificates often are of poor quality.

Recommendations

Only a limited number of studies address the essential aspects of sick leave, and SBU recognizes the need for qualitatively better research (such as longitudinal studies and intervention studies at the individual and group levels, eg, at workplaces).

Methods

A systematic search and assessment of scientifically published studies was undertaken by a multidisciplinary, 11-member team. The search for studies was broad, using literature databases (MEDLINE, PsycINFO, SSCI), reference lists, and personal contacts. The quality of studies found to be relevant, were analyzed according to criteria established for this report.

Written by Anders Norlund, SBU, Sweden

Title	**Surgical Simulation; A Systematic Review**
Agency	**ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical** PO Box 688, North Adelaide, South Australia 5006, Australia; Tel +61 8 8239 1144, Fax +61 8 8239 1244, college.asernip@surgeons.org; www.surgeons.org/asernip-s
Reference	ASERNIP-S Report Number 29. ISBN 0 909844 60 7 Full text available: http://www.surgeons.org/asernip-s/publications2.htm

Aim

To assess the effectiveness of surgical simulators in comparison to each other, no training, or other methods of surgical training.

Conclusion and results

Evidence rating: Poor – there was insufficient evidence since most of the RCTs were flawed and outcomes were often not comparable.

Efficacy: Cannot be determined – the inconclusive outcome of this review may be related to small sample sizes and the validity and reliability of outcome measurements.

Results: 26 RCTs with 668 participants were included, although RCT quality was often poor. Computer simulation generally showed better results than no training, but was not convincingly superior to standard training (eg, surgical drills) or video simulation (particularly when assessed by operative performance). Video simulation did not show better results than no training, and data were insufficient to show if video simulation was superior to standard training or use of models. Model simulation may have been better than standard training, and cadaver training may have been better than model training. None of the RCTs compared computer simulation vs. model training.

Methods

Search strategy: Studies were identified by searching MEDLINE, PREMEDLINE, EMBASE, PsycINFO, CINAHL, Current Contents, Cochrane Library, Science Citation Index Expanded from inception to week 3, 2003. NHS Centre for Research and Dissemination (UK), NHS Health Technology Assessment (UK), and the National Research Register (UK) were searched on 25/03/2003. Additional articles were identified in the reference sections of the studies retrieved.

Study selection: RCTs assessing any training technique using at least some elements of surgical simulation compared to any other methods of surgical training, or no surgical training, were included for review. Articles needed to address at least one of the following outcome measures: surgical task performance, objective or subjective, or satisfaction with training techniques.

Data collection/analysis: Data from studies were extracted by an ASERNIP-S researcher using standardized data extraction tables developed *a priori* and checked by a second researcher. Results were not pooled across studies since outcomes were not comparable. Relative risks for dichotomous outcome measures or weighted mean differences for continuous outcome measures with 95% confidence intervals were calculated for some outcomes in individual RCTs.

Further research/reviews required

Further research was recommended in the context of training for particular performance standards. Ideally, studies should be multicenter trials with standardized approaches and sufficient participants. The skills being evaluated should be part of a standard surgical skills training course, not just stand-alone technical skills. Once efficacy has been determined, cost-benefit analyses could be attempted.

Written by Dr Leanne Sutherland et al, ASERNIP-S, Australia

Title **Systematic Review of Post-vasectomy Testing to Confirm Sterility**

Agency **ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical**

PO Box 688, North Adelaide, South Australia 5006, Australia; Tel +61 8 8239 1144, Fax +61 8 8239 1244, college.asernip@surgeons.org; www.surgeons.org/asernip-s

Reference ASERNIP-S Report Number 39. ISBN 0 909844 59 3

Full text available: www.surgeons.org/asernip-s/publications.htm

Aim

To make evidence-based recommendations on the appropriate protocol for post-vasectomy testing to confirm sterility.

Conclusions and results

The review included 65 studies, whereof 2 were comparative and 63 were case series or case reports. The quality of the evidence was poor. The evidence base was weakened by the lack of comparability among studies and losses to followup (with some studies reporting up to 66% loss). While compliance varied greatly among studies, it did not appear to depend on the number of tests in the post-vasectomy testing protocol or the timing of the first or last tests.

The time taken to reach azoospermia varied widely, although the median percentage of azoospermic patients consistently stayed over 80% from 3 months onward and after 20 ejaculations. The percentage of patients reaching azoospermia between the first and second tests always increased, and this increase got smaller when the initial tests were conducted later.

A small proportion of patients exhibited persistent non-motile sperm, and some patients showed the reappearance of sperm after azoospermia had been shown. The reappearance of sperm occurred up to 22 months post-vasectomy.

Pregnancies that were confirmed by DNA analysis showed that pregnancy could occur 10 years post-vasectomy.

Recommendations

The evidence presented in this review supports a post-vasectomy testing protocol with only one test (showing azoospermia) at 3 months post-vasectomy and after a minimum of 20 ejaculations. If the sample is positive at 3 months, then periodic testing can continue until azoospermia is reached. In patients who do not reach azoospermia after prolonged testing, cautious assurance of success could be given provided only low levels of non-motile sperm are present. No evidence was found to support a recommendation of histological testing of the excised vas deferens. The proposed protocol could considerably reduce costs of post-vasectomy testing.

Methods

Searching Current Contents, EMBASE, MEDLINE and The Cochrane Library until March 2003 identified relevant literature on post-vasectomy semen analysis. Studies reporting time to azoospermia, number of ejaculations to azoospermia, time to loss of sperm motility, pregnancy, repeat vasectomy patient compliance with test protocol, sperm function post-vasectomy, and histological analysis of vas specimens were included for review. Studies, with no language restrictions, detailing comparative studies, case series and case reports were included (no RCTs were available).

Written by Griffin et al, ASERNIP-S, Australia

Title **Vacuum-assisted Closure for the Management of Wounds: An Accelerated Systematic Review**

Agency **ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical**

PO Box 553, Stepney 5069, Australia; Tel +61 8 83637513, Fax +61 8 83622077; www.surgeons.org/asernip-s

Reference ASERNIP-S Report Number 37. ISBN 0 909844 61 5. Full text: www.surgeons.org/asernip-s/publications.htm

Aim

To assess whether the management of non-healing wounds using vacuum-assisted closure (VAC) therapy will improve efficacy and safety outcomes compared to conventional methods.

Conclusions and results

Six RCTs of VAC on four indications (pressure sores/ulcers, diabetic foot ulcers, skin grafts, chronic/complex wounds) were reviewed. Also included were 4 nonrandomized comparative studies (sternal wounds, skin grafts) and 7 case series studies (skin grafts, chronic wounds, pressure sores/ulcers, diabetic foot ulcers, sternal wounds). Regarding pressure sores/ulcers, no difference was found between VAC and traditional gauze dressings or the Healthpoint (HP) system. Foot ulcers managed with VAC significantly decreased in surface area versus those managed with saline-moistened gauze, which increased. VAC therapy appeared to be more effective than Opsite and bolster dressings in skin graft management. Patients managed with VAC had higher reepithelialisation rates, and fewer patients required repeat split thickness skin graft to the same site. VAC was more effective than WM gauze in chronic/complex wounds (significantly greater reduction in wound volume, depth, and treatment duration). Comparative studies on sternal wounds suggest that VAC may be more cost effective than traditional dressings or closed drainage and irrigation (VAC required fewer dressing changes, fewer flaps to close the wound, and shorter treatment time & hospitalization). This could reduce healthcare costs and enhance patient satisfaction and quality of life. A major complication for patients whose wounds failed to heal with VAC was amputation. Cases of periwound maceration and infection were reported (unclear if VAC-related). Some patients reported minor discomfort with pressure exceeding 100 mmHg.

Recommendations

Although most studies were probably too small to detect significant differences, some findings showed VAC to result in better healing than standard methods, with few serious complications. With proper training to ensure appropriate and competent use, VAC is simple to use and appears to be a promising option for managing various wound types.

Methods

MEDLINE, PREMEDLINE, EMBASE, Current Contents and PubMed were searched from inception up to July 2003. The Cochrane Library Issue 3, 2003 was searched for randomized controlled trials (RCTs) comparing VAC with an alternative treatment. The York (UK) Centre for Reviews and Dissemination databases, Clinicaltrials.gov, National Research Register, Grey Literature Reports, relevant online journals, and the Internet were searched in July 2003. Searches had no language restrictions. Studies with safety and efficacy data on the VAC technique were included (RCTs, other controlled or comparative studies, and case series with consecutive patients and stating the type of wound). Accelerated systematic reviews use the same methodology as full systematic reviews, but may restrict the types of studies to produce the review in less time.

Further research/reviews required

Rigorous studies with larger sample sizes assessing the use of VAC therapy on different wound types are required.

Written by Pham CT et al, ASERNIP-S, Australia

Title **The Organization of Troponin Testing in Acute Coronary Syndromes**

Agency **NHS QIS, NHS Quality Improvement Scotland**
Delta House, 50 West Nile Street, Glasgow G1 2NP, Scotland, UK;
Tel: +44 (0)141 2256999, Fax: +44 (0)141 2483778;
Enquiries: comments@nhshealthquality.org

Reference Craig et al. 2004 Health Technology Assessment Report 4, Glasgow: NHS Quality Improvement Scotland. ISBN 1–903961–42–4

Aim

To determine whether troponin testing (TT) is clinically and cost effective in managing patients presenting with acute coronary syndromes (ACS) and, if so, to consider how such a service could be optimally organized for Scotland.

Conclusions and results

Clinical evidence strongly supports the conclusion that troponin is superior to other cardiac enzyme tests in detecting myocardial damage. There is evidence that measuring cardiac troponin to rule out myocardial damage is only effective at least 12 hours after the onset of symptoms. Evidence also suggests that TT on admission to hospital in cases of suspected ACS identifies about 50% of patients who will have a positive troponin result 12 hours later. Current evidence indicates that few of the quantitative troponin point-of-care analyzers, and none of the qualitative troponin point-of-care readers, are sufficiently sensitive and precise to assess risk or rule out myocardial necrosis.

A cost-consequence analysis showed that if the variable costs of conducting point-of-care tests are less than £8.40, it would be cost effective to measure troponin on admission in patients with symptoms suggestive of ACS but with no high-risk clinical or ECG markers.

Recommendations

- Troponin testing should be available in all Scottish hospitals receiving patients with suspected ACS, including patients with ST elevation myocardial infarction.
- Troponin should be used in conjunction with clinical and ECG risk markers to inform diagnostic decisions and to assess risk and suitability for medical or invasive treatment in patients with suspected or diagnosed ACS.
- Timing and diagnostic value of TT depends on the clinical characteristics of patients.
- A troponin testing service should meet local needs, may be laboratory based or provided at the point of care, and will depend on local hospital requirements.
- Protocols should be developed/applied to ensure appropriate and optimal use of TT and equitable access to catheterization facilities.
- Health professionals should explain to patients/carers; the diagnosis (using consistent terms) and how it was made, treatment options, actions to take if symptoms return after discharge, and should check that patients understand the information. These discussions should be supported by written information.
- Consensus on the definition of myocardial infarction is urgently required.

Methods

The scientific literature was systematically searched to identify evidence (e.g. submissions from experts, professional and patient groups, manufacturers, and focus groups.) Evidence was critically appraised. Cost-consequence analyses were performed, and an economic model was constructed to inform the organization of a cost-effective TT service.

Further research/reviews required

Further research should investigate the effect of replacing 'any biochemical marker' by troponin in existing scoring systems and estimating the interaction between troponin level and treatment with small molecule glycoprotein inhibitors licensed for medical management of patients with non-ST elevation ACS.

Written by Joyce Craig and Emma Riches, NHS QIS, UK

Title **Colorectal Cancer Screening: Integrating Coloscopy/Simoidoscopy into the Austrian Preventive Medical Checkup**

Agency **ITA, Institute of Technology Assessment of the Austrian Academy of Sciences**
HTA Unit, Strohgasse 45, A-1030 Vienna, Austria; Tel: +43 1 51581/6586; sjonas@oeaw.ac.at

Reference Jonas S, Rafetseder O, Wild C, 2003, Früherkennung von Dickdarmkrebs. Integrierung der Darmspiegelung in die österreichische Gesundenuntersuchung. Ein Kurz-Assessment. Institut für Technikfolgen-Abschätzung, Wien, Dezember. www.oeaw.ac.at/ita/ebene5/d2-2b25.pdf

Aim

To evaluate coloscopies/sigmoidoscopies performed in Austria, to describe and analyze the current Austrian approach to early diagnosis of colorectal cancer, and to develop recommendations for a screening program considering the scientific literature.

Conclusions and results

Colorectal cancer has become the most common type of cancer worldwide. Early detection of colorectal cancer is predestined for a screening program, but screening procedures are carried out in clinically healthy persons and are potentially risky. As of spring 2002, no population-based colorectal cancer screening program on a national basis had yet been established. Now, national screening programs are established in Germany and Italy. In Austria, endoscopic colorectal cancer screening will be part of preventive health checkups. In 2002, over 120 000 endoscopic examinations of the colon were done. Due to traditional circumstances, colonoscopy is preferred over sigmoidoscopy in Austria. Colorectal cancer screening reduces the mortality rate from colorectal cancer. The effectiveness of fecal occult blood testing (FOBT) is best documented scientifically in contrast to endoscopy. Current scientific evidence based on randomly controlled studies does not show whether sigmoidoscopy or coloscopy should be preferred as a screening method. Cost-effectiveness studies favor screening compared to the cost of no screening.

Recommendations

There is a need to act locally on the following points: The introduction of organized, age-group specific colorectal cancer screening is necessary since a healthcare benefit is only achieved if a describable and measurable health profit for the population arises, and this is not possible with opportunistic screening. Also, a strategic concept needs to be developed for the colorectal cancer screening program considering necessary investments, quality control, documentation, evaluation, and transparent and understandable risk information and communication. The screening coloscopies in Austria should be centralized in competent centers at specialized medical practices and hospitals.

Methods

A systematic literature search of medical data banks focused on HTAs, guidelines, and screening programs followed by analyses. In addition, primary data were collected on endoscopy rates in Austria in 2002.

Further research/reviews required

Studies on colorectal cancer screening in daily practice are needed.

Written by Dr Susanna Jonas, ITA, Austria

Title	**Screening for Fragile X Syndrome: A Literature Review and Modelling Study**
Agency	**NCCHTA, National Coordinating Centre for Health Technology Assessment** Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom; Tel: +44 2380 595586, Fax: +44 2380 595639
Reference	Health Technol Assess 2003;7(16). Aug 2003. www.ncchta.org/execsumm/summ716.htm

Aim

To compare the effectiveness, estimate the associated costs, and summarize available evidence about the feasibility and acceptability of different screening strategies in England and Wales. To establish a model for estimating effectiveness and costs of these different strategies.

Conclusions and results

Simulation results by the FXS Model showed that, over the first 10 years, 4% of premutation (PM) females and 70% of full mutation (FM) females could be detected by active cascade screening (versus 10% and 58%, respectively, by prenatal screening). The maximal detection rate for FM carriers by active cascade screening is higher than that by prenatal screening (91% versus 71%). However, the maximal rate of detection of female PM carriers by active cascade screening (6%) is much lower than that by prenatal screening (60%). During the first 10 years of simulation, the estimated direct cost per year to the NHS in England and Wales is £0.7–0.2 million by active cascade screening and £14.5–9.1 million by a program of prenatal screening. The incremental cost per extra carrier detected (using current practice as the reference standard) is, on average, only £165 by active cascade screening versus £7543 by prenatal screening. The incremental cost per FXS birth avoided is, on average, £8494 by active cascade screening versus £284 779 by prenatal screening.

Recommendations

The empirical evidence suggested that both prenatal screening and cascade screening are feasible and acceptable. They both can reduce births of FXS children and save cost in the long term. Population-based prenatal screening is more efficacious and has a greater impact on the population, but also costs more than active cascade screening. The active cascade screening of affected families is more efficient, cheaper, but less effective than population-based prenatal screening.

Methods

e assessed the published literature. Efforts focused on developing a model that could be used to synthesize data from various sources, estimate the cost effectiveness of different strategies, and conduct sensitivity analyses according to different assumptions.

Further research/reviews required

It is suggested that both strategies be evaluated in large-scale trials, which might also help to determine whether and how the different strategies could be simultaneously or sequentially combined.

Written by Dr Fujian Song, Dept of Public Health and Epidemiology, University of Birmingham, UK

Title **Systematic Review of the Clinical Effectiveness and Cost-effectiveness of Tension-free Vaginal Tape for Treatment of Urinary Stress Incontinence**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(21). Sept 2003. www.ncchta.org/execsumm/summ721.htm

Aim

To evaluate the effectiveness and cost effectiveness of tension-free vaginal tape (TVT) in comparison with the standard surgical interventions currently used.

Conclusions and results

Based on limited data from direct comparisons with TVT and from systematic reviews, laparoscopic colposuspension and traditional slings have broadly similar cure rates to TVT and open colposuspension, whereas injectable agents appear to have lower cure rates. TVT is less invasive than colposuspension and traditional sling procedures and is also usually performed under regional or local anesthesia. The principal operative complication is bladder perforation. No data beyond 2 years post-surgery are yet available from randomized controlled trials (RCTs). Hence, long-term effects are not reliably known. TVT was more likely to be considered cost effective compared with the other surgical procedures.

Recommendations

The long-term performance of TVT is not reliably known, although the short- to medium-term effectiveness appears to approach that of alternative procedures currently available, and the cost is lower. Possibly, some women who would currently be managed non-surgically will be considered eligible for TVT as it is less invasive. Increased adoption of TVT will require additional surgeons proficient both in the technical aspects of the procedure and the choice of women suitable for the operation. It is likely that some of the higher complication rates are related to a 'learning curve'.

Methods

A systematic review was conducted of studies including comparisons of TVT with any of the comparators. Alternative treatments considered were abdominal retropubic colposuspension (including both open and laparoscopic colposuspension), traditional suburethral sling procedures, and injectable agents (periurethral bulking agents). The studies were critically appraised and their results summarized. A Markov model comparing TVT with the comparators was developed using the results of the review of effectiveness and data on resource use and costs from previous studies. The Markov model was used to estimate costs and quality-adjusted life-years for up to 10 years following surgery, and it incorporated a probabilistic analysis and a sensitivity analysis around key assumptions of the model.

Further research/reviews required

Further research suggestions include unbiased assessments of longer term performance from followup of controlled trials or population-based registries; more data from methodologically sound RCTs using standard outcome measures; a surveillance system to detect longer term complications, if any, associated with the use of tape; and rigorous evaluation before extending the use of TVT to women who are currently managed non-surgically.

Written by Ms June Cody, Health Services Research Unit, University of Aberdeen, UK

Title **A Randomised Controlled Trial to Assess the Impact of a Package Comprising a Patient-orientated, Evidence-based Self-help Guidebook and Patient-centred Consultations on Disease Management and Satisfaction in Inflammatory Bowel Disease**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;

Reference Health Technol Assess 2003;7(28). Oct 2003. www.ncchta.org/execsumm/summ728.htm

Aim

To determine if informed patients who are given patient-centered care and open access to outpatient clinics had a better quality of life (QoL) and made more cost-effective use of NHS services compared to a control group of patients who received normal care.

Conclusions and results

At 12 months the intervention had no impact on QoL, but resulted in significantly fewer hospital visits ($p<0.001$). The number of GP visits did not change, and the intervention did not increase anxiety or depression scores. Both groups reported similar satisfaction with consultations, but those in the intervention group had greater confidence to cope with their condition. Qualitative interviews explored the success of different strategies used in the intervention. Our results suggest that the guidebook was effective since it increased support for patients. Qualitative data suggest that more attention should be given to self-referral and access. Control needs to be redistributed to patients via greater adherence to patient-centered norms by consultants. Our approach to self-management was found to be more cost effective than standard management of IBD. Scarce NHS resources may be best allocated using this self-management model. The model is more likely to be cost effective than existing practice.

Recommendations

A whole-systems approach toward introducing self management leads to a significant and cost-effective reduction in hospital visits and an increase in patients' ability to manage (enablement) without changing QoL or increasing anxiety and depression. Both patients and their consultants preferred the new system of care.

Methods

The design was a two-armed pragmatic multicenter trial with randomization by treatment center. The components of the intervention included: provision of a guidebook, a written self-management plan, a patient-centered approach, and direct self-referral to services. Seven hundred patients with established IBD were recruited. Qualitative interviews with 30 intervention patients and all consultants from the intervention hospitals were used to understand the whole experience of the intervention.

Further research/reviews required

The health service must respond to the changing demographics of disease and the changing expectations of patients by modifying traditional practices which have often been physician-centered and disempowering to patients. Further research is needed to:

- Study long-term effects of self-management in empowered patients with chronic illness.
- Establish efficient operating systems in secondary and primary care to allow self-managers to self-refer and to keep them informed of new treatments.
- Explore models to train health professionals in methods to promote and support self-care.

Written by Dr Anne Kennedy, National Primary Care Research & Development Centre, University of Manchester, UK

Title **The Effectiveness of Diagnostic Tests for the Assessment of Shoulder Pain due to Soft Tissue Disorders: A Systematic Review**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(29). Oct 2003. www.ncchta.org/execsumm/summ729.htm

Aim

To evaluate the evidence for the effectiveness and cost effectiveness of newer diagnostic imaging tests in addition to clinical examination and patient history for diagnosing soft tissue shoulder disorders.

Conclusions and results

Studies show that prevalence of rotator cuff (RC) disorders was high, partial verification of patients was common, and many patients were selected retrospectively. Sample sizes were small. Reference tests were often inappropriate (many studies used arthrography alone). Ten cohort studies were found that examined either the accuracy of individual tests or clinical examination as a whole. Individual tests were either good at ruling out RC tears when negative (high sensitivity), or at ruling in such disorders when positive (high specificity). However, the small sample sizes yielded no conclusive evidence. Ultrasound was investigated in 38 cohort studies and was most accurate when used to detect full-thickness tears. Sensitivity was lower in detecting partial-thickness tears. For MRI, 29 cohort studies were included. For full-thickness tears, overall pooled sensitivities and specificities were fairly high, and the studies were not statistically heterogeneous. However, the pooled sensitivity estimate was much lower in detecting partial-thickness RC tears. Results from 6 MRA studies suggested that it may be accurate in detecting full-thickness RC tears, but less consistent in detecting partial-thickness tears. Direct evidence comparing the performance of one test with another is limited.

Recommendations

The results suggest that clinical examination by specialists can rule out the presence of a RC tear, and that either MRI or ultrasound could be used to detect full-thickness RC tears, although ultrasound may be better at picking up partial tears. Ultrasound also may be more cost effective in a specialist hospital to identify full-thickness tears.

Methods

Studies were identified that evaluated clinical examination, ultrasound, magnetic resonance imaging (MRI), or magnetic resonance arthrography (MRA) in patients suspected of having soft tissue shoulder disorders. Outcomes assessed were detection of clinical impingement syndrome or RC tear. Only cohort studies were included. The methodological quality of test-accuracy studies was assessed. Findings were extracted in duplicate using a predesigned, piloted data extraction form to avoid errors. Sensitivity, specificity, and positive and negative likelihood ratios with 95% confidence intervals were calculated for each study. Pooled estimates of sensitivity, specificity, and likelihood ratios were calculated using random effects methods. Potential sources of heterogeneity were investigated by subgroup analyses.

Further research/reviews required

Large, well-designed, prospective studies of the diagnosis of shoulder pain. In particular, a followup study of patients with shoulder pain in primary care and a prospective cohort study of clinical examination, ultrasound, and MRI, alone and/or in combination.

Written by Ms Jacq. Dinnes, Wessex Institute for Health Research & Development, University of Southampton, UK

Title **The Value of Digital Imaging in Diabetic Retinopathy**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(30). Nov 2003. www.ncchta.org/execsumm/summ730.htm

Aim

To assess the performance of digital imaging compared with other modalities in screening for and monitoring the development of diabetic retinopathy.

Conclusions and results

Manual grading of 35-mm color slides produced the highest sensitivity and specificity figures, with optometrist examination recording most false negatives. Manual and automated analysis of digital images had intermediate sensitivity. Both manual grading of 35-mm color slides and digital images yielded sensitivities above 90% with few false positives. Digital imaging produced 50% fewer ungradable images than color slides did. This part of the study was limited as patients with the more severe levels of retinopathy opted for treatment. There was an increase in the number of microaneurysms in those patients who developed from mild to moderate. There was no difference between the turnover rate of either new or regressed microaneurysms for patients with mild or with sight-threatening retinopathy. It was not possible in this study to ascertain whether digital imaging systems determine when treatment is warranted.

Recommendations

In the context of a national screening program for referable retinopathy, digital imaging is an effective method. In addition, technical failure rates are lower with digital imaging than with conventional photography. Digital imaging is also a more sensitive technique than slit-lamp examination by optometrists. Automated grading can improve efficiency by correctly identifying just under half the population as having no retinopathy.

Methods

Imaging was acquired at a hospital assessment clinic. Subsequently, study optometrists examined the patients in their own premises. A subset of patients also had fluorescein angiography performed every 6 months. A repeat assessment was carried out of all patients 1 year after their initial assessment. Patients who had more severe forms of retinopathy were monitored more frequently for evidence of progression.

Further research/reviews required

Recommendations for future research include investigating:

- Whether the nasal field is required for grading
- If automated grading can safely perform as a first-level grader (a large screening program is required)
- If color improves the performance of grading digital images
- Methods to ensure effective uptake in a diabetic retinopathy screening program.

Written by Professor Peter Sharp, Department of Biomedical Physics, University of Aberdeen, UK

Title **Lowering Blood Pressure to Prevent Myocardial Infarction and Stroke: A New Preventive Strategy**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(31). Nov 2003. www.ncchta.org/execsumm/summ731.htm

Aim

- To investigate the screening performance of measuring blood pressure and other variables in identifying those who will develop, or die from, ischemic heart disease and stroke.
- To quantify the extent to which blood pressure lowering drugs will reduce the risk of ischemic heart disease and stroke in those designated 'screen positive'.

Conclusions and results

Lowering blood pressure (BP) by 5 mmHg diastolic reduces the risk of stroke by an estimated 34% and ischemic heart disease by 21% from any pre-treatment level. These estimates, from cohort studies, have been corroborated by the results of randomized trials in persons with high, average, and below average BP levels. Blood pressure is a poor predictor of cardiovascular events. Its poor screening performance is illustrated by findings in the largest cohort study where persons in the top 10% of the distribution of systolic BP experienced only 21% of all ischemic heart disease events and 28% of all strokes at a given age. Combining several reversible risk factors adds little to the screening performance of BP alone, eg, the 25% of men aged 55–64 years at highest computed risk (≥1% per year) experience only 46% of all ischemic heart disease events. The main screening methods should identify everyone with a history of cardiovascular disease events (eg, identifying patients at the time of hospital discharge following a first myocardial infarction (MI) detects 50% of all heart disease deaths in a population at a false positive rate of 12%) and use a person's age. Identifying everyone with a history of MI or stroke in a population and everyone aged 55 years or more would include 98% of all deaths from ischemic heart disease and stroke. The five main categories of blood pressure lowering drugs, ie, thiazides, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin-II receptor antagonists, and calcium channel blockers, significantly reduce BP from all pre-treatment levels although the extent of the BP reduction increased with pre-treatment BP. The reductions were similar at standard dose for the five categories; average reduction was 9.1 systolic and 5 diastolic. The effect on BP of combining two drugs was additive. No effect of age was apparent. There were no serious metabolic consequences of using these drugs in standard dose.

Recommendations

The evidence indicates that 3 drugs in combination may reduce stroke by about two-thirds and ischemic heart disease by half. The report suggests avoiding the term hypertension since it is not a disease and falsely implies another category ("normotensives") that would not benefit from lowering BP. Since BP reduction using combinations of safe, well-established drugs is effective in preventing cardiovascular events, it is suggested that such preventive therapy be used more widely in people who are at risk of heart attack or stroke regardless of initial BP.

Methods

Relevant cohort studies and randomized trials were identified and analyzed. Statistical analysis was used to determine drug efficacy and adverse effects.

Further research/reviews required

Further research is required on treatment effectiveness and the economic implications of policy options.

Written by Dr Malcolm Law, St Bart's & The Royal London School of Medicine, UK

Title **Clinical and Cost-effectiveness of New and Emerging Technologies for Early Localised Prostate Cancer: A Systematic Review**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2003;7(33). Nov 2003. www.ncchta.org/execsumm/summ733.htm

Aim

To evaluate the clinical and cost effectiveness of new and emerging technologies for early, localized prostate cancer.

Conclusions and results

For neoadjuvant hormonal therapy, no evidence of benefit was found in terms of biochemical disease-free survival. For adjuvant hormonal therapy, no evidence of benefit was found in terms of survival, but some conflicting evidence showed that higher risk patients might benefit. The largest number of studies reported results for brachytherapy, where some evidence suggested that it may be more effective than standard treatments for lower risk patients, although less effective for intermediate- and high-risk patients, in terms of biochemical disease-free survival. Lower quality evidence reported fewer complications than for standard treatments. Higher quality evidence suggested that disease-specific quality of life (QoL) for brachytherapy patients was lower than for patients receiving standard treatments. The review of three-dimensional conformal radiotherapy (3D-CRT) considered treatment-related morbidity, where significantly fewer gastrointestinal complications occurred than with standard radiotherapy. It was suggested that higher radiation doses achieved better disease control, although patient characteristics were often reported as independent indicators of control. The review of intensity-modulated conformal radiotherapy suggested that late gastrointestinal toxicity might be reduced compared with 3D-CRT. For cryotherapy, high rates of impotence were reported. Owing to the paucity and poor quality of evidence identified for other interventions, conclusions regarding their clinical effectiveness cannot be drawn.

Cost-effectiveness estimates were based on the impact of adverse events on quality-adjusted life-years and the assessment was restricted to brachytherapy, 3D-CRT, and cryotherapy compared with standard treatments. Of the new treatments included, only cryotherapy appeared not to be potentially cost effective compared with traditional treatments, owing to the associated high incidence of impotence.

Recommendations

It is difficult to draw conclusions on the relative benefits of the newer technologies owing to the lack of substantive evidence of any quality and the lack of comparisons between the newer technologies and standard treatments.

Methods

A list of new and emerging technologies was identified and agreed. A systematic review was undertaken and selected studies were reviewed against a set of criteria. An economic model was developed and used to compare specified newer treatments and traditional approaches.

Further research/reviews required

Areas recommended for further research are: RCTs with sufficient followup to measure benefits in terms of overall survival (including QoL measurement); identification of prognostic risk factors in men diagnosed with early prostate cancer; QoL studies to compare the utility of health states among patients on active monitoring, patients receiving treatment, and the comparable healthy population; the relationship between surrogate end-points and survival; and the adoption of standard definitions for adverse events.

Written by Ms Suzy Paisley, School of Health and Related Research, University of Sheffield, UK

Title **Routine Ultrasound Scanning Before 24 Weeks of Pregnancy**

Agency **NHS QIS, NHS Quality Improvement Scotland**
Delta House, 50 West Nile Street, Glasgow G1 2NP, Scotland, UK;
Tel: +44 (0)141 225 6988, Fax: +44 (0)141 221 3262, http://www.nhshealthquality.org

Reference Ritchie et al., 2004. Health Technology Assessment Report 5, Glasgow: NHS Quality Improvement Scotland. ISBN 1-903961-44-0

Aim

To determine the most clinically and cost-effective program of routine ultrasound scanning and screening which can be offered to women in Scotland before 24 weeks of pregnancy.

Conclusions and results

Strategies involving a scan in the first trimester and an anomaly scan in the second trimester are more expensive than single-scan strategies, but maximize the identification of fetal abnormalities at an acceptable false-positive rate. A first trimester test for chromosomal abnormalities involving nuchal translucency measurement is more effective than the second trimester double test currently used in Scotland. Women value early screening and would also welcome the opportunity to have a second trimester scan in addition to a first trimester scan.

Recommendations

- All women in Scotland should be offered a first trimester scan and test for chromosomal abnormalities and a second trimester scan as part of routine antenatal care.
- Appropriate written information should be available, with time for the pregnant woman to consider and discuss this with a health professional prior to ultrasound examination.
- Women who decide to participate in all or part of an antenatal screening program should provide written informed consent.
- The first trimester scan should be offered between 10 and 13 completed weeks' gestation to confirm fetal viability, assess gestational age, and identify multiple pregnancy.
- Nuchal translucency measurement should be offered as part of the first trimester scan. The results and maternal serum screening (PAPP-A and free β-hCG) should be combined with gestational age (at scan) and maternal age to assess the risk of chromosomal abnormalities.
- Women who present after 13 completed weeks' gestation should be offered an ultrasound scan to assess gestational age at presentation and second trimester serum screening (alphafetoprotein and hCG) for chromosomal abnormalities.
- The second trimester scan is to exclude or detect identifiable common fetal abnormalities and should be done between 18 and 22 weeks' gestation (target is 20 weeks' gestation). It should not include detection of soft markers to assess risk of chromosomal abnormalities.
- Formally trained staff with suitable scanning equipment should perform the recommended program of scanning and screening. There should be consistent record keeping in maternity services to facilitate internal and external quality assurance and audit.

Methods

NHS maternity units in Scotland were surveyed to ascertain current practice. The literature was systematically searched to identify clinical effectiveness data. No accurate data were available from NHSScotland or from the literature review to inform on the cost of different ultrasound scans. Hence, a bottom up costing methodology was adopted using data from the best available sources. A mathematical model was constructed to estimate the costs and benefits of 6 screening policy options for congenital abnormalities. A literature review and focus groups were used to determine women's views on ultrasound scanning in pregnancy.

Written by Karen Ritchie and Susan Quinn, NHS QIS, UK

Title **Suicide Prevention Strategies: Evidence from Systematic Reviews**

Agency **AHFMR, Alberta Heritage Foundation for Medical Research**
HTA Unit, Suite 1500, 10104-103 Avenue NW, Edmonton, Alberta T5J 4A7 Canada;
Tel: +1 780 423 5727, Fax: +1 780 429 3509; info@ahfmr.ab.ca, http://www.ahfmr.ab.ca

Reference HTA 28, February 2003 (English). ISBN 1-896956-68-8 (print);
ISBN 1-896956-70-X (online): http://www.ahfmr.ab.ca/programs.html

Aim

To identify what types of suicide prevention (SP) strategies have been evaluated in the research and to determine which suicide prevention strategies are effective.

Conclusions and results

Ten systematic reviews published since 1990 were analyzed: 2 covered a wide range of SP strategies, 3 focused on school-based SP strategies for adolescents, and 5 focused on psychological/ pharmacological treatments for highly suicidal patients. Three of the ten reviews received a 'good' quality rating. Nearly thirty types of SP strategies have been evaluated in the research, and more than half fall into the 'treatment' category of the prevention framework. The evidence was insufficient to ascertain whether any single prevention strategy was more effective than another in reducing suicide rates. The 3 'good' quality systematic reviews found that school-based prevention programs directed toward at-risk students enhanced protective factors and reduced risk factors and suicidal behavior. Findings from small clinical studies suggested that some psychological/pharmacological treatments, such as problem-solving, provision of an emergency contact card, dialectical behavior therapy, flupenthixol administration, and cognitive behavior therapy were promising in reducing rates of repeated self-harm among suicide attempters. The authors of the reviews noted many methodological limitations in the research.

Recommendations

Limited evidence indicated that no single strategy appeared to be effective in reducing suicide rates. School-based prevention strategies directed toward at-risk students were promising in enhancing protective factors and reducing suicide behavior and risk factors. Some psychological/ pharmacological treatments reduced rates of repeated self-harm in patients who had previously attempted suicide. Given that suicide is complex and multifaceted, a broad array of suicide prevention strategies addressing different risk factors at various levels will be required to achieve an overall reduction in the population's long-term suicide rate.

Methods

This was a qualitative systematic review of systematic reviews. One researcher extracted data from the reviews, and two researchers independently assessed the methodological quality of the reviews. Suicide prevention strategies identified from the reviews were presented in a prevention framework that incorporated prevention (universal, selective, and indicated), treatment (case identification and standard treatment), and maintenance (compliance and after-care).

Further research/reviews required

Future research challenges include: standardizing assessment protocols for identifying at-risk populations, developing universal definitions for suicide-related terms, and defining formally validated outcome measures. It may also be necessary to develop a conceptual framework when planning and establishing provincial suicide prevention strategies.

Written by Bing Guo, Ann Scott, Samantha Bowker, AHFMR, Canada

INAHTA Briefs

Issue 2004/19

Prevalence of Chronic Pain: An Overview

Agency AHFMR, Alberta Heritage Foundation for Medical Research
HTA Unit, Suite 1500, 10104-103 Avenue NW, Edmonton, Alberta T5J 4A7 Canada;
Tel: +1 780 423 5727, Fax: +1 780 429 3509; info@ahfmr.ab.ca, http://www.ahfmr.ab.ca

Reference HTA 29, December 2002 (English). ISBN 1-896956-62-9 (print);
ISBN 1-896956-64-5 (online): http://www.ahfmr.ab.ca/programs.html

Aim

To analyze and critically appraise the published evidence on the prevalence of non-malignant chronic pain (CP) in the general population. A secondary objective was to summarize information on the characteristics of CP and the use of health services by CP sufferers.

Conclusions and results

Thirteen primary studies were analyzed, most of which reported prevalence estimates for adolescent and adult populations (aged 15 to 86 years). Two studies provided prevalence data for elderly populations (over 65 years), while one study addressed the prevalence of CP in children (0 to 18 years). In general, the studies were of acceptable methodological quality. The CP prevalence estimates varied from 10.1% to 55.2%. Calculation of severe CP prevalence was possible in 5 studies that utilized both the International Association for the Study of Pain (IASP) definition of CP and proxy definitions of severity. The prevalence of severe CP varied little among study populations (8% in children, 11% in adults, and 15% in the elderly). These estimates were similar to those reported in 3 studies that used the American College of Rheumatology (ACR) criteria (11.8%, range 10% to 13%). The definitions of CP in the studies were very heterogeneous. Even when similar criteria were used to define CP, the phrasing and ordering of questions in the assessment tool often differed. The study populations and their associated comorbidities also varied greatly among studies. The main methodological problems were a lack of validity and reliability of information on the data collection instruments; failure to report confidence intervals for the prevalence values; and low response rates.

Recommendations

The lack of consensus on basic definitions, inconsistencies in measurement, and wide variation in prevalence estimates made it impossible to generate precise CP prevalence numbers or generalize the findings to a regional context.

Methods

A quasi qualitative/quantitative systematic review was undertaken. Data on a set of predetermined variables were extracted from each study. Studies were divided based on criteria used to define CP (IASP, ACR). Weighted mean estimates based on the study sample size and adjusted according for potential confounding variables were reported for each subgroup of studies.

Further research/reviews required

Prospective epidemiological studies are needed to estimate the prevalence of CP in Alberta. The number and characteristics of people with CP and the proportion of people with disabling, limiting, or severe CP must also be quantified. Studies that used telephone or face-to-face interviews reported lower prevalence rates than those that used postal questionnaires to collect data. However, information was insufficient to assess the direction and magnitude of this trend. Also, the effect on the prevalence estimate of the order and content of the questions used in the data collection tool needs further investigation.

Written by Maria Ospina, Christa Harstall, AHFMR, Canada

Title	**Chronic Hepatitis C. Combination Therapy IFN and Ribavirin**
Agency	**DACEHTA, Danish Centre for Evaluation and Health Technology Assessment** National Board of Health, P.O. Box 1881, DK-2300 Copenhagen S, Denmark; Tel: +45 72 22 74 48, Fax: +45 72 2274 13, www.dacehta.dk
Reference	DACEHTA Report 2002;2(2). Danish, English summary. ISBN 87-91232-05-8 (print); ISBN 87-91232-06-6 (online): www.sst.dk/applikationer/cemtv/publikationer/docs/kroniskhepatitisc/indhold_til_net.pdf

Aim

An estimated 2000 people in Denmark suffer from chronic hepatitis C infection. This study aims to assess combination treatment of chronic hepatitis C using alpha-interferon (IFN) and ribavirin, which was licensed in 1999.

Conclusions and results

Combination treatment with IFN and ribavirin can permanently eliminate the hepatitis C virus (HCV) from the blood and thereby cure and prevent liver disease in about 40% of all treated patients. Combination treatment has numerous side effects, some of which can be serious or permanent, ie, interference with thyroid function. Patients generally perceive that the treatment itself is good, and it is good to be offered the treatment. Patients will recommend this treatment to others, despite its side effects.

Combination treatment for all patients who could potentially benefit from it can be offered within the existing framework of health services. A decision to offer treatment is not considered to require organizational changes within the departments/clinics, among departments, or at the hospital level.

IFN and ribavirin prices are high. Economic analysis using conservative estimates of costs related to the health care of patients with advanced liver disease, shows that combination treatment with IFN and ribavirin will be beneficial (from a health economic perspective) only in the very long term.

Recommendations

Based on all of the stated considerations, the working group will recommend that combination treatment with IFN and ribavirin should be offered to patients with chronic hepatitis C where HCV can be detected for more than 6 months, the liver enzyme ALT has increased (exceeding the upper normal value) at least twice in 6 months, and where a liver biopsy shows inflammation and/or formation or connective tissue or cirrhosis. Excluded are persons with present drug or alcohol abuse, and cirrhosis with liver failure.

Methods

The effect of treatment with IFN plus ribavirin was compared to treatment with IFN alone. This was carried out as a systematic literature review within the framework of the international Cochrane Collaboration. Patient-related aspects were analyzed by literature studies and interviews. The economic analysis employed a Markov model.

Written by Weis N, Krogsgaard K, Kjærsgaard LL et al, DACEHTA, Denmark

Title **Photodynamic Treatment of Subretinal New Vessels of Choroidal Origin in Age-related Macular Degeneration – An HTA**

Agency **DACEHTA, Danish Centre for Evaluation and Health Technology Assessment**
National Board of Health, P.O. Box 1881, DK-2300 Copenhagen S, Denmark;
Tel: +45 72 22 74 48, Fax: +45 72 2274 13, www.dacehta.dk

Reference DACEHTA Report 2002;2(3). Danish, English summary. ISBN 87-91093-73-2 (online): www.sst.dk/applikationer/cemtv/publikationer/docs/fotodynamiskbehand/148545.pdf

Aim

Age-related Macular Degeneration (AMD) is the leading cause of visual impairment and blindness in industrialized countries. Until recently, the only therapy available for AMD was the destructive photothermal coagulation of new vessels growing under the retina. A new, more lenient method for non-thermal selective closure (photodynamic therapy) of subretinal new vessels (CNV) is the subject of this HTA.

Conclusions and results

Controlled trials demonstrate that few patients will experience an improvement in visual acuity during the course of treatment, but a significant reduction in the rate of visual loss has been documented over an observation period of 2 years. Furthermore, a beneficial effect of photodynamic therapy for CNV is found for diseases other than AMD.

A cost-effectiveness analysis demonstrates that the cost per quality-adjusted life-year is 250 000 Danish kroner (DKK). This is comparable to other moderately expensive therapies across different medical specialties. Previous epidemiological studies and recent data from Copenhagen County indicate that the total direct costs per year in Denmark for treating CNV secondary to AMD by photodynamic therapy were estimated to range between 20.7 and 38.3 million DKK in 2003, if implemented to its full potential.

Recommendations

The assessment indicates that photodynamic therapy for CNV secondary to AMD should be continued where it has already been established as a therapeutic modality, and that this new treatment should be made equally available throughout Denmark by promoting dynamic collaboration between primary care ophthalmologists and secondary ophthalmological referral centers. Proper diagnosis and administration of therapy depends on subspecialty skills, experience, and volume. The necessary equipment is widely available, or can be installed at low cost. The critical medical task is to distinguish treatable from untreatable conditions. The new treatment is mechanistically akin to photocoagulation, and it is likely to be incorporated gradually into the general spectrum of therapeutic modalities. However, it will remain a task for the subspecialized ophthalmologist.

Methods

The HTA covers four basic elements, ie, technology, patients, organization, and economics. The technology part describes the photodynamic therapy of CNV and the effects of treatment according to available documentation. The economic aspects were investigated and discussed in terms of expected savings and increased expenses in healthcare and social agencies, based on how the new treatment affected patients and the health service organization.

Written by Haaeman P, Larsen M, Juhl HH, Svenning AR, DACEHTA, Denmark

Title **Chlamydia Screening with Home Testing – An HTA**

Agency **DACEHTA, Danish Centre for Evaluation and Health Technology Assessment**
National Board of Health, P.O. Box 1881, DK-2300 Copenhagen S, Denmark;
Tel: +45 72 22 74 48, Fax: +45 72 2274 13, www.dacehta.dk

Reference DACEHTA Report 2002;2(4). Danish, English summary. ISBN 87-91232-69-4 (print); ISBN 87-91232-70-8 (online): http://www.sst.dk/publ/Publ2003/klamydia/klamydia.pdf

Aim

Chlamydia trachomatis constitutes a significant health problem. In Denmark, about 13 000 chlamydial infections are diagnosed annually. An estimated 24 000 infections among young women and men aged 16 to 25 years remain undetected. Untreated infections may result in complications such as infertility among women (risk 2.4%), ectopic pregnancy (risk 1.6%), and chronic abdominal pain (risk 3%).

Diagnostic methods are available that enable an individual to obtain a sample at home and mail it to the laboratory without consulting a medical doctor (home sampling). Only patients with a positive test result need to contact their doctor.

This report describes the consequences of continuing the present diagnostic strategy (general practitioners testing based on symptoms or clinical indication) versus a screening strategy involving the group aged 16 to 25 years and based on yearly home sampling with subsequent notification of the possible source of infection, the partner.

Conclusions and results

With the present diagnostic strategy, the frequency of chlamydial infections and the number of complications will remain unchanged. If, in addition, the home sampling screening strategy described above is offered, the prevalence of chlamydial infections would possibly decline to an insignificant level within 10 years.

The costs during this period will be 380 million Danish kroner (DDK), whereof first-year costs are 42.5 million DKK. Concurrently, it will be possible to save 238 million DKK as a consequence of 57 000 fewer complications. This corresponds to a net cost of 141 million DKK. If reduced loss of production is included, a further 376 million DKK will be saved after 10 years of screening. The strategy will be cost saving after the fourth year of screening.

Home sampling is generally well accepted by the target group. However, due to stigmatization issues, the target group should have immediate access to information and advice. The screening strategy should be accompanied by general information concerning the prevention of sexually transmitted diseases. Special consideration should be given to ethnic minorities. A strategy of home sampling is relatively easy to introduce in the present organization of the Danish health services. Major barriers are not expected.

Methods

The HTA covers four basic elements, ie, technology, patient, organization, and economics. The HTA is based on literature reviews, internally designed and accomplished studies, and statements from recognized Danish experts.

Written by Østergaard L, Andersen B, Møller JK, Olesen F, DACEHTA, Denmark

Title	**Preimplantation Genetic Diagnosis – An HTA**
Agency	**DACEHTA, Danish Centre for Evaluation and Health Technology Assessment** National Board of Health, P.O. Box 1881, DK-2300 Copenhagen S, Denmark; Tel: +45 72 22 74 48, Fax: +45 72 2274 13, www.dacehta.dk
Reference	DACEHTA Report 2002;2(1). Danish, English summary. ISBN 87-91232-00-7 (print); ISBN 87-91232-01-5 (online): http://www.sst.dk/Applikationer/cemtv/publikationer/docs/Praeimplantation/præimplant.pdf

Aim

The overall purpose was to contribute with information and input for decision making by analyzing the literature on preimplantation genetic diagnosis (PGD) and evaluating the experience obtained during a 2-year project at a Danish university hospital offering PGD to couples with selected hereditary diseases. Another issue concerns the ethical questions derived from PGD and attitudes toward PGD among potential consumers of the technique compared to prenatal diagnosis (PND). Furthermore, it was decided to analyze the present organization of PGD in Denmark and in the Nordic countries in an attempt to outline a future organization of PGD in Denmark. Finally, using a model-based, health economic analysis, it was intended to evaluate the economic implications for the public healthcare system of introducing PGD to couples at risk of offspring with a particular hereditary disease – cystic fibrosis.

Conclusions and results

Using PGD, members of families with hereditary diseases can reduce their risk of having an affected child from 25%–50% to 1% or lower. Technologically, preimplantation diagnosis can be introduced in Denmark, but not without increasing costs for the healthcare sector. However, these extra costs are moderate, especially when compared with the costs of many new pharmaceuticals.

The PGD technique is very much demanded by potential users (families at risk of having a diseased child), but presumably the method will be employed by a limited group of people at risk of having a child with relatively severe disease. From a gradualistic perspective (ie, human life has a gradually increasing moral value from fertilization to birth) the method is ethically preferable. A minor uncertainty concerning the possible long-term risk associated with PGD does not justify a reservation. PGD can be introduced in the public healthcare sector at a relatively moderate extra cost, which must be balanced against the advantages of the method, eg, avoided legal abortions.

Methods

A systematic HTA approach was used covering the following aspects of PGD, ie, technology, patient, organization, and economics. The technology analysis was based on a literature review covering existing knowledge and experience with prenatal and preimplantation diagnosis. Ethical analyses focused on: *ethically relevant characteristics* of PGD as a technology, ethical *problems* related to the ethically relevant characteristics, and *ethical assessment*. Attitudes and preferences to PGD and PND among potential users were investigated by a survey. The health economic analysis (a cost-minimization analysis and two cost effectiveness analyses) included experiences with PGD from Denmark and Europe. Furthermore, PGD-related organizational aspects and the influence on processes and structure in health care were analyzed.

Written by Ingerslev HJ et al, DACEHTA, Denmark

Title	**Rheumatoid Arthritis – Health Technology Assessment of Diagnosis and Treatment**
Agency	**DACEHTA, Danish Centre for Evaluation and Health Technology Assessment** National Board of Health, P.O. Box 1881, DK-2300 Copenhagen S, Denmark; Tel: +45 72 22 74 48, Fax: +45 72 2274 13, www.dacehta.dk
Reference	DACEHTA Report 2002;4(2). ISBN 87-91232-54-6 (print); ISBN 87-91232-55-4 (online): http://www.sst.dk/publ/Publ2003/SST_leddeg_AS5.pdf

Aim

In Denmark, about 35 000 persons are affected by rheumatoid arthritis (RA). Traditional treatment encompasses pharmacotherapy with slow-acting anti-rheumatic drugs, joint surgery, physiotherapy, occupational therapy, psychological therapy, and patient education. The appearance of a new type of biological anti-rheumatic drug precipitated the need for a broad assessment – not only of the new drugs, but covering the entire treatment spectrum.

Conclusions and results

Traditional drugs reduce disease activity in most RA patients. The effect is improved by early and intensive treatment. Insufficient effect is found in 10% to 20% of the patients treated by rheumatologists. The new drugs, besides having a rapid effect on symptoms, diminished or arrested the development of joint erosion. Staff requirements and costs are at least twice as high for Model I (new drugs for all patients treated for RA) as Model II (new drugs only for non-responders to traditional drugs). Non-medical treatments do not affect the disease itself, but are mainly effective in relieving symptoms.

Recommendations

At present, based on the evidence and an overall assessment, the expert group recommends Model II as the best basis for RA treatment – combined with efforts to improve early referral to specialists and early diagnosis. (Some countries, eg, England, have similar limitations on the use of the new drugs.)

Further recommendations are:

- Centralization of new drug treatment to a single rheumatology department at one hospital in each of the 14 Danish counties.
- Improvement of early diagnosis, eg, better informed GPs, immediate referrals to specialists, and prompt first appointments.
- Equal access to relevant physiotherapy, occupational therapy, and surgical evaluation – even for patients living in outlying districts.
- Establishment of a national clinical database for patients on treatment with new drugs.

Methods

The HTA, carried out by an interdisciplinary group of 20 experts, included systematic literature reviews of clinical effectiveness and patient aspects (including ranking of evidence) and evaluations of organizational and economic consequences. Two alternative management models structured the analyses: new drugs for all patients treated for RA (Model I) and new drugs only for non-responders to traditional drugs (Model II).

Written by A project group in DACEHTA. Project Managers: Lange M, Sigmund H, DACEHTA, Denmark

Title **Type 2 Diabetes. A Health Technology Assessment of Screening, Diagnosis and Treatment**

Agency **DACEHTA, Danish Centre for Evaluation and Health Technology Assessment**
National Board of Health, P.O. Box 1881, DK-2300 Copenhagen S, Denmark;
Tel: +45 72 22 74 48, Fax: +45 72 2274 13, www.dacehta.dk

Reference DACEHTA Report 2003;5(1). ISBN 87-91361-38-9 (print). ISBN 87-91361-39-7 (online).
www.cemtv.dk/publikationer/docs/Diabetes/type_2_diabetes.pdf

Aim

In Denmark, as in many other Western countries, the prevalence of type 2 diabetes (T2D) is rapidly increasing. Studies estimate that in a Danish population of 5.3 million, between 100 000 and 150 000 individuals are diagnosed with T2D, and a similar number are undiagnosed. On this basis, DACEHTA initiated an HTA project to provide broad, evidence-based input to decision making on how to approach this health problem.

Conclusions and results

Population-based screening for T2D has no well-documented effect on hard endpoints, and cost-effectiveness studies show that the cost per avoided complication is high. T2D patients with atherosclerosis and/or albuminuria have a documented effect from individualized, intensive polypharmacological therapy. The extra costs of intensive therapy vary between 42 and 105 million USD depending on the intensity of strategy applied. Systematic screening for diabetic retinopathy is expensive, but cost effective. The evidence on most nonpharmacological interventions proved poor and inconclusive.

Recommendations

A general recommendation is that efforts should be made to establish a uniform organization and structure that ensures coherent patient care with regular controls. Population-based screening is not recommended. Intensified clinical case finding is recommended instead. Furthermore, it is recommended that T2D patients with atherosclerosis and/or albuminuria should receive individualized, intensive, polypharmacological therapy, and that patients with T2D should be screened for retinopathy by fundus photography on a regular basis. Specific recommendations concerning nonpharmacological treatment are difficult to make due to poor documentation of most nonpharmacological interventions. With this in mind, it is recommended that a low-fat hypocaloric diet, physical activity, and smoking cessation comprise a basic offer to patients with T2D. Furthermore, regular foot therapy, therapeutic shoes, and custom insoles are recommended to high-risk patients to avoid foot ulcers and amputation. Patient education should be offered to all T2D patients, but establishment of more schools should await thorough evaluation of existing diabetes schools.

Methods

Systematic literature reviews were conducted on clinical effectiveness and patient aspects, combined with economic evaluations and analyses of organizational aspects. The literature was rated by level of evidence.

Further research/reviews required

Well-designed and sufficiently large multicenter studies addressing the value of nonpharmacological treatment, including its organization, are required.

Written by A project group in DACEHTA. Project Manager: Hansen NW, DACEHTA, Denmark

INAHTA Member Agencies

AÉTMIS

Scientific Director: Dr. Véronique Déry
Contact person: Dr. Véronique Déry
Agence d'Évaluation des Technologies et des Modes d'Intervention en Santé
2021, avenue Union, bureau 1040
Montréal (Québec), H3A 2S9 **CANADA**
Tel: +1 514 873 2563 Fax: +1 514 873 1369
E-mail: aetmis@aetmis.gouv.qc.ca
Internet: www.aetmis.gouv.qc.ca

AETS

Contact person: Dr. José Maria Amate Blanco
Agencia de Evaluación de Tecnologias Sanitarias
Instituto de Salud "Carlos III"
Calle Sinesio Delgado 4
ES-28029 Madrid **SPAIN**
Tel: +34 9 1 387 7800 Fax: +34 9 1 387 7841
E-mail: jamate@isciii.es
Internet: www.isciii.es

AETSA

Director: Dr. José A. Valverde
Contact Person: Dr. José A. Valverde
Agencia de Evaluación de Tecnologías Sanitarias de Andalucía
Avda. de la Innovación, s/n. Edificio Arena-1
ES-41020 Sevilla **SPAIN**
Tel: +34 95 500 6638 Fax: +34 95 500 6677
E-mail: joseantonio.valverde@juntadeandalucia.es
Internet: www.juntadeandalucia.es/salud/

AHFMR

Director: Mr. Don Juzwishin
Contact person: Mr. Don Juzwishin
Alberta Heritage Foundation for Medical Research
10104-103 Avenue, Suite 1500
Edmonton Alberta, T5J 4A7 **CANADA**
Tel: +1 780 423 5727 Fax: +1 780 429 3509
E-mail: djuzwish@ahfmr.ab.ca
Internet: www.ahfmr.ab.ca

AHRQ

Director: Mr.Douglas Kamerow
Contact person: Mr. Martin Erlichman
Agency for Healthcare Research and Quality
Center for Outcomes & Evidence
540 Gaither Road
Rockville, M.D. 20850 **USA**
Tel: +1 301 427 1610 Fax: +1 301 427 1639
E-mail: merlichm@ahrq.gov
Internet: www.ahrq.gov

ANAES

Director: Mr. Alain Coulomb
Contact person: Dr. Bertrand Xerri
French National Agency for Accreditation and Evaluation in Healthcare
2, avenue du Stade de France
FR-93218 Saint-Denis La Plaine CEDEX **FRANCE**
Tel: +33 1 55 93 71 72 Fax: +33 1 55 93 74 38
E-mail: b.xerri@anaes.fr
Internet: www.anaes.fr

ASERNIP-S

Director: Prof. Guy Maddern
Contact person: Prof. Guy Maddern
Australian Safety and Efficacy Register of New Interventional Procedures - Surgical
PO Box 553
Stepney SA 5069 **AUSTRALIA**
Tel: +61 8 8363 7513 Fax: +61 8 8362 2077
E-mail: College.asernip@surgeons.org
Internet: www.surgeons.org/asernip-s

CAHTA

Director: Dr. Joan Pons
Contact person: Mr. Antoni Parada
Catalan Agency for Health Technology Assessment and Research
Esteve Terradas, 30, Recinte Parc Sanitari Pere Virgili
Edifici Mestral, 1a planta
ES-08023 Barcelona **SPAIN**
Tel: +34 93 2594200 Fax: +34 93 2594201
E-mail: tparada@aatrm.catsalut.net
Internet: www.aatrm.net

CCOHTA

Director: Dr. Jill Sanders
Contact person: Dr. Jill Sanders
Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600
Ottawa, ON K1S 5S8 **CANADA**
Tel: 613-226-2553 Fax: 613-226-5392
E-mail: jills@ccohta.ca
Internet: www.ccohta.ca

CEDIT

Director: Dr. Elisabeth Fery-Lemonnier
Contact person: Dr. Elisabeth Fery-Lemonnier
Comité d'Evaluation et de Diffusion des Innovations Technologiques
Assistance Publique Hôpitaux de Paris
3, avenue Victoria
FR-75004 Paris R.P. **FRANCE**
Tel: +33 1 40 27 31 09 Fax: +33 1 40 27 55 65
E-mail: elisabeth.fery-lemonnier@sap.ap-hop-paris.fr
Internet: http://cedit.aphp.fr

CMS

Director: Dr. Sean Tunis
Contact person: Dr. Steven Berkowitz (Director, CAG)
Coverage and Analysis Group, CAG
Centers for Medicare and Medicaid Services (OCSQ)
Office of Clinical Standards and Quality
7500 Security Blvd. Mailstop C1-09-06
Baltimore, MD 21244, **USA**
Tel: +1 410 786 2281 Fax: +1 410 786 9286
E-mail: SBerkowitz@cms.hhs.gov
Internet: www.cms.hhs.gov

CMT

Director: Prof. Jan Persson
Contact person: Prof. Jan Persson
Center for Medical Technology Assessment
Department of Health and Society
Linköping University
SE-581 83 Linköping **SWEDEN**
Tel: +46 13 22 49 93 Fax: +46 13 22 49 95
E-mail: Jan.Persson@ihs.liu.se
Internet: www.cmt.liu.se

CRD

Director: Prof. Jos Kleijnen
Contact person: Ms. Julie Glanville
Centre for Reviews and Dissemination
University of York
York, YO10 5DD **UNITED KINGDOM**
Tel: +44 1904 321040 Fax: +44 1904 321041
E-mail: jmg1@york.ac.uk
Internet: www.york.ac.uk/inst/crd

CVZ

Director: Mr. J.L.P.G. van Thiel
Contact person: Dr. Albert Boer
College voor zorgverzekeringen
Postbus 320
NL-1110 AH Diemen **THE NETHERLANDS**
Tel: +31 20 797 8555 Fax: +31 20 797 8500
E-mail: bboer@cvz.nl
Internet: www.cvz.nl

DACEHTA

Director: Prof. Finn Børlum Kristensen
Contact person: Prof. Finn Børlum Kristensen
Danish Centre for Evaluation and Health Technology Assessment
National Board of Health
P.O. Box 1881, Islands Brygge 67
DK-2300 Copenhagen S **DENMARK**
Tel: +45 72 22 74 48 Fax: +45 72 22 74 07
E-mail: dacehta@sst.dk,
Internet: www.dacehta.dk

DAHTA@ DIMDI

Director: Dr. Alric Rüther
Contact person: Dr. Alric Rüther
German Agency for Health Technology Assessment at the German Institute for Medical Documentation and Information
Waisenhausgasse 36-38a
DE-50676 Cologne **GERMANY**
Tel: +49 221 472 41 Fax: +49 221 4724 444
E-mail: dahta@dimdi.de
Internet: www.dahta.dimdi.de

DSI

Director: Prof. Jes Søgaard
Contact person: Dr. Henrik Hauschildt Juhl
Danish Institute for Health Services Research and Development
Dampfærgevej 27-29 P.O. Box 2595
DK-2100 Copenhagen **DENMARK**
Tel: +45 35 29 8400 Fax: +45 35 29 8499
E-mail: hhj@dsi.dk
Internet: www.dsi.dk

ETESA

Director: Dr. Gloria Ramirez Donoso
Contact person: Dr. Gloria Ramirez Donoso
Unidad De Tecnologias De Salud
Ministerio De Salud De Chile
Mac Iver 541, oficina 58
Santiago de Chile **CHILE**
Tel: +56 2 630 0447 Fax: +56 2 638 5186
E-mail: etesa@minsal.cl
Internet: www.minsal.cl

FinOHTA

Director: Prof. Marjukka Mäkelä
Contact person: Prof. Marjukka Mäkelä
Finnish Office for Health Care Technology Assessment
STAKES, P.O. Box 220
FIN-00531 Helsinki **FINLAND**
Tel:+358 9 3967 2290 Fax:+358 9 3967 2278
E-mail: marjukka.makela@stakes.fi
Internet: www.stakes.fi/finohta

GR

Director: Dr. Menno van Leeuwen
Contact person: Dr. Menno van Leeuwen
Health Council of the Netherlands
Gezondheidsraad Postbus 16052
NL-2500 BB Den Haag **THE NETHERLANDS**
Tel: +31 70 3407520 Fax: +31 70 3407523
E-mail: m.van.leeuwen@gr.nl
Internet: www.gr.nl

HSMTA
Director: Dr. Egils Lavendelis
Contact person: Dr. Egils Lavendelis
Health Statistics and Medical Technology Agency
Duntes 12/22, Riga, LV-1005 **LATVIA**
Tel: +371 7501590, Fax: +371 7501591
E-mail: agentura@vsmta.lv
Internet: www.vsmta.lv

HunHTA
Director: Dr. László Gulácsi
Contact person: Dr. László Gulácsi
Unit of Health Economics and Health Technology Assessment
Department of Public Policy and Management
Budapest University of Economic Studies
Fövam tér 8
HU-1093 Budapest **HUNGARY**
Tel: +36 1 218 8197 Fax: +36 1 218 1466
E-mail: lgulacsi@bkae.hu

IAHS
Director: Prof. Adrian Grant
Contact person: Prof. Norman Waugh
Institute of Applied Health Sciences
University of Aberdeen
c/o Department of Public Health
Medical School Buildings, Foresterhill
Aberdeen AB25 2ZD **UNITED KINGDOM**
Tel: +44 1224 555998 Fax: +44 1224 662994
E-mail: N.R.Waugh@abdn.ac.uk

ICTAHC
Director: Prof. Joshua Shemer
Contact person: Prof. Joshua Shemer
Israel Center for Technology Assessment in Health Care
The Gertner Institute, Sheba Medical Center
Tel-Hashomer 52621 **ISRAEL**
Tel: +972 3 530 3278 Fax: +972 3 635 41 36
E-mail: shukis@gertner.health.gov.il

INHEM
Director: Prof. Mariano Bonet
Contact person: Prof. Mariano Bonet
Instituto Nacional de Higiene Epidemiologia y Microbiologia
Infanta #1158 c/ Llinás y Clavel
Centro Habana CP 10300
C. Habana **CUBA**
Tel: +537 781479 Fax: +537 66 2404
E-mail: director@heinsa.sld.cu
Internet: www.sld.cu/instituciones/inhem2

ITA
Director: Prof. Dr. Gunther Tichy
Contact person: Dr. Claudia Wild
HTA Unit of the Institute of Technology Assessment
ITA of the Austrian Academy of Science
Strohgasse 45/3. Stock
A-1030 Vienna **AUSTRIA**
Tel: +43 1 5158 16582 Fax: +43 1 710 98 83
E-mail: cwild@oeaw.ac.at
Internet: www.oeaw.ac.at/ita/hta

KCE
Director: Prof. Dr. Dirk Ramaekers
Contact person: Prof. Dr. Dirk Ramaekers
Belgian Federal Health Care Knowledge Centre
Résidence Palace (A, 10th floor)
Wetstraat 155, B-1040 Brussels **BELGIUM**
Tel: +32-2-2873397 Fax +32-2-2873385
E-mail: info@kenniscentrum.fgov.be

MSAC
Director: Dr Stephen Blamey
Contact person: Dr Stephen Blamey
Medical Services Advisory Committee
MDP 107, GPO Box 9848
Canberra ACT 2601 **AUSTRALIA**
Tel: +61 2 6289 6811 Fax: +61 2 6289 8799
E-mail: msac.secretariat@health.gov.au
Internet: www.msac.gov.au

MTU/SFOPH
Director: Dr. Pedro Koch
Contact person: Mr. Christoph Künzli
Swiss Federal Office of Public Health
Medical Technology Unit
Effingerstrasse 20
CH-3003 Bern **SWITZERLAND**
Tel: +41 31 322 1586 Fax: +41 31 322 7880
E-mail: christoph.kuenzli@bag.admin.ch
Internet: www.snhta.ch

NCCHTA
Director: Prof. John Gabbay
Contact person: Ms. Lynn Kerridge
National Coordinating Centre for HTA
Mailpoint 728, Boldrewood
University of Southampton
Southampton SO16 7PX **UNITED KINDGOM**
Tel: +44 2380 595586; Fax: +44 2380 595639
E-mail: lk1@soton.ac.uk
Internet: www.hta.nhsweb.nhs.uk

NHSC
Director: Dr. Claire Packer
Contact person: Dr. Claire Packer
National Horizon Scanning Center
Department of Public Health and Epidemiology
The University of Birmingham
Edgbaston, Birmingham B15 2TT **UNITED KINGDOM**
Tel: +44 121 414 7831 Fax: +44 121 2269
E-mail: c.packer@bham.ac.uk
Internet: www.publichealth.bham.ac.uk/horizon

NHS QIS
Interim Director HTA: Dr Harpreet Kohli
Contact person: Mr. Jim Slattery
NHS Quality Improvement Scotland
Delta House, 50 West Nile Street
Glasgow G1 2NP Scotland, **UNITED KINGDOM**
Tel: +44 141 225 6980 Fax: +44 141 248 3778
E-mail: jslattery@htbs.org.uk
Internet: www.nhshealthquality.org

NICE

Director: Mr. Andrew Dillon
Contact person: Mr. Andrew Dillon
National Institute for Clinical Excellence
MidCity Place, 71 High Holborn
London WC1V 6NA **UNITED KINGDOM**
Tel +44 20 7067 5800 Fax: +44 20 7067 5801
E-mail: nice@nice.nhs.uk
Internet: www.nice.org.uk

NZHTA

Director: Dr. Ray Kirk
Contact person: Dr. Ray Kirk
New Zealand Health Technology Assessment
Department of Public Health & General Practice
Christchurch School of Medicine & Health Sciences
PO Box 4345
Christchurch **NEW ZEALAND**
Tel: +64 3 364 36 78 Fax: +64 3 364 36 97
E-mail: nzhta@chmeds.ac.nz
Internet: http://nzhta.chmeds.ac.nz

OSTEBA

Contact person: Dr. Rosa Rico
Basque Office for Health Technology Assessment
Department of Health, Basque Government
Calle Donostia 1
ES-01010 Vitoria-Gasteiz **SPAIN**
Tel: +34 9 45 01 9250 Fax: +34 9 45 01 9280
E-mail: rosarico-osteba@ej-gv.es
Internet: www.euskadi.net/sanidad/osteba

SBU

Director: Dr. Nina Rehnqvist
Contact person: Ms. Margareta Nordwall
Swedish Council on Technology Assessment in Health Care
P.O. Box 5650
SE-114 86 Stockholm **SWEDEN**
Tel: +46 8 412 32 00 Fax: +46 8 411 32 60
E-mail: nordwall@sbu.se
Internet: www.sbu.se

SMM

Director: Dr. Berit S Mørland
Contact person: Dagny Fredheim
Norwegian Health Services Research Centre
HTA and Dissemination Department
Universitetsgata 2, Postbox 7004 St. Olavs plass
NO-0310 Oslo **NORWAY**
Tel: +47 23 25 50 83 Fax: +47 22 06 79 79
E-mail: dagny.fredheim@kunnskapssenteret.no
Internet: www.sintef.no/smm

TA-SWISS

Director: Dr. Sergio Bellucci
Contact person: Dr. Sergio Bellucci
Swiss Science and Technology Council/Technology Assessment
Birkenweg 61
CH-3003 Berne **SWITZERLAND**
Tel: +41 31 322 9966 Fax: +41 31 323 3659
E-mail: sergio.bellucci@swtr.admin.ch
Internet: www.ta-swiss.ch

TNO

Director: Dr. A. Dijkstra
Contact person: Dr. Taeke Van Beekum
TNO Prevention and Health
P.O. Box 2215
NL-2301 CE Leiden **THE NETHERLANDS**
Tel: +31 71 518 18 18 Fax: +31 71 518 19 20
E-mail: WT.vanBeekum@pg.tno.nl
Internet: www.tno.nl

UETS

Director: Elena Andradas
Contact person: Elena Andradas
Unidad de Evaluación Tecnologías Sanitarias, Agencia Laín Entralgo
Lain Entralgo Agency
C/ Gran Vía 27, 8ª, ES-28013 Madrid **SPAIN**
Tel: +34 91 3089418 FAx: +34 91 3089458
E-mail: elena.andradas@salud.madrid.org
Internet: www.madrid.org/lainentralgo

VATAP

Director: Dr. Karen Flynn
Contact person: Dr. Karen Flynn
VA Technology Assessment Program
Office of Patient Care Services (11T)
VA Boston Healthcare System Room 4D-142
150 South Huntington Avenue
Boston, MA 02130 **USA**
Tel: +1 617 278 4469 Fax: +1 617-264-6587
E-mail:vatap@med.va.gov, Karen.Flynn@med.va.gov
Internet: www.va.gov/vatap

ZonMw

Director: Mr. Henk J. Smid
Contact person: Dr. Jetty Hoeksema
Health Care Research and Development Agency Council for Medical and Health Research
PO Box 93245
NL-2509 AE The Hague **THE NETHERLANDS**
Tel: +31 70 349 5260 Fax: +31 70 349 5389
E-mail: hoeksema@zonmw.nl
Internet: www.zonmw.nl

INAHTA SECRETARIAT

Network Manager: Ms. Margareta Nordwall
International Network of Agencies for Health Technology Assessment
c/o SBU. PO Box 5650, Tyrgatan 7
SE-114 86 Stockholm **SWEDEN**
E-mail: nordwall@sbu.se
Internet: www.inahta.org

www.inahta.org

INAHTA

c/o SBU
PO Box 5650
Tyrgatan 7
SE-114 86 Stockholm
Sweden

www.inahta.org